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Aspirin Quality Control

Abstract Titration with sodium hydroxide permits precise determination of the mass of active ingredient in aspirin pills, acetyl salicylic acid. Advertised mass content is confirmed within specific quality limits, demonstrating the successful use of the tablet as a uniform vehicle for delivery of a specific aspirin dosage.

Introduction

In medicine, aspirin and other medicines must be prescribed with regard to precise dose to be used to a particular effect. Thus, aspirin is usually incorporated into a vehicle that can deliver the precise amount of drug that makes up a common dosage, a pill or tablet. The manufacture of aspirin pills may vary the amount of non-active ingredients, but it should adhere to the marketed dosage of aspirin within acceptable limits. In this experiment, a method is devised and followed to assure the accuracy of a marketed dosage deemed to be in each pill, 0.325g aspirin. Quality of a batch of pills is the accuracy of its aspirin mass with respect to the printed dosage mass. By using a batch of pills presumably subjected to quality control, the limits set for acceptable variation by the manufacturer are inferred from the observed range of measured aspirin content per pill; if this experiment were used as a quality control procedure, the results could be used to determine whether a batch of product meets or exceeds such quality constraints.

Molarity of the titrant sodium hydroxide is precisely found by titration with the standard potassium hydrogen phthalate.

(a) $HO_2CC_6H_4CO_2K_{(aq)} + NaOH_{(aq)} \rightarrow Na^+_{(aq)} + O_2CC_6H_4CO_2K^-_{(aq)} + H_2O$

Aspirin tablets are then massed and reacted with sodium hydroxide in subsequent titrations.

(b) $HO_2CC_6H_4CO_2CH_{3\,(aq)} + NaOH_{(aq)} \rightarrow Na^+_{(aq)} + O_2CC_6H_4CO_2CH_3^-{}_{(aq)} + H_2O$

Both reactions have reached an end point when the basic indicator phenopthalein indicates persistent presence of unreacted sodium hydroxide in either titrated solution. Both reactions occur momentarily at room temperature as the aqueuous hydroxide ions in the titrant diffuse into either acidic solution.

Both acids are monoprotic, reacting in one to one mole ratio with the titrant. Thus, after determining the precise molar concentration of hydroxide ions in solution, the active ingredient in each dissolved tablet may be directly calculated from the precise volume of sodium hydroxide solution titrated to bring the aspirin solution to the threshold of a detectable basic pH.

Method

A 50 mL burette is filled with approximately 0.1M sodium hydroxide solution to a precise volume and primed to remove air bubbles. The standard acid, potassium hydrogen phthalate, is precisely massed and stirred into solution in a 100 mL beaker no more than half filled with deionized water. Calculation based on reaction (a) is applied to use only a mass of the standard necessary to produce a solution of similar or lesser molarity in comparison to the sodium hydroxide, thus guaranteeing completion of the titration in the beaker. One drop of phenolphthalein is added to indicate pH.

The sodium hydroxide solution is then titrated with the standard, one drop at a time, allowing time to observe dissipation or persistence of hydroxide ions in solution as indicated by pink phenolphthalein. When the first drop of reagent hydroxide ions is not consumed by reaction (a), a pink hue remains and the titration may be deemed complete. This standard or control titration is then used to calculate a more precise molarity of the sodium hydroxide solution.

Each titration is an iteration producing data about one the aspirin content of one massed pill containing aspirin. A pill of aspirin is massed and then pulverized using mortar and pestle. The entire content of the pill is washed into a clean beaker with deionized water and stirred into solution. This solution and a drop of phenolphthalein is titrated with the sodium hydroxide solution of experimentally determined molarity. In these titrations, reaction (b) occurs and reaches an end point when the protons from acetyl salicylic acid are completely consumed by reaction with hydroxide ions. Again, this point is indicated when the phenolphthalein indicates persistent hydroxide ions in solution, remaining a very faint pink hue. This titration is repeated as many times as necessary to determine a likely limiting range of varying aspirin content in the tested batch of pills.

Results

Table 1: Dissolved Mass of Reactants and Corresponding Titration Volumes

Acid Reactant	Mass in Solution	NaOH Start Level	NaOH Completion	NaOH Consumed (ΔmL)
$HO_2CC_6H_4CO_2K$ (std.)	0.4233g	14.09 mL	25.765 mL	11.68 mL
Aspirin pill no. 1	0.3727g	2.02 mL	22.42 mL	20.40 mL
Aspirin pill no. 2	0.3755g	4.10 mL	35.94 mL	31.84 mL

$HO_2CC_6H_4CO_2K$ (standard reactant) molar mass = 204.23g/mol
$HO_2CC_6H_4CO_2CH_3$ (experimental reactant) molar mass = 180.17 g/mol
NaOH (titrant) molar mass = 39.998g / mol

Beaker weight* = 58.8621g

The mole ratio of hydrogen to hydroxide ions in each titration is 1 to 1 (i=1). Thus, a certain number of moles of sodium hydroxide completely reacting with the standard or experimental indicates that number of moles of the reactant participated and was the total amount present in the solution. Thus, the standard gives (0.4233g) / (204.23 g/ mol) = 0.002073 mol of standard, and also 0.002073 mol of NaOH in 0.01168L solution, or 0.1775M NaOH solution.

The titration of the two pills then gives the following moles of aspirin present:

(20.40 mL NaOH) x (0.1775M NaOH) x (1) = 0.003621 mol aspirin in pill 1
(31.84 mL NaOH) x (0.1775M NaOH) x (1) = 0.005652 mol aspirin in pill 2

(0.003621 mol aspirin) x (180.17 g/mol aspirin) = 0.6524g aspirin in pill 1*
(0.005652 mol aspirin) x (180.17 g/mol aspirin) = 1.018g aspirin in pill 2*

Mass varies between the pills, so the ratio of active ingredient mass to total mass is pertinent in determining whether discrepancy is due to inaccurate experimental measurement, or inconsistent pill manufacturing techniques.

*Greater than the total massed pill. Because of experimental or calculation error, no percent mass of aspirin in the pill can be determined!

Conclusion

This experiment did not accurately determine the content of aspirin in a given batch of pills. The reasons for this are likely due to a number of reasons. First, the beaker used to hold the reactant solutions may have been contaminated by dry residue from earlier experiments, though this is not likely. What was observed however, was an air bubble that did not prime out of the burette and remained until the middle of the titration with pill one. While this should not effect the determination of molarity of the hydroxide solution, it adds significant error to calculations effecting pill 1. Unfortunately, it was observed that pill two was not completely washed from the mortar it was pulverized in. It did not show until the mortar dried completely. While some attempt was made to calibrate this error by repeating the same mistake and then finding the difference between a clean mortar and a mortar with similarly missed reactant, the mass was above the maximum on the scales. In retrospect, results from a more careful process should result in finding a limit on the extent that there is proportionality between the moles of aspirin in a set of pill and that pills' original mass, indicating the range of accuracy that the manufacturer's process achieves, advertising 0.325g aspirin per pill.