Investigating the effects of different solvents used for recrystallization of Aspirin (Acetylsalicylic acid)

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Introduction

In this investigation, an experiment will be conducted in order to determine the purity of lab synthesized Aspirin recrystallized by five different solvent. The crude Aspirin produced in laboratory will undergo recrystallization process and its purity will be determined with method of spectrophotometry. The experimental values obtained will allow for establishing the relationship between different solvents and determining percentage yield.

I have chosen this IA topic because, I had severe headaches in last couple of months, and therefore I want through many medical checkups in order to determine reasoning behind by constant headaches. Before I was diagnosed, I had to use painkillers multiple times a day to be able for normal functioning. The one I used most frequently was Aspirin, but I never knew how does it ease my headaches and what is the procedure of synthetizing it. Therefore, I wanted to learn more about its relieving effects and production of it. Additionally, I was aware that this research will give me more lab experience that will be needed in my future career as I want to be a chemical engineer. Due to everything aforementioned this topic takes my great personal interests.

Research question:

How does the use of different solvents (H_2O, C_2H_5OH, C_3H_6O, C_3H_8O, and $C_3H_8O_3$) affect the purity of the product as well as the percentage yield of crude aspirin through recrystallization of Acetylsalicylic acid whilst employing the spectrophotometric analysis?

Background information

Aspirin is a common medication used to reduce various types of pain, and it belongs to chemical group of compounds called salicylates. In chemistry, otherwise known as acetylsalicylic acid or 2-Acetoxybenzoic acid (IUPAC), with a chemical formula of $C_9H_8O_4$, with a molar mass of 180.16 g/mol it has melting point of $135\ °C$ and boiling point of $140\ °\ C$. Rapid decomposition of Aspirin occurs in solutions of carbonates, citrates, acetates, or hydroxides of alkali metals. It is stable on the room temperature, however if exposed to moisture or higher temperature it degrades to its components, acetic and salicylic acids. The main ingredient of Aspirin, salicylic acid is produced from Spiraea plant. In alkali solutions, acetate and salicylate hydrolyze rapidly. This reaction produces clear solutions that consist of acetate and salicylate solely.

In 1897, Felix Hoffman, a German chemist working for the Bayer Company, was able to modify salicylic acid to create acetylsalicylic acid, which was named aspirin[1]. Because of its anti-

[1]Miner, J., & Hoffhines, A. (2007). *The discovery of aspirin's antithrombotic effects*. Texas Heart Institute journal. Retrieved February 13, 2022, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1894700/#:~:text=In%201897%2C%20Felix%20Hoffman%2C%20a,1).

inflammatory, analgesic (pain-relieving), and antipyretic (temperature-lowering) qualities, the chemical is one of the most extensively used drugs. Aspirin was very early on recognized as a high potential drug, and further investigations of modern research on this late 19th century developed drug proved its effectiveness in cancer and cardiovascular diseases preventions. Aspirin is synthesized by the reaction of salicylic acid (lipophilic monohydroxy benzoic acid, $C_7H_6O_3$) with excess acetic anhydride. In organic chemistry a reaction for Aspirin synthesis is called esterification. Additionally, sulfuric or phosphoric acids are added to the reaction, and they behave as catalyst.

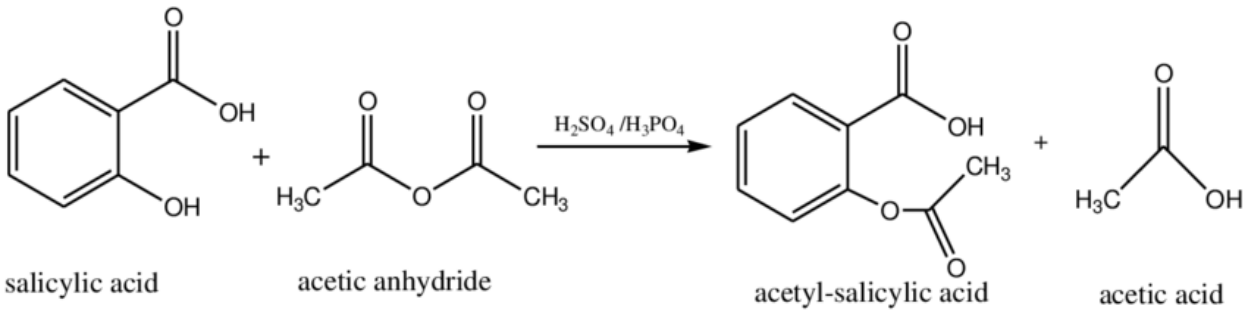

Figure 1. Synthesis of Aspirin[2]

Recrystallization is the process of purifying the product in a solvent. Solvents are mainly liquid substances in which a solutes gets dissolved. In the investigation crude aspirin is solute that will be treated with five different solvents in order to be recrystallized. Acetylsalicylic acid is a polar compound due to two polar functional groups: aromatic carboxylic acid and aromatic ester. However, the compound is partially polar. This is the result of compound having both polar and non-polar regions. The polar groups are being attached to the benzene ring which as a non-polar region significantly influences properties of the whole molecule, therefore Acetylsalicylic acid dissolves very well in semipolar solvents. Furthermore, polarity within the molecule allows for a solubility in polar solvents such as water. Due to the listed properties, both polar and semipolar solvents will be used, such as water, ethanol, acetone, isopropanol and glycerol (H2O, C2H5OH, C3H6O, C3H8O, and C3H8O3).

Semipolar solvents are generally strong dipolar compounds that usually make no hydrogen bonds. They can cause non-polar molecules to become polar (both solutes and solvents). Aldehydes, ketones, certain esters, and nitro-compounds are examples of semipolar solvents. The dielectric

[2] *Synthesis of acetyl-salicylic acid from salicylic acid and ... (n.d.). Retrieved February 14, 2022, from https://www.researchgate.net/figure/Synthesis-of-acetyl-salicylic-acid-from-salicylic-acid-and-acetic-anhydride_fig2_316038270*

constant (ε, no units) of a solvent is a measure of its polarity. Polar solvents have dielectric constant value above fifty whereas semipolar solvents have it between twenty and fifty.

Pure aspirin will result in white solid crystals, whereas the light tan Aspirin indicates presence of impurities. In commercial production, Aspirin is synthesized from salicylic acid and acetic anhydride, while hot aqueous ethanol is used in recrystallization process. Despite non-polar regions, the whole Aspirin is a polar molecule with dipole-dipole attraction bonds and hydroxyl group.

Due to a hydroxyl (OH) group that forms hydrogen bonds with other molecules, ethanol is a very polar molecule. Whereas, ethyl group (C2H5) is non-polar, which allows ethanol to be used as a solvent for both polar and non-polar molecules.

Aspirin being polar makes it non-addictive drug since it cannot be absorbed by non-fatty lipid tissue of the brain. As a result it has no psychoactive effect since it does not bind to any certain respirators in the brain that deal with sensation of pleasure which would create addiction.

To be able to determine purity of every sample spectrometric analysis will be essential part of the investigation. Spectrophotometry is a quantitative measurement method for determining chemical substance absorbance. It works on the principle of measuring the light intensity that passes through a sample solution. Each substance absorbs and transmits light of a specific wavelength. Light is electromagnetic wave that radiates energy. Visible light is a transverse wave, which means that the displacement is at right angles to the direction of energy transfer. White light is composed from all wavelengths within visible light spectrum. Wavelength denoted by the Greek letter lambda (λ) and unit nanometer, is a measure of distance between two consecutive crests of a wave. An instrument used for measuring the amount of absorbed or transmitted light is called Spectrophotometer and it consists of spectrometer and photometer that work separately. The spectrometer creates a range of wavelengths, by sending a beam of light through prism that splits it into several wavelengths, and only chosen wavelengths get transmitted. The purpose of the photometer is to detect the absorbance and show the readings on a display.

Optical density, better known as Absorbance (A), is the quantity of light absorbed by a solution. Transmittance, amount of light passing through solution and Absorbance are closely related in spectrophotometry, and their relationship can be expressed by using the following formula.

$$A = log_{10}\left(\frac{1}{T}\right) \qquad (1)$$

A – Absorbance [Au]

T – Transmittance

Relationship between the absorbance and the concentration of the substance is described by Beer-Lambert law.

$$A = \epsilon lc \qquad (2)$$

ϵ – Molar absorptivity $\left[\frac{L}{mol \cdot cm}\right]$

l – Light path length [cm]

c – Concentration $\left[\frac{\text{mol}}{L}\right]$

Hypothesis:

As like substances dissolve like substances the products recrystallized with polar solvents, should have higher purity. Moreover, according to the background theory, the product of the highest percentage purity should be the ethanol recrystallized product.

Methodology

Aspirin is produced by reacting salicylic acid with an excess of acetic anhydride. A little dose of a strong acid is utilized as a catalyst, which will lower the energy of transition for this reaction. Sulfuric acid will serve as the catalyst in this lab synthesis. The excess acetic acid will be neutralized by the addition of water. Since aspirin has a lower solubility in water, it will precipitate when water gets added. Furthermore, acetic acid will be easily removed from the product as it is highly soluble in water. This is a vigorous exothermic reaction and therefore extra caution should be taken. The aspirin separated in this step is the crude product. Like substances dissolve like substances therefore, the crude product can be recrystallized in hot ethanol to produce purified product. Furthermore, this product can be analyzed through the method of spectrophotometry, which will enable calculating the percentage purity of the product.

Apparatus	**Chemicals**
- Scale (milligram scale, uncertainty $\pm 0.1 \times 10^{-5}$ kg) - Filter papers - Boiling flask (250ml) - Pipette (5ml, uncertainty ± 0.01ml) - Heater - Stand clamp holder - Reflux condenser - Constant water supply - Erlenmeyer flask (125ml, uncertainty ± 5ml) - Volumetric flasks (100ml, uncertainty ± 0.08ml) - Thermometer (uncertainty ± 0.5 C^{o})	- Concentrated sulfuric acid - Salicylic acid - Acetic anhydride - Sodium hydroxide solution, 1M - Iron (II) chloride, 0.02M

Variables	Impact upon the investigation	How the variable will be changed/measured/controlled
Independent variable Polarity of solvents Polarity is a measure of electric charge separation that leads to dipole moment. Polar molecules Net dipole is a characteristic of polar molecules whereas non polar molecules have a symmetrical arrangement of polar bonds.	The most significant impact on the investigation is the polarity of the solvents, since Acetylsalicylic acid is a polar molecule and like substances dissolve like substances. Therefore the aspirin which has both polar and non-polar regions needs at least partly polar solvents to be dissolved.	Variety of different solvents are used in the investigation, out of which two are polar (H2O, C3H8O) and three are semipolar (C2H5OH, C3H6O, C3H8O3). These two polar solvents will result in good solubility since they have similar polar behavior. Moreover, due to phenyl ring, aspirin will be able to dissolve in acetone, ethanol and glycerol.
Dependent variable Absorbance (A) [*Au*] Absorbance is a measure of amount of light absorbed by a certain substance. It can be utilized to determine an unknown substance as well as its amount. This is possible due to the fact that every compound transmits and absorbs light of definite wavelength range.	The absorbance is used to find concentrations of different Aspirin products that are diluted in a complex ion. The values of Absorbance obtained with spectrophotometric device will be used in Beer Lambert's formula. The absorbance values have a significant impact on the investigation since the purity of lab synthesized aspirin is deduced over these values. Additionally spectrophotometer has an uncertainty of ≈3%.	The wavelength (λ) is adjusted to a constant value of 550nm and the absorbance is measured using a spectrophotometric analysis method. The Aspirin absorbs ultra-violent light and therefore it was converted to colored complex and measured by spectrophotometer that works in visible spectrum.
Dependent variable Molar Concentration of products (C) [*mol/L*] Concentration of a chemical species in a certain solution is called molarity or molar concentration.	The concentration of Aspirin in all 5 five lab-made products is utilized to calculate mass of Aspirin per product, which will be used to find percentage purity of acetylsalicylic acid in every experimentally obtained, recrystallized Aspirin sample.	Throughout the experiment, a constant quantity of 0.32g for every experimentally obtained Aspirin is used. This mass is dissolved into 100ml, and then four samples of (1.0/2.0/3.0/4.0) ml are transferred to cuvette and filled with 0.2M iron(III) chloride to 10.0 ml mark
Dependent variable Purity of samples The essential part of pharmaceutical chemistry is purity which allows for successful research. Moreover, purity standards are established through quality control that assures consumers' safety while using the pharmaceutical product.	The purity of products is the aim of the research, and it can be determined through different methods. Its results are of great significance since it determines the relationship between the solvents used and their characteristics. Furthermore, the use of purity analysis is crucial to pinpoint the presence or identity of any impurities within the samples.	There are a couple of methods to determine the purity of the product. The one used in the investigation is colorimetry, which determines the concentration of colored compounds in a solution. This method is based on the Beer-Lambert law, which states the proportionality between the solute's concentration and absorbance. The absorbance will be measured with a spectrophotometer.

Table 1. Variables

Variables	Impact upon the investigation	How the variable will be changed/measured/controlled
Controlled variable Mass of sample Aspirin (m) [*kg*] Product	Mass of Aspirin is used in order to calculate the percentage purity for each product and concentration of pure Aspirin, which is required to monitor absorption of experimentally obtained samples.	Throughout the experiment, a constant quantity of 0.32g of pure aspirin is maintained, which is weighted using a laboratory weighing scale with a ± 0.001 g error.
Controlled variable Mass of Salicylic acid (m) [*kg*] Limiting reagent	The mass of the crude aspirin produced in the experiment depends on the amount of Salicylic acid used in the experiment. This directly influences absorbance values as well as purity of final product.	The mass of Salicylic acid was 4.00 grams and it was measured using a laboratory scale with a ± 0.001 g error.
Controlled variable Volume of acetic anhydride (V) [*ml*] Reagent in excess	The volume of Acetic anhydride is constant and it influences the amount of crude product. It is the reagent in excess for this reaction and therefore the volume used in experiment depends on the mass of limiting reagent (Salicylic acid).	Throughout the experiment, a constant quantity of 8ml was used in every lab synthetized aspirin. It was measured by 5ml pipette with uncertainty ± 0.01ml.
Controlled variable Volume of solvents (V) [*ml*]	Different solvents of same volume were used in recrystallization process to establish effects on the purity. To achieve maximum purity, a sufficient amount of solvent must be used to dissolve the crystals and retain the impurities in the solution after cooling. Minimize the quantity of solvent used to ensure that as little sample as feasible remains in solution after cooling to maximum yield.	The volume of every solvent used was kept constant at 20ml because higher or lower volume of solvent would change the purity of product. The volume of solvent was measured with 5ml pipette with uncertainty ± 0.01ml.
Controlled variable Temperature of solvents (T) [C^o]	The temperature of solvents has a significant impact on the investigation, since the solubility of crude aspirin increases with an increase in temperature. The more crude aspirin dissolves the higher purity is achieved.	The temperature of warm bath was kept constant at 70 C^o for every solvent. It was measured with thermometer that has uncertainty of ± 0.5 C^o.

Table 2. Variables (continued)

Figure 2.Experimental setup

Procedure for preparation of Aspirin

Pre lab Synthesis:

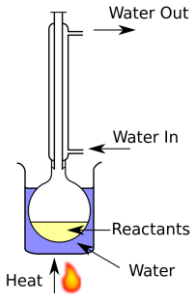

Figure 3. Reflux condenser scheme

1. Make a clear working space and build the experimental setup as shown in Figure 2.
2. Weigh accurately 4g of 2-hydroxybenzoic acid (Salicylic acid) and put it inside a 250ml Florence/Boiling flask.
3. With use of a pipette pour 8cm^3 of acetic anhydride into same 250ml boiling flask.
4. Add ten drops of concentrated sulfuric acid (H_2SO_4) and swirl to mix.
5. Put boiling flask on the heater.
6. Connect a reflux condenser with a flask and attach it to the stand clamp holder.
7. Make sure that reflux condenser is properly attached to water flow. (Figure 3.)[3]
8. Turn on the heater and heat the mixture for about 10 minutes on medium temperature or until everything dissolves.
9. Without cooling carefully (vigorous exothermic reaction) add 2cm^3 of distilled water down the condenser. Addition of distilled water will hydrolyze any ethanoic anhydride left in excess.
10. Turn off the heater and let the solution and boiling flask to cool down.
11. Put the boiling flask into an ice-water bath and let the aspirin crystalize.
12. Filter off the crystals by vacuum filtration and leave to dry.

[3] Chua, S. (2015, January 17). *Organic Chemistry - what is reflux? - A-level H2 chemistry tuition by 10 Year Series Author*. A. Retrieved February 14, 2022, from https://www.alevelh2chemistry.com/organic-chemistry-what-is-reflux/

Recrystallization:

1. The crude Aspirin obtained in previous steps is scaled (weight should be around 2.5 grams) and placed into a 100 cm3 flask.
2. 20ml of ethanol /isopropanol/water/ acetone/glycerol is added to the flask which is exposed to heat in water bath at 70 C^o.
3. The flask is removed from bath and 50ml of water is added to the solution which is left to cool down to room temperature.
4. Put the flask in the ice water bath until crystals appear.
5. Filter off the crystals by vacuum filtration and wash them with distilled water.
6. Collected crystals are left to dry and purified product is obtained. This process is known as recrystallization.

Colored complex and Spectrophotometry

1. 0.32g of purified product is taken and transferred into a 125ml Erlenmeyer flask
2. Add 10ml of 1M sodium hydroxide ($NaOH$) to the flask and heat the mixture until recrystallized aspirin dissolves.
3. After the purified product gets dissolved, transfer it to a 100ml volumetric flask and dilute with water until 0.1L mark.
4. Take four cuvettes for spectrophotometric measurements and make samples filled with 1.00/2.00/3.00/4.00 ml of mixture from previous step.
5. Dilute all four samples up to 10.0ml mark with 0.02M iron (II) chloride.
6. Repeat the whole process for remaining solvent recrystallized samples and pure aspirin.
7. Sort all 24 cuvettes and analyze them one by one with the spectrophotometer, which wavelength is manually set to 550nm.
8. Collect the data for absorbance value and use it to determine purity of products.

Safety and Ethical considerations:

The experiment demands a lot of time, and one needs to be careful whilst conducting it. The apparatus consists of many parts, and several hazardous chemicals, thus everything has to be handled with additional caution. Special caution should be executed whilst using acetic anhydride and concentrated sulfuric acid, due to corrosion. Therefore gloves, apron and goggles must be worn at all times. The addition of distilled water to the reflux condenser will cause a vigorous exothermic reaction, which requires this process to be completed slowly and carefully. Furthermore, solvents used (acetone, isopropanol, and ethanol) during the recrystallization process should be dealt with care due to their detrimental effects on health. There should be specific attention and caution whilst heating the ethanol in the laboratory. Ethanol is very flammable substance and therefore it has to be heated in warm bath at constant temperature of 70 degrees Celsius and cannot exceed this due to the fact its boiling point is 78 degrees Celsius. This way risk of any incident occurring is reduced to minimum. Due to the aforementioned, the first trial of the complete experiment should be conducted with the supervision of the teacher.

Data Collection and Processing:

Qualitative data:

Five recrystallized samples obtained in the experiment appeared in different forms. Glycerol recrystallized sample deviates the most in physical comparison. The sample has a strong yellow color that clearly indicates high impurity percentage. Moreover, many crystals are merged into a big one which has a very dense and asymmetric structure. The water sample had really powdery structure, and the sample lacked crystal form (turned into the sand when pressed). The yellow-pink color indicated presence of impurities however it was not as yellow as in glycerol sample.

In the remaining three samples increase in purity could be noticed, since the color for isopropanol sample was just a bit yellow and crystal form was obtained. For the samples of ethanol and acetone highest purity can be noticed since both samples had very clear crystal form that by appearance was closest to theoretical one. Moreover, the color of both samples was indicating very low number of impurities compared to other three samples, as the color was very close to white.

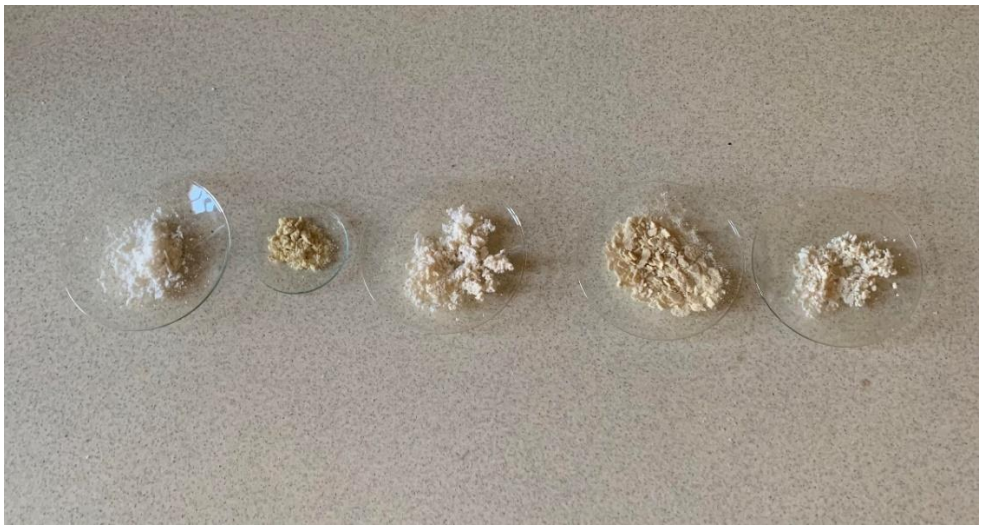

Figure 4. Final products in order C2H5OH, C3H8O3, C3H6O H2O, C3H8O

Without spectrophotometric analysis assumptions about purity of samples can be deduced from Figure 4. Referring to the background theory, white crystals indicate low presence of impurities, thus the sample of highest purity should be the ethanol recrystallized sample (furthest to the left).

$$C_7H_60_{3(s)} + C_4H_60_{3(l)} \xrightarrow{H_2SO_4} C_9H_8O_{4(s)} + C_2H_4O_{2(l)}$$

The reaction for lab synthesis of crude aspirin is shown, and it can be used to deduce percentage yield of crude aspirin.

Quantitative raw data:

Salicylic acid is a limiting reagent for the above reaction and therefore one mole of Salicylic acid ($Mr = 138.12g/mol$) produces one mole of Acetylsalicylic acid ($Mr = 180.16g/mol$). Since 4.00 grams of Salicylic acid were used in the experiment theoretical yield can be calculated:

$$138.12g/mol(C_7H_60_3): 180.16g/mol(C_9H_8O_4) = 4.00g(C_7H_60_3): xg(C_9H_8O_4)$$

$$x = 5.22g, (theoretical\ yield)$$

However, after the lab synthesis, the measured mass of crude aspirin was 2.44g (actual yield). Now theoretical yield can be determined:

$$\%Yield = \frac{Actual\ yield}{theoretical\ yield} \cdot 100\% = \frac{2.44g}{5.22g} \cdot 100\% = 46{,}7\% \approx 47\% \qquad (3)$$

The five recrystallized samples of Aspirin, in addition with pure Aspirin were diluted in iron (III) chloride solution up to volumes of 1ml, 2ml, 3ml, 4ml. The samples were then put in cuvettes and analysed in spectrophotometer, with a manually set, constant wavelength of 550 nm as coloured complex transmits violet light.

The values of absorbance obtained in the measurements are collected and presented in table below:

Diluted volumes [ml]	Absorbance (± 0.001 Au)					
	Pure Aspirin	Ethanol sample	Acetone sample	Isopropanol sample	Glycerol sample	Water sample
1	0.560	0.536	0.498	0.534	0.406	0.357
2	0.763	0.724	0.624	0.675	0.575	0.553
3	1.074	1.027	0.921	0.982	0.783	0.732
4	1.396	1.356	1.225	1.287	1.022	1.003

Table 3. Raw absorbance data for diluted volumes of six different aspirin products

When dividing the mass of the sample by the initial volume and the molar mass of the substance, the stock concentration of pure aspirin can be determined:

$$c_1 = \frac{m}{VM} = \frac{0.32g}{0.1L \cdot 180.2g/mol} = 0.0178M, \frac{mol}{L} = M \qquad (4)$$

Furthermore, the diluted concentration of pure Aspirin can be calculated by assuming that the number of moles stays constant.

$$c_2 = \frac{c_1 \cdot V_1}{V_2} = \frac{0.0178\text{mol/L} \cdot 5/4/3/2/1\text{ml}}{10\text{ml}} \quad (5)$$

The absorbance data for each diluted concentration read from the spectrophotometer are shown in Table 2. These values will be used to plot the Beer-Lambert graph:

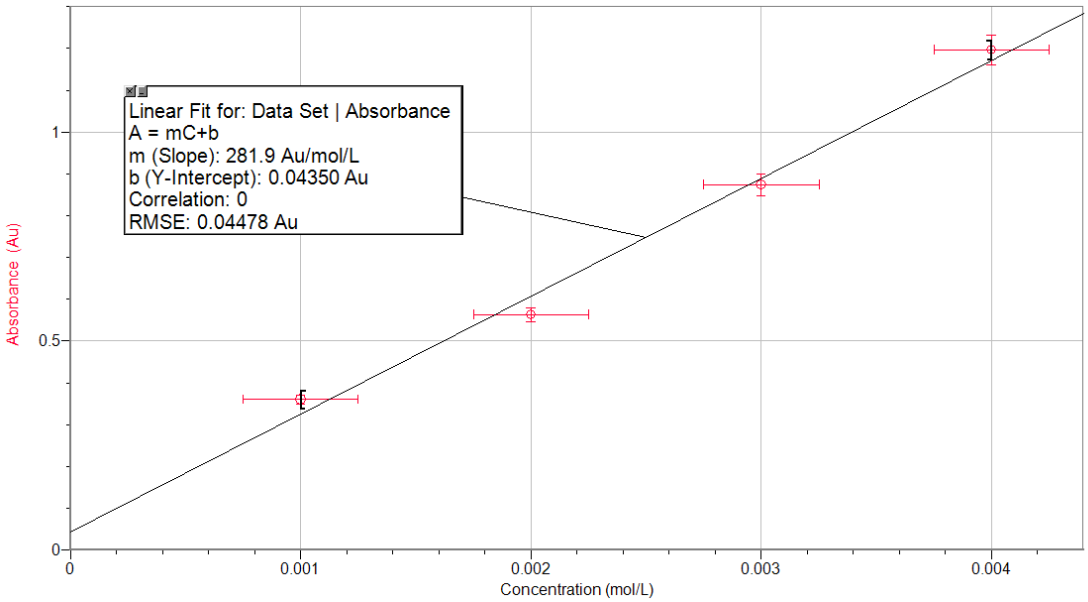

Figure 5. Beer-Lambert graph of Absorbance vs Concentration

The graph represents Beer-Lambert law. From the graph, it can be deduced that absorbance increases with an increase in concentration, due to the fact that the slope is positive. The y-intercept is not big, close to zero and therefore it can be concluded that absorbance and concentration are linearly proportional. This can also be seen in linear fit form A = mC + b, value of b is very close to 0. This indicates linear proportionality stated by Beer-Lambert law. If graph is observed carefully, it can be noticed that linear fit passes through all error bars. Through the linear function of the graph the linear fit relationship is established. A spectrophotometer is used to assess the absorbance of diluted lab-produced aspirin. To determine diluted concentrations, absorbance values will be subtracted from the y-intercept value and divided by the slope of the Beer-Lambert graph.

This graph will be used in order to find concentrations of experimentally produced Aspirin, synthesized in lab. The graph shows relation of absorbance on the y-axis and concentration on the x-axis. The linear equation $y = mx + c$ of the graph is going to be used in calculations to obtain diluted values of five different samples, by inputting different absorbance values instead y for recrystallized Acetylsalicylic acid.

$$y = 281.9\frac{mol}{AuL}x + 0.0435Au \quad (6)$$

A sample calculation of the diluted concentration, x (C_2)of water recrystallized aspirin for absorbance value, $y = 1.003Au$:

$$x = \frac{1.003 - 0.0435}{281.9}\text{mol/L} = 0.0034\text{ mol/L}$$

Since $C_1V_1 = C_2V_2$, stock concentration of pure Aspirin(C_1)within lab synthetized Aspirin can be determined by using diluted concentration values for volume, $V_2 = 4ml$:

$$c_1 = \frac{x \cdot V_2}{V_1} = \frac{0.0034\text{ mol/L} \cdot 10ml}{4ml} = 0.0085\text{mol/L}$$

These calculations are done for all five solvent recrystallized samples by using every absorbance value for diluted volumes (1.00, 2.00, 3.00, and 4.00) ml in order to obtain the stock concentrations. The determined stock concentrations for all five samples are summed up and divided with number of trials to obtain average stock concentration, which is shown in the table:

Samples stock concentrations [mol/L]				
Ethanol	Water	Acetone	Isopropanol	Glycerol
0.0164	0.0111	0.0161	0.0139	0.0129
0.0121	0.0092	0.0103	0.0094	0.0094
0.0116	0.0081	0.0104	0.0099	0.0087
0.0116	0.0085	0.0105	0.0113	0.0087
Average Values				
0.0129	0.0092	0.0118	0.0111	0.0099

Table 4. Average stock concentrations of five different solvents

The mass of Aspirin in ethanol sample as well as percentage purity are calculated in the following by using the average concertation value from Table 4.

$$C = \frac{n}{V}, n = \frac{m}{M} \Longrightarrow m = C \cdot M \cdot V$$

Molar mass of Aspirin $C_9H_8O_4$ is $M = 180.14\frac{g}{mol}$ and $V = 0.1l$

$$m = 0.0129\frac{mol}{L} \cdot 0.1L \cdot 180.14\frac{g}{mol} = 0.2323g$$

There are 0.23 grams of pure Aspirin within, ethanol recrystallized sample.

Percentage purity can be calculated with following formula:

$$\frac{mass\ of\ recystallized\ aspirin}{mass\ of\ pure\ aspirin} \cdot 100\% = \frac{0.2323}{0.3200} \cdot 100\% \approx 73\%$$

Sample calculation for random error of H20 sample:

$$Random\ error = \%m_{impure}(AS) + \%AB + \%V(A.A.) + \%m(S.A.) \qquad (7)$$

The percentage uncertainty of crude aspirin was calculated by dividing scale uncertainty with measured mass.

$$\%m_{impure}(AS) = \frac{\Delta m}{m} \cdot 100\% = \left(\frac{0.001}{0.320}\right) \cdot 100\% = 0.313\%$$

Sample calculation for percentage uncertainty for absorbance of water was calculated in following way:

$$\%AB_W = \left(\frac{\Delta A}{A_1} + \frac{\Delta A}{A_2} + \frac{\Delta A}{A_3} + \frac{\Delta A}{A_4}\right) \cdot 100\%$$

$$\%AB_W = \left(\frac{0.001}{0.357} + \frac{0.001}{0.553} + \frac{0.001}{0.732} + \frac{0.001}{1.003}\right) \cdot 100\% = 0.7\%$$

The same procedure was followed for other samples of acetone, isopropanol, glycerol, and ethanol. By adding up all the values, the percentage uncertainty for absorbance is obtained:

$$\%AB = \%AB_W + \%AB_A + \%AB_I + \%AB_G + \%AB_E \qquad (8)$$

$$\%AB = 0.70\% + 0.55\% + 0.51\% + 0.65\% + 0.50\% = 2.91\%$$

Percentage uncertainty for volume of acetic anhydride used in the experiment was calculated by dividing the uncertainty of pipette with volume of acetic anhydride used in synthesis:

$$\%V(A.A.) = \left(\frac{\Delta V}{V}\right) \cdot 100\% = \left(\frac{0.01}{8.00}\right) \cdot 100\% = 0.125\%$$

Percentage uncertainty for mass of salicylic acid was obtained by following:

$$\%m(S.A.) = \frac{\Delta m}{m} \cdot 100\% = \left(\frac{0.001}{4.000}\right) \cdot 100\% = 0.025\%$$

Random error is calculated by summing up all values of percentage uncertainty obtained in the previous steps, by using the equation (7):

$$Random\ error = 0.313\% + 2.91\% + 0.125\% + 0.025\% = 3.373\% \approx 3.4\%$$

$$Absoulte\ uncertainty = random\ error \cdot percentage\ purity \quad (8)$$

$$Absolute\ uncertainty = 0.034 \cdot 52\% = \pm 1.8$$

The same calculations were performed for the rest of the solvents to obtain the following table:

Solvent used	Percentage purity [%]
H2O	52.0 ± 1.8
C3H8O3	56.0 ± 1.9
C3H8O	62.0 ± 2.1
C3H6O	67.0 ± 2.3
C2H5OH	73.0 ± 2.5

Table 5. Percentage purity values with absolute uncertainty

Data analysis

The bar chart below gives percentage purity of all solvent recrystallized samples obtained from experimental calculations and spectroscopy.

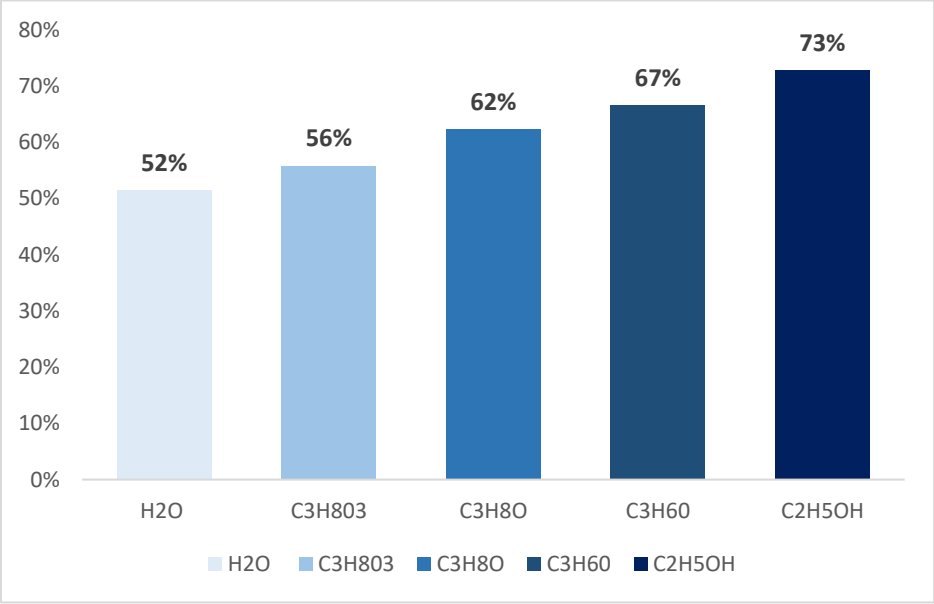

Figure 6. Percentage purity of samples.

The ethanol recrystallized sample resulted in highest purity value of 73%. This result was anticipated, before the final calculations and due to the colour and the shape of crystals in recrystallization process that indicated low impurities level. Moreover, after the spectrophotometric analysis, ethanol had highest absorbance value out of all solvent recrystallized

samples. However, the product consists of around 27% impurities. These impurities could be the result of unintended oxidation that occurred during the synthesis through the heating process. Another reason for these impurities was the system which was not isolated enough from external effect.

Solvent	P' value
Water	10.2
Acetone	5.1
Acetonitrile	5.8
Ethanol	4.3
2-Propanol	3.9
Methanol	5.1
Tetrahydrofuran	4.0

Figure 7. Polarity index of solvents[4]

The sample recrystallized with acetone has the second highest purity compared to all five samples. It has purity of 67 % that was determined with spectrophotometric analysis. From these it is seen that first and second products of highest purity are actually semipolar. While polar solvents such as water and isopropanol are giving products of lower purity. The third purest sample was recrystallized with isopropanol and it gave purity of 62%.

In spite the fact that glycerol is a semipolar molecule it resulted in higher purity than water which is the most polar solvent. Glycerol recrystallized product had a purity of 56% and water product gave the lowest purity of 52%. Moreover, by looking at polarity index table Figure 7. it can be seen that water is indeed of highest polarity and it is around 2.4 times more polar than ethanol which yielded highest percentage purity. Water being most polar but giving least purity indicates that there are other factors that influence purity of products.

Conclusion:

The goal of this investigation was to determine effects of both polar and semipolar solvents on recrystallization process of Acetylsalicylic acid. The emphasis was put on the purity of the products that was determined over spectrophotometric analysis. This method allowed for in depth research of the topic. The absorbance values read from spectrophotometer together with plotted

[4] Teutenberg, T., Wiese, S., Wagner, P., & Gmehling, J. (2020, November 27). *Table 3 polarity values (literature data according to Ref. [18]).* ResearchGate. Retrieved April 7, 2022, from https://www.researchgate.net/figure/Polarity-values-literature-data-according-to-Ref-18_tbl2_38014625

Beer-Lambert law graph Figure 5. enabled for purity calculations of every sample. From these calculations it was determined that ethanol yields a product of highest purity. This goes in accordance with the hypothesis, since ethanol sample had a purity of 73%, which was the highest compared to other four samples. Furthermore, the final results of the investigation showed that generally semipolar solvents will give higher purity than polar ones. This can be seen in the percentage purity chart bar Figure 6. since glycerol, a semipolar molecule produced a sample of higher purity than the water, which is most polar solvent in the research. To get a better representation of the distribution of electrical charge over the molecules polarity index table Figure 7. was introduced. From these it was concluded that the polarity is not the only factor that affects purity of the samples.

Despite the fact that a hundred percent purity of a pharmaceutical product is not obtainable, analytical methods like spectrophotometry (colorimetric method) are used to determine the presence of any impurities within the product. Impurities refer to organic and inorganic components that are not active substances of a certain product.

Besides the spectrophotometric analysis that was used to determine the percentage purity of the products, a physical comparison was used additionally. This is a more simple method that allows for understating the purity of a sample. It is based on a comparison between an experimentally obtained sample and a pure sample. In the investigation, all five samples were compared with pure aspirin and it was deduced that acetone and ethanol have the biggest correlation due to their crystalline structure and almost white color. Subsequently, results of spectrophotometric analysis supported the claims of physical comparison with absorbance values that were close to those of pure aspirin.

Multiple studies prove that ethanol is the most effective solvent in process of aspirin production, as it has the highest absorbance value in spectrophotometric analysis. Ethanol dissolves many both polar and non-polar compounds. Quick evaporation is a characteristic due which ethanol leaves minimal impurities, compared to other solvents. The results of the investigation indicate that ethanol indeed produces the most pure Aspirin sample in recrystallization process. Moreover, this was proved experimentally and is supported with data reference[5].

Evaluation:

Random error in the investigation was calculated by summing up all percentage uncertainty values, resulting in 3.4% which slightly affects preciseness of the measurements. This is not necessarily

[5] Ltd, A. A. (2021, December 31). *Preparation of recrystallization of aspirin*. UK Essays. Retrieved March 27, 2022, from https://www.ukessays.com/essays/biology/preparation-of-recrystallization-of-aspirin-biology-essay.php#:~:text=Ethanol%20has%20been%20chosen%20as,also%20dissolve%20non%2Dpolar%20substances

an indicator of mistakes during the investigation but a natural part of the experiment instead. There were many variability throughout the research due to fluctuations in the environment and instruments used. The biggest impact on random error was percentage uncertainty of spectrophotometer which was around 2.9%, and since it is the error of the instrument it cannot be minimized.

Absolute uncertainty of percentage purity for five samples was obtained by multiplying the random error with percentage purity value. The increase of the percentage purity resulted in increase of absolute uncertainty. Therefore the lowest absolute uncertainty is obtained in water sample ± 1.8 and the highest in ethanol sample ± 2.5.

The main source of systematic error throughout the whole investigation is that 0.32g of "pure" aspirin used was just set to be pure for the purposes of Beer-Lambert relationship. The tablets used, were not 100% aspirin but were taken as a referent value in order to establish values that can be compared with sample values. Furthermore, this means that percentage purity determined in the experiment, is significantly lower than it was calculated due to the fact that each pill consists of 50mg of pure Aspirin.

Strengths:

The data collected throughout the experiment is reliable since the physical comparison of samples (color and structure) was supported with absorbance values obtained through spectrophotometric analysis. Also, 4 different volumes of each sample were used in the experiment, thus random error was reduced due to increased number of trials. The error bars on the graph Figure 5. are not that significant in y-axis as they are in x-axis due to big difference in length. The error bars in x-axis have significant impact due to spectrophotometer that makes uncertainty of around 3%. However since the liner fit passes through all four points on the graph and y-intercept is very small (close to zero), it can be concluded that the research was conducted well. Despite the limitations and weakness present in the experiment values obtained go in accordance with both theory and hypothesis. Furthermore, it is important to put emphasis that the experiment itself was conducted with extreme caution and there were no side effects suggesting that safety measures were well respected.

Weaknesses:

The whole investigation was very time consuming due to methodology consisting of many steps and all safety measures that need to be respected. Moreover, five different solvents were used to obtain better results, and for each 4 trials were made. The Aspirin tablets compared with samples values were not pure aspirin and therefore higher values were obtained. Therefore the use of more concentrated acetylsalicylic acid source would give off more accurate results. The system in which lab-synthesis of crude aspirin was conducted got influenced by outside effects. Inadequate

isolation of the system resulted in oxidation, and green and orange color of crude aspirin. This made experiment more time consuming as such crude aspirin was not used due to high probability of bad absorbance values. Synthesizing the aspirin on a lower room temperature would be experiment less time consuming. While washing off the crystals with distilled water in vacuum filtration, there was a certain amount of crystals that got dissolved, and this could be prevented by using multiple filter papers. Additionally to get more accurate results, another analytical method could be used, which results would support the result of the initial method.

Extension:

The samples made in the experiment could be used to measure melting point of each sample. By introducing this comparative method, new results would be obtained and they would additionally support the claims of my investigation.

Besides measuring the melting point of the samples any different methodology that has a similar experiment or answer to the research question could be used. Some of the analytical purity testing methods include titration, infrared spectroscopy, paper chromatography, and optical rotation, among others[6].

This investigation could be improved even more by using different solvents, especially non-polar ones. The results obtained from change in solvent would be used to determine the detailed impact of polarity in synthesis of aspirin.

Green chemistry solvents could be used instead of the ones that create waste, for example Polyethylene glycol (PEG) which is a typical green and inexpensive solvent which application is present in various chemical synthesis. It is a polar eco-friendly solvent with low toxic level. Due to its structure with polar oxygen atom and non-polar $CH2$ group it would potentially be a very good solvent for Aspirin that as well has both polar and non-polar regions.

[6] *Top 5 methods of assessing chemical purity*. Moravek, Inc. (2019, June 13). Retrieved April 10, 2022, from https://www.moravek.com/top-5-methods-of-assessing-chemical-purity/

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