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參展科別 **化學**

作品名稱 **The effects of Different Synthesis Methods and Catalysts on Crude Aspirin**

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關鍵詞

1. Introduction

Aspirin is one of the most used and well-known medicines world-wide. It can be synthesized by reacting acetic anhydride and salicylic acid in a warm temperature of around 60-80°C. This reaction is usually catalyzed by sulfuric or phosphoric acid. This paper will investigate alternative catalysts, safer and more environmentally friendly, as well as compare different synthesis methods with different heat mediums, one using a water bath and the other a microwave. By doing so, the effects of the catalyst and the method of synthesis on the yield, purity and environmental consequence of crude aspirin synthesis will be deduced. The targeted outcome is to find the alternative method as more energy efficient, and to find a greener safer catalyst to sulfuric and phosphoric acid. Further background information, exploration, and explanation is in the appendix. **The targeted outcome** will be to find a viable alternative catalyst that is safer and more environmentally friendly, and to find that the microwave synthesis method consumes less energy.

2. Methodology

The procedure used in this investigation has been inspired by several sources and changed to fit the investigation better (Experiment 8; Abdelshaheed; Aspirin Synthesis).

2.1 Water bath

A hot water bath of 80°C was prepared. 15 test tubes were prepared, 3 for each catalyst. Approximately 2 g of salicylic acid put into each test tube. The specific mass of salicylic acid that went into each test tube were recorded. The catalysts were put into the test tubes. For liquid catalysts, 3 drops were added to the salicylic acid, and for $Al(NO_3)_3 \cdot 9H_2O$, 0.03-0.04 g were added. Afterwards, 2 cm^3 of acetic anhydride were added into each test tube. And the test tubes were put into the 80°C water bath for 20 minutes as can be seen in Fig. 5.

Fig. 5: "Water Bath" (Candidate, 8/6/2021)

The catalysts were added before the acetic anhydride. This ensures that an acidic environment was established before the reaction started. 2 cm^3 of acetic acid was added because this reaction has a 1:1 ratio of reactants, with the acetic anhydride needing to be in excess to ensure the reaction goes to equilibrium and the salicylic acid is used. The excess acetic anhydride does not affect the dried products as it decomposes in H_2O, and the products were rinsed with cold distilled water during the filtration process. After 20 minutes, 2 cm^3 of cold distilled water was added to each test tube to terminate the reaction and decompose any excess acetic anhydride.

Flasks and filters were set up. The filter papers were weighed and recorded before being put into the funnels. The filter papers were lined with cold distilled water.

After the hot water bath, the test tubes were put into an ice bath for 10 minutes to induce crystallization. Using a stirring rod and cold distilled water, the products in the test tubes were

extracted. They were rinsed with cold distilled water to both help the products get into the funnel for gravitational filtration, and to decompose the excess acetic anhydride.
The excess acetic anhydride decomposes into acetic acid, and goes through the filter, becoming the filtrate. After filtration, the filter papers were put on watch glasses and left to dry, as can be seen in Fig. 6.

Fig. 6: "Dried Water Bath Method Aspirin" (14/6/2021)

2.2 Microwave

The adding of the reactants and the catalysts into the test tubes, were all done in the same order as described in section 3.1. Acetic anhydride was added to groups of 3 test tubes, and the test tubes with all the chemicals required were then put in a beaker to hold them upright, as can be seen in Fig. 7. The 3 test tubes were microwaved for 3 minutes at the 75% setting. As the microwave used was old, % setting referred to the % of time the magnetron in the microwave was on during the 3 minutes (Lam). After 3 minutes in the microwave, the 3 test tubes were then put into an ice bath for 10 minutes to induce crystallization.

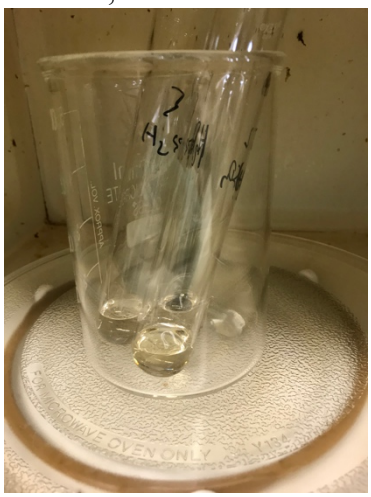


Fig. 7: "Microwave Trial" (Candidate, 9/6/2021)

The solution at the bottom of the test tubes did not recrystallize by themselves, and the cold solution was thus further stimulated by scratching the bottom of the test tube with a stirring rod, leading to crystallization. This was done 5 times in batches of 3, for a total amount of 15 trials.

The trials of aspirin made using the microwave were subject to the same extraction and filtration process. The dried products can be seen in Fig. 8.

Fig. 8: "Dried Microwave Method Aspirin" (14/6/2021)

2.3 Analysis of Trials

The purities of each trial of crude aspirin were analyzed using a melting point analysis [MPA] and a ferric chloride test. Explanations and results of the ferric chloride test have been placed in the appendix.

The MPA was done using two melting point apparatuses. Samples of each trial of crude aspirin were collected using capillary tubes. MPA was then done with three capillary tubes at a time. After a batch, to save time, while one melting point apparatus cooled down, the other was used. The final melting point of the crude aspirin was recorded when the trial inside of the capillary tubes turned completely clear and see through.

2.3.1 Explanation of the Melting Point Analysis

Conducting a MPA with each trial will provide insight as to how pure each trial is. This will be done through analyzing the melting point range [MPR], and how similar the melting point of each trial is to those of commercial aspirin, and salicylic acid.

For pure solids, a MPR is very narrow, often between 1°C -2°C whereas for impure solids, the range can be much broader, and differs based on how impure the substance is (Brittain). Furthermore, impure solids with crystalline structures such as ASA will also have a lower MPR than its pure version, as the impurity causes defects in the crystalline structure of the solid, decreasing the amount of energy needed to overcome the intermolecular forces and interactions between the molecules (Brittain).

3. Results and observations

Qualitative observations have been placed in the appendix.

Key: W = Water bath, M = Microwave, and numbers are for each respective trial.
Table 2: "Sample of Raw Data for Final Mass of Filter Paper taken from Appendix 2"
Source: Candidate, 3/10/21

Catalyst	Trials	Mass Salicylic Acid ±0.01 g	Volume Acetic Anhydride ±0.1 ml	Starting Mass of Filter Paper ±0.01 g
None	W1	1.99	2.0	0.99
	M1	2.07	2.0	0.73
H_2SO_4	W1	2.04	2.0	0.95
	M1	2.03	2.0	0.69
HCH3CH2COO	W1	2.08	2.0	0.92
	M1	2.02	2.0	0.71
H_3PO_4	W1	2.05	2.0	0.93
	M1	2.09	2.0	0.71
$Al(NO_3)_3 \cdot 9H_2O$	W1	2.08	2.0	0.92
	M1	2.00	2.0	0.81

Table 3: Sample Raw Data for the Results of the Melting Point Analysis taken from Appendix 3" Source: Candidate, 3/10/21

Catalyst	Trials	Start to melt ± 1 °C	Finish Melting ± 1 °C
None	W1	101	119
	M1	117	123
H_2SO_4	W1	93	105
	M1	92	105
HCH3CH2COO	W1	90	105
	M1	111	124
H_3PO_4	W1	95	111
	M1	114	125
$Al(NO_3)_3 \cdot 9H_2O$	W1	109	125
	M1	108	117
Aspirin Tablet	1	120	130
Salicyclic Acid	1	143	152

4. Analysis

4.1 Mass and Percentage Yield

Calculating the Mass of Crude Aspirin Produced and Percentage Yield:

To find the mass of crude aspirin produced, the starting mass of the filter paper must be subtracted from the final mass of the filter paper. Using H_2SO_4 Trial W1, this would look like:

$$3.28\pm0.01\text{g} - 0.95\pm0.01\text{g} = 2.33\pm0.02\text{ g}$$

This calculation was done for all the trials.

Calculating the % Yield of the Aspirin Synthesis Process:

To find the % Yield, the theoretical Aspirin yield of the process must be found first. 2 grams of salicylic acid (138.12 $gmol^{-1}$) and 2 milliliters of acetic anhydride (102.09$gmol^{-1}$ and 1.08gcm^{-1}) were used. The molecular mass of Aspirin is 180.16$gmol^{-1}$).

Determining the amount of salicylic acid used:

$$\frac{2g}{138.12\text{g}mol^{-1}} = 0.0145\ mol\ Salicylic\ Acid$$

Determining the amount of acetic anhydride used:

$$2\ millilters = 2cm^3, \therefore 2cm^3 \times 1.08gcm^{-3} = 2.16g\ acetic\ anhydride$$

$$\frac{2.16g}{102.09\text{g}mol^{-1}} = 0.0212mol\ Acetic\ Anhydride$$

Determining limiting reactant:

As this reaction is 1:1 ratio between reactants, the limiting reactant is the Salicylic Acid, which exists in a lower amount than the acetic anhydride in this reaction. The process was designed to be as such.

Determining the mass of Aspirin Produced:

$$0.0145mol \times 180.16\text{g}mol^{-1} = 2.61g\ Aspirin$$

The Percentage Yield Formula:

$$\frac{Experimental\ Yield}{Theoretical\ Yield} \times 100\%$$

Example Using None Trial W3:

$$\frac{2.41 \pm 0.02\ g}{2.61\ g} \times 100\% = 92.3\%$$

Table 6: "Sample of The Masses of Crude Aspirin Produced and % Yield of Each Trial taken from Appendix 5"
Source: Candidate, 3/10/21

Catalyst	Trials	Mass of Aspirin Produced g ±0.02 g	% Yield
None	W1	2.93	112
	M1	2.35	90.0
H_2SO_4	W1	2.33	89.1
	M1	2.76	106
HCH3CH2COO	W1	2.51	96.3
	M1	2.11	80.8
H_3PO_4	W1	2.42	92.8
	M1	2.44	93.5
$Al(NO_3)_3 \cdot 9H_2O$	W1	2.16	82.7
	M1	2.15	82.4

Determining Averages for Mass of Crude Aspirin Produced and % Yield:
The average mass produced and % yield was calculated for each respective catalyst group by taking a total of masses and % yields and dividing by the number of trials in the group.
Example for the $Al(NO_3)_3 \cdot 9H_2O$ water bath group:
Calculating average mass of crude aspirin produced:

$$\frac{2.16 \pm 0.02g + 2.16 \pm 0.02g + 2.45 \pm 0.02g}{3} = 2.26 \pm 0.02g$$

Calculating average % yield:

$$\frac{82.7\% + 82.8\% + 93.8\%}{3} = 86.4\%$$

Table 7: "Average Mass of Crude Aspirin Produced Using Water Bath and Microwave" Source: Candidate, 3/10/21		
Catalyst	Average Mass produced Using Water Bath ± 0.02g	Average Mass produced Using Microwave ± 0.02g
None	2.33	2.18
H_2SO_4	2.16	3.05
H_3PO_4	2.63	2.23
HCH3CH2COO	2.57	2.23
$Al(NO_3)_3 \cdot 9H_2O$	2.26	2.25

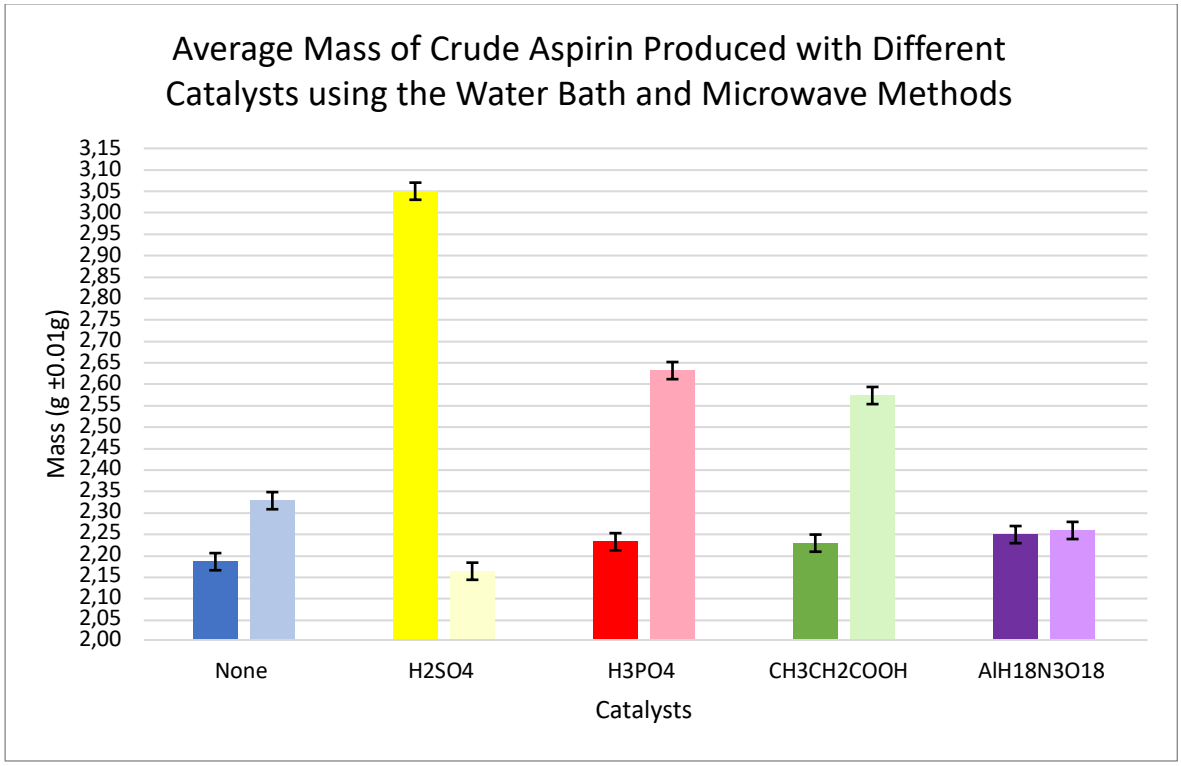
Table 8: "% Yield of Crude Aspirin Produced Using Water Bath and Microwave" Source: Candidate, 3/10/21		
Catalyst	Average % Yield Using Water Bath	Average % Yield Using Microwave
None	89.1	83.7
H_2SO_4	82.8	117
H_3PO_4	101	85.4
HCH3CH2COO	98.5	85.3
$Al(NO_3)_3 \cdot 9H_2O$	86.4	86.1

Graphs Regarding Mass Produced and % Yield:

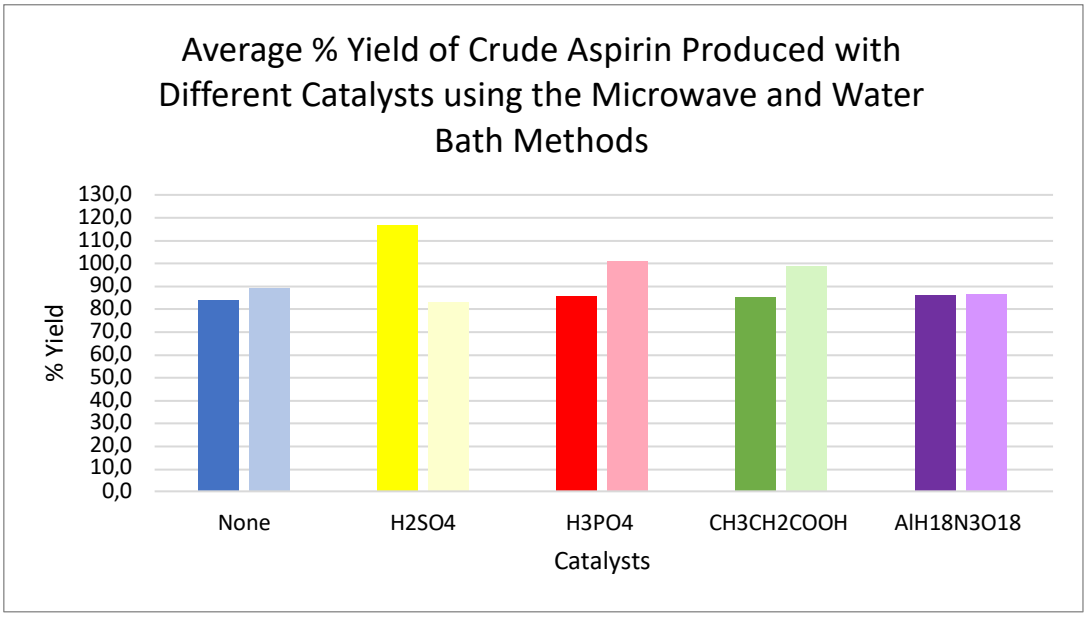
Key: The averages from the microwave trials have been colored a lighter version of its water bath counterpart.

Graph 1: "Average Mass of Crude Aspirin Produced with Different Catalysts using the Water Bath and Microwave Method Made with Data Taken from Table 7"

Source: Candidate, 4/10/21



Graph 2: “Average % Yield of Crude Aspirin Produced with Different Catalysts using the Microwave and Water Bath Methods Made with Data Taken from Table 8”
Source: Candidate, 4/10/21



4.2 Melting Point Analysis

Calculating the Melting Point Range and Difference Between Aspirin Tablet:
The time when the trial first started melting and finished melting was taken, and the MPR was calculated from these two values. Furthermore, the difference between the final melting points of each respective trial and the Aspirin tablet was calculated.
Using H_3PO_4 W1 as an Example, Calculating Range:

$$111 \pm 1°C - 95 \pm 1°C = 16 \pm 2°C$$

Calculating Difference Between Final Melting Points of Trial and Aspirin Tablet:

$$130 \pm 1°C - 111 \pm 1°C = 19 \pm 2°C$$

Table 9: “Sample Melting Point Range and Comparison of Trial and Aspirin Tablet taken from Appendix 4” Source: Candidate: 9/10/21

Catalyst	Trial	Range ± 2°C	Difference Between Final Melting Points of Trial and Aspirin Tablet ± 2°C
None	W1	18	11
	M1	6	7
H_2SO_4	W1	12	25
	M1	13	25
HCH3CH2COO	W1	15	25
	M1	13	6
H_3PO_4	W1	16	19
	M1	11	5
$Al(NO_3)_3 \cdot 9H_2O$	W1	16	5
	M1	9	13
Aspirin Tablet	1	10	-
Salicyclic Acid	1	9	-

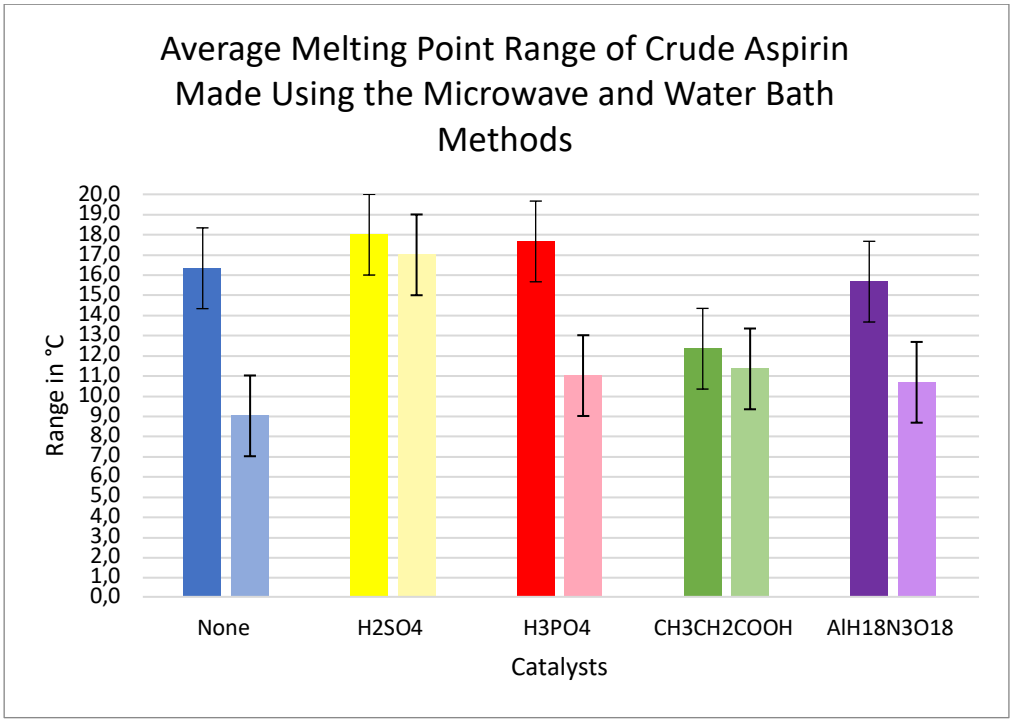
Data Tables Regarding Average Melting Point Range and Difference Between Commercial Aspirin:

Table 10: "Average Melting Point Range with Different Methods and Catalysts" Source: Candidate, 9/10/21		
Catalyst	Water Bath Average Melting Point Range ± 2°C	Microwave Average Melting Point Range ± 2°C
None	16.3	9.0
H_2SO_4	18.0	17.0
H_3PO_4	17.7	11.0
HCH3CH2COO	12.3	11.3
$Al(NO_3)_3 \cdot 9H_2O$	15.7	10.7

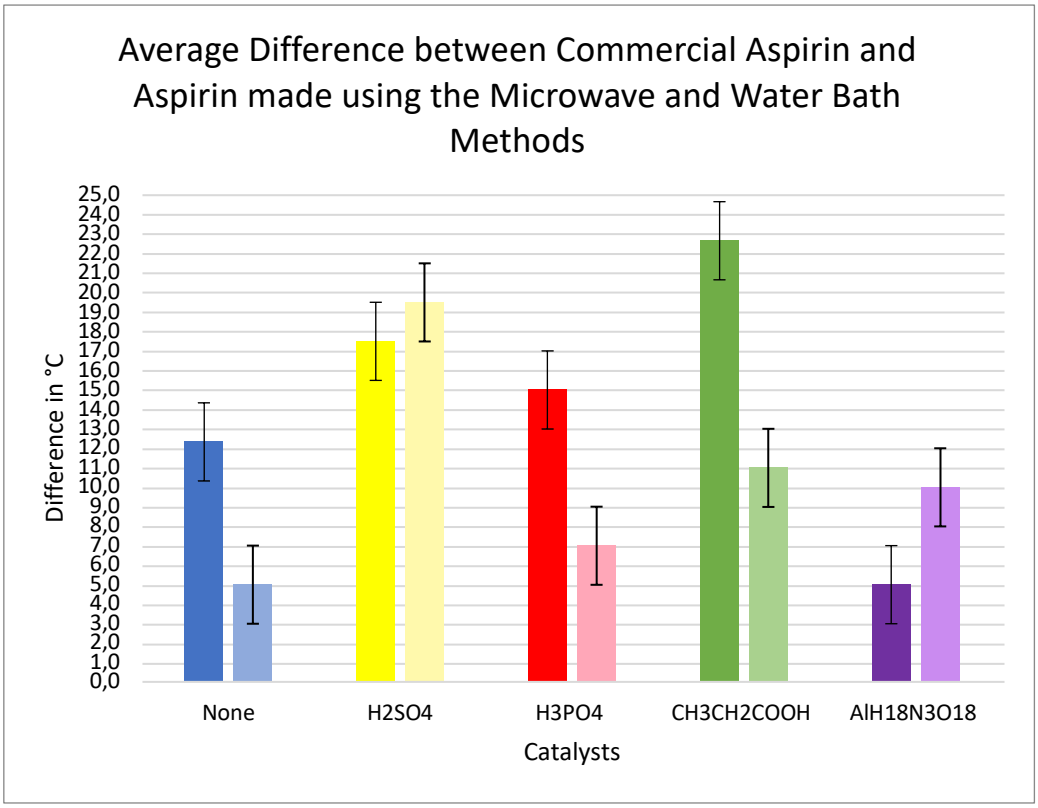
Table 11: "Average Difference Between Aspirin Tablet and Crude Aspirin Trials" Source: Candidate, 9/10/21		
Catalyst	Water Bath Average Difference to Aspirin Tablet ± 2°C	Microwave Average Difference to Aspirin Tablet ± 2°C
None	12.3	5.0
H_2SO_4	17.5	19.5
H_3PO_4	15.0	7.0
HCH3CH2COO	22.7	11.0
$Al(NO_3)_3 \cdot 9H_2O$	5.0	10.0

Graphs Regarding Average Melting Point Range and Difference Between Commercial Aspirin:

Graph 3: "Average Melting Point Range of Crude Aspirin Made Using the Microwave and Water Bath Methods Made with Data Taken from Table 10" Source: Candidate, 9/10/21



Graph 4: “Average Difference between Commercial Aspirin and Aspirin made using he Microwave and Water Bath Methods Made with Data Taken from Table 11”
Source: Candidate, 9/10/21



4.3 Energy Use

Water bath:

The water bath used 3 liters of room temperature (23°C) water and was heated up to 80°C. To calculate the amount of energy needed to do this, the specific heat capacity formula will be used.

Specific heat capacity formula:

$Q = mc\Delta T$

Where:
Q = heat energy
m = mass in kg
c = specific heat capacity (of the substance being heated)
ΔT = change in temperature

Determining ΔT:

$\Delta T = 80°\text{C} - 23°\text{C} = 57°\text{C}$ or $353K - 296K = 57K$

Determining Mass of Water Used in KG:

$$3\ Liters\ of\ Water = 3\ Kilograms\ of\ Water$$

And finally, as the component being heated is water, water’s specific heat capacity is:

$$4.18kJkg^{-1}K^{-1}$$

Finding Q, the heat energy used to synthesize 15 trials of crude aspirin:

$$Q = 3KG \times 57\text{K} \times 4.18kJkg^{-1}K^{-1} = 714.78kJ\ or\ 714280J$$

It should be mentioned that the real energy used is much higher than the one presented above, as the energy used for keeping the water hot and loss to the surroundings are not incorporated in the calculations.

Microwave:
To find out how much energy the microwave used, its power rating in Watts or in other words Joules per second will be multiplied by the amount of time it was turned on. The power rating of the microwave is 700W, and it was used at 75% for 3 minutes 5 times.
Determining the number of seconds the microwave was actively heating:

$$3\ minutes \times 0.75 = 2.25\ minutes$$

$$2.25\ minutes = 135\ seconds$$

Determining energy used for 1 batch (3 Trials):

$$135\ seconds \times 700W = 94500\ Joules$$

Determining energy used for 15 trials:

$$94500\ Joules \times 5 = 472500\ Joules\ or\ 472.5\ kJ$$

It should be mentioned that this calculation assumes 100% energy efficiency, Therefore, is a good estimate of the energy that was used but is higher than what was absorbed by the reactants.

4.4 Energy Use Comparison of the Two Methods

Energy Microwave Method used to synthesize 15 Trials of Crude Aspirin: 472.50 kilojoules
Energy Water Bath Method used to synthesize 15 Trials of Crude Aspirin: 714.78 kilojoules

5. Conclusion

To what extent does the method and catalyst used in aspirin synthesis influence the yield, purity, and environmental consequences of the crude aspirin produced? As a general trend, the catalysts and the method of synthesis influence the yield, purity and the environmental consequences of the crude aspirin produced to a certain extent. The microwave method decreases the environmental impact of synthesizing crude aspirin as it uses much less energy than the water bath method, to be specific, 242.28 kJ less to produce 3 trials. Furthermore, using no catalyst or propanoic acid as a catalyst given that it is very biodegradable, is much more environmentally friendly than the orthodox option of using sulfuric or phosphoric acid as catalysts in the ASA synthesis process.

For the trials which used H_3PO_4, HCH_3CH_2COO and no catalyst, the microwave method had both a higher % yield and a higher purity, sporting a narrower MPR with smaller differences between its MPR and that of commercial aspirin, seen in Graphs 2, 3 and 4.

For H_2SO_4, the water bath method provided a higher % yield, as illustrated in Graph 2. As for the purity, deduced from Graph 3 and 4, the water bath method had a larger melting point range, but also presented less of a difference to commercial aspirin. These results which go against the trend could be explained by the uncertainties associated with the MPA.

For trials which used $Al(NO_3)_3 \cdot 9H_2O$ as a catalyst, the microwave method presented a higher mass produced and % yield than the water bath method seen in Graph 1 and 2, however, even though the MPR seen in Graph 3 is narrower, the microwave method has a bigger difference to the MPR of commercial aspirin than the water bath method as shown in Graph 4. As the uncertainties in this case cannot explain this, this might be due to specific formations and

defects in the crystalline structure. Furthermore, as it has a light brown color, there is a high possibility that the solid $Al(NO_3)_3 \cdot 9H_2O$ has remained in the crude aspirin, affecting its properties, and making it impure.

It would be more profitable to use the microwave method, as it uses much less energy than the water bath method and provides a purer product with a higher % yield when some specific catalysts are used. It would also have the least environmental consequence as it uses less energy, showing a greener approach to aspirin synthesis.

In the green chemistry aspect, the best trial would be the trials with no catalyst used in the microwave method. It provides the purest crude product and the 4th highest % yield out of the trials attempted, and complies best with the principles of green chemistry, as it shows higher energy efficiency, is the least hazardous chemical synthesis process, prevents any possible additional waste and pollution, and is the best regarding accident prevention as no additional measures need to be taken.

It should be mentioned that the trial with the highest purity would be the best trial regardless of energy consumption or environmental effects, as the most important aspect of a medicine is its ability to work as intended for the consumer. Alongside this, it should also be mentioned the produced ASA in this investigation would present a much higher purity if they were recrystallized.

6. Evaluation

The following paragraphs describe faults and points that could be improved in the experiment in order of significance.

The recrystallisation process was attempted twice but was unsuccessful both times. Combined with the time constriction, as a result, the data analysis and the conclusions drawn within this investigation are only relevant to crude aspirin. Although the information gathered might still have some relevance to recrystallized aspirin, the only meaningful and reliable data deduced in this investigation is for crude aspirin.

During the MPA, one of the machines used had a foggy observation glass with crystalline structures on it, making it difficult to determine the exact temperature at which the trials started to and finished melting. This would affect the recorded data about the purity of the crude aspirin trials, which might be misrepresented due to both human and systematic error. This could be improved by using cleaner equipment.

Errors that could have affected the final mass of the crude aspirin recorded include:

- Spillages that happened as the wet filter papers were placed on the watch glasses. There were also cases where the solution spilled through the filter paper and on to the watch glasses.

- Even though the filter papers were lined with cold distilled water before hand, some of the crude aspirin solution passed through between the funnel and the filter paper. This led to there being crystalline aspirin formations left in the filtrate.

Both errors would indicate that the recorded mass produced is slightly lower than it should be for affected trials. This could be improved by making sure crude aspirin solution is properly filtered and making sure they are dry enough before being placed on the watch glass.

When the masses of the filter papers were being measured, a balance that measured into the 3rd decimal place was used, however, after the masses of the filters for some of the water bath trials were measured, it was observed that the balance had calibration problems, as the readings would be constantly and infinitely be going either upwards or downwards. As their masses were still accurate after measuring with a slightly less accurate balance, the original masses were kept, however, one decimal point was removed, with rounding done when necessary. This could have affected the recorded mass produced of crude aspirin and the % yield. Can be improved by using the same balance to measure all masses.

Further questions and additional investigations that could be done to explore this topic and gather more relevant data has been placed in the appendix.

Appendix

Background Exploration and Explanation

1.1.1 Acetylsalicylic Acid

Acetylsalicylic acid (ASA) is an odorless white solid, also known as aspirin, and is one of the most used medicines (PubChem [CID 2244]). It was created by adding an acetyl group to salicylic acid from acetic anhydride, which reduced its irritant and acidic properties and made it safer and easier for consumption, while keeping its medicinal value (Goldberg; Eschner).

ASA works by binding to, and acetylating residues of serine, a non-essential amino acid used in metabolic reactions and muscle growth in cyclooxygenases, an enzyme that catalyzes reactions which trigger physiological and pathophysiological responses (PubChem [CID 2244]; PubChem [CID 5951]; Cyclooxygenase Structure). The acetylation of serine in cyclooxygenases result in decreased synthesis of prostaglandin, and platelet aggregation, which causes, aspirin to exhibit analgesic, antipyretic, anti-inflammatory and anticoagulant properties (Cyclooxygenase Structure; PubChem [CID 2244]).

Commonly prescribed to alleviate pain, fever, or inflammation, aspirin is available in many different doses and administration forms (PubChem [CID 2244]). Because of its anticoagulant properties, it can be used as a preventative measure against blood clots and therefore strokes and heart attacks (Goldberg). Furthermore, the long-term use of Aspirin may decrease the risk of different cancers (Eschner). Fig. 1 shows the structure of ASA, where the acetyl group R-CH_3CO can be seen.

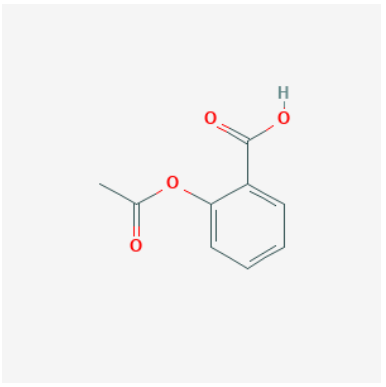


Fig. 1: “Structure of Acetylsalicylic Acid” (Chemical Structure [Aspirin])

1.1.2 Salicylic Acid

Historically used as pain and fever relief as well as anti-inflammatory medicine, examples of administering salicylic acid are chewing on or brewing tea from willow tree barks (Eschner; Salicylic Acid: Properties, Uses and History; C
however there are health problems related to the prolonged use of
acidity, it often led to gastrointestinal irritation, with symptoms of nausea, vomiting, bleeding, and ulcers (Goldberg). Due to these risks, a “better” salicylic acid started to be researched in the late 1800s (Eschner). The most important difference between ASA and salicylic acid can be seen in Fig. 2, showing the absence of the acetyl group.

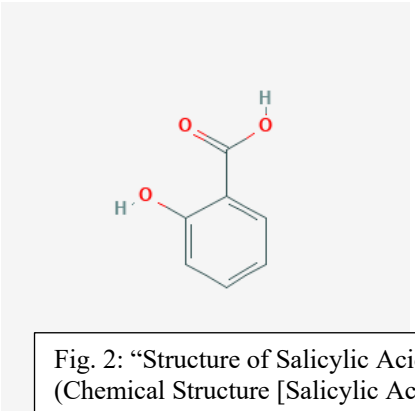


Fig. 2: “Structure of Salicylic Acid” (Chemical Structure [Salicylic Acid])

1.2 Reaction Summary of the Synthesis of Acetylsalicylic Acid

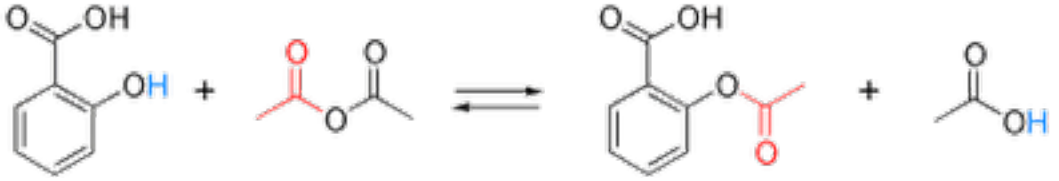


Fig. 1: "Aspirin Synthesis Reaction" (Aspirin Synthesis Reaction)

Salicylic Acid	Acetic Anhydride	Acetylsalicylic Acid	Acetic Acid
$C_7H_6O_3$	$C_4H_6O_3$	$C_9H_8O_4$	$C_2H_4O_2$
138.12 $gmol^{-1}$	102.09$gmol^{-1}$	180.16$gmol^{-1}$	60.05$gmol^{-1}$

To synthesize ASA, salicylic acid is acetylized through an esterification reaction with acetic anhydride, illustrated in Fig. 3. The hydroxyl group R-OH in the salicylic acid is replaced by an ester group R-OCOCH$_3$, creating ASA, an ester (Synthesis of Aspirin). This reaction can be described as the acetyl group on acetic anhydride and the hydrogen in the hydroxide group of salicylic acid swapping places. This reaction has an equilibrium and is reversible, as the products can react to produce the reactants (Synthesis of Aspirin). This causes aspirin synthesis to have a low yield.

The reactants will react with each other without a catalyst; however, it takes a longer time (Abdelshaheed). Therefore, the reactants are usually heated up to 70°C-100°C, and an acidic catalyst such as H_2SO_4 or H_3PO_4 is used (Experiment 8). These catalysts provide a proton for the reaction and provide a pathway with lower activation energy for the reaction (The Editors of Encyclopaedia Britannica, et al.). This decreases the reaction time and causes the faster establishment of equilibrium. Although the catalyst loses a proton and is therefore chemically "changed" during the process, it is reassembled at the end of the mechanism, as can be seen in Fig. 4.

The mechanism illustrated:

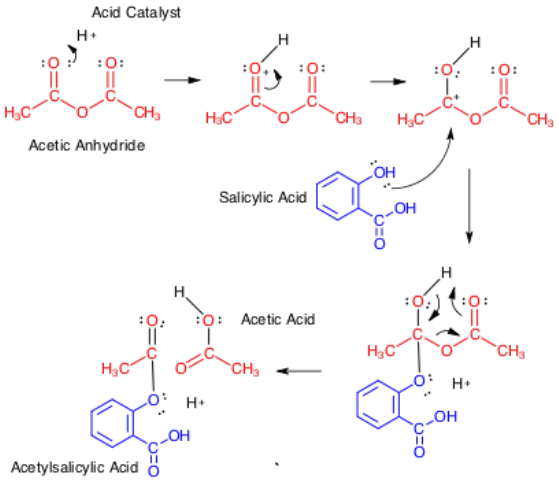


Fig. 4: "Synthesis Mechanism" (The Catalyst Mechanism)

1.3 Reactants:

Salicylic Acid:

Description	White crystals, usually in fine needles, or fluffy, white, crystalline powder (MEDISCA).
Melting/Freezing Point	157-161°C (MEDISCA)
Water solubility (25°C)	2240mg/L (MEDISCA)
Ethanol solubility (21°C)	34870mg/L (Salicylic Acid)
Density (20°C)	1.44 gcm^{-3} (PubChem [338])

Acetic Anhydride:

Description	Clear, colorless liquid with a vinegar-like odor (Fisher Scientific [Acetic Anhydride])
Melting/Freezing Point	-73°C (Fisher Scientific [Acetic Anhydride])
Water solubility	Decomposes in water (Fisher Scientific [Acetic Anhydride])
Density	1.08gcm^{-3} (Fisher Scientific [Acetic Anhydride])

1.4 Products

Acetylsalicylic Acid:

Description	Odorless white powder (Fisher Scientific [Acetylsalicylic Acid]).
Melting/Freezing Point	134-136°C (Fisher Scientific [Acetylsalicylic Acid])
pH	3.5 (Fisher Scientific [Acetylsalicylic Acid])
Water solubility (25°C)	4600mg/L (Sigma-Aldrich [Acetylsalicylic Acid])
Ethanol solubility	50000mg/L (A5376 Acetylsalicylic Acid)

1.5 Hazard and Safety Considerations

As the chemicals used in this investigation can cause severe skin, eye and lung damage, personal protective equipment was used, including a fume hood, goggles, and nitrile rubber gloves. Further information can be found in Section 1.6 regarding the catalysts used.

1.6 Green Chemistry

Green chemistry is an approach to chemistry and chemical processes, concerned with environmental friendliness more than standard techniques. Green chemistry helps chemical processes become more environmentally friendly in several ways; developing processes that reduce pollution, give alternatives to hazardous substances, introduce processes that reduce waste and usage of diminishing resources, and processes that use less energy (Green Chemistry). This is important since resources on the earth are finite.

This investigation will be concerned with several of the "12 Principles of Green Chemistry". The principles most important to this investigation are: "less hazardous chemical synthesis", through the investigation of greener alternatives to H_2SO_4 and H_3PO_4, "design for energy

efficiency", through using a microwave instead of a water bath in aspirin synthesis (Green Chemistry.

1.6 Catalysts

Table 1: "Relevant Information on the Catalysts Used",
Sources: Listed in table (Fisher Scientific [Phosphoric Acid]; Sigma-Aldrich [Aluminium Nitrate Nonahydrate]; Sigma-Aldrich [Sulfuric Acid]; Sigma-Aldrich [Propionic Acid])

Catalysts	Molecular Formula	Environmental Impacts and Precautions	Concentration
Sulfuric Acid	H_2SO_4	Shall not be classified as toxic to the aquatic environment. Endangers drinking-water supplies if allowed to enter water or soil in large quantities. IMDG Marine Pollutant: no Do not let product enter drains. (Sigma-Aldrich [Sulfuric Acid])	14 $moldm^{=3}$
Phosphoric Acid	H_3PO_4	Do not release into the water, may cause algae growth and depleted oxygen in the environment. Also toxic at high concentrations. IMDG Marine Pollutant: no Prevent from reaching drains. (Fisher Scientific [Phosphoric Acid])	14 $moldm^{=3}$
Propanoic Acid	HCH3CH2COO	IMDG Marine Pollutant: no No data on other adverse effects. Aerobic biodegradability: 93% in 20 days. (Sigma-Aldrich [Propionic Acid])	98.5 %
Aluminum Nitrate Nonahydrate	$Al(NO_3)_3 \cdot 9H_2O$	IMDG Marine pollutant: no Hazard for drinking water supplies. (Sigma-Aldrich [Aluminium Nitrate Nonahydrate])	Solid
None	----------	None	None

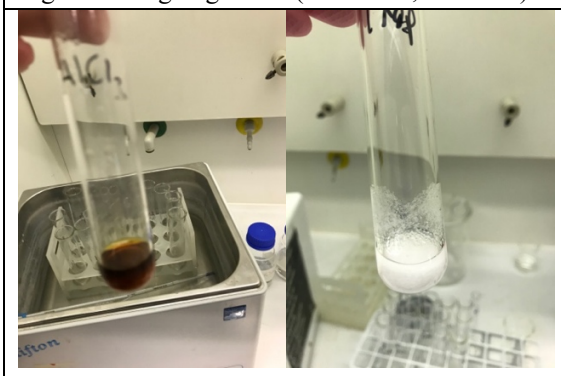
Qualitative Observations

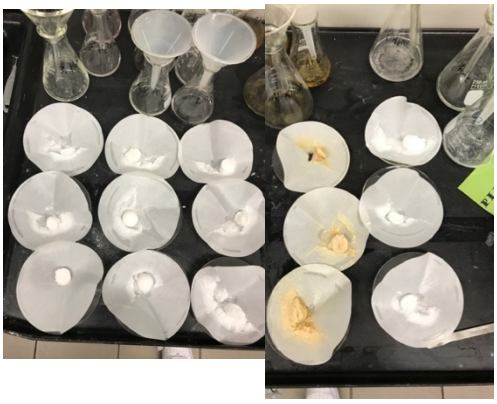
Table 4: "Sample Raw Data for the Results of the Ferric Chloride Test taken from Appendix 1" Source: Candidate, 3/10/21

Catalyst	Trials	Colour Observed
None	W1	red

	M1	orange
H_2SO_4	W1	red
	M1	orange
HCH3CH2COO	W1	red
	M1	orange
H_3PO_4	W1	red
	M1	orange
$Al(NO_3)_3 \cdot 9H_2O$	W1	red
	M1	orange
Aspirin Tablet	1	orange
Salicyclic Acid	1	red

Table 5: "Qualitative Observations" Source: Candidate, 3/10/21

Image/Description	Explanation and Significance
 Fig.11: "Weighing Boat" (Candidate, 8/6/2021)	After using the weighing boat to add in the salicylic acid to a test tube, there would be a little bit lweft over on the weighing boat, as can be seen in Fig. 11. Although this small amount is not very significant, it still indicates that the specific data for salicylic acid added might be slightly higher than it is.
 Fig.12: "Al(NO3)3 ·9H2OTrial" (Candidate, 8/6/2021) Fig.13: "HCH3CH2COO Trial" (Candidate, 9/6/2021)	All catalyst trials produced a milky white solution when the acetic anhydride was first added, shown in Fig. 13, except $Al(NO_3)_3 \cdot 9H_2O$, which was brown, seen in Fig. 12. This color change is also reflected in the product of trials which used this catalyst, which were light brown This indicates that this catalyst affected the purity negatively, as it is not consistent with the description aspirin.
Image/Description	Explanation and Significance
When the 2 milliliters of water were added to the Microwave trials, the water boiled as soon as it made contact with the first trial out of the 3. It did not for the other 2 trials. This was true for all 5 batches.	This means that the microwave heated the solutions inside the test tubes to just above water's boiling temperature, 100°C, which is 20°C higher than what the water bath's temperature was set as. This could have differing effects on the % yield and purity of the microwave trials. This could have also happened because of the

	decomposition of the excess acetic anhydride, however, seeing this did not take place in any water bath trials, the prior possibility is more likely.
After the cold water/ice bath, the microwave trials did not crystallize on their own, and crystallization had to be stimulated by scratching the bottom of the test tube with a stirring rod.	This indicates super saturation in the solution, which could mean that the concentration of the ASA in the solution is higher than it normally would be at that temperature. This could lead to a higher % yield and higher purity in the microwave trials being observed.
 Fig.13: "Wet Water Bath Trials" (Candidate, 8/6/2021) Fig.14: "Wet Water Bath Trials 2" (Candidate, 8/6/2021)	Figures 13 and 14 are images of the water bath trials before they were crushed up for analysis. All trials have a small ball that is harder than the rest of the white crystalline powder on the filter paper. Assuming that this is not ASA, and rather salicylic acid, the % yield of the water bath trials should be higher than usual and have a lower purity. Furthermore, these "balls" were already present at the bottom of the test tubes, segmented from the rest of the softer, product. This could also be further supported by the densities of salicylic acid, aspirin, and water in relation to one another. One explanation for this might be that salicylic acid is denser, although slightly, than aspirin. Salicylic acid is also much denser than water.

Ferric Chloride Test

A ferric chloride solution was prepared with the addition of solid $FeCl_3$ into 0.1 $moldm^{-3}$ NaOH. This solution tests for phenols, and if positive, the $FeCl_3$ changes color from red to light brown (Test for Phenolic Group). Phenols are present in salicylic acid. $FeCl_3$ is therefore used to confirm the existence of salicylic acid in the crude aspirin.

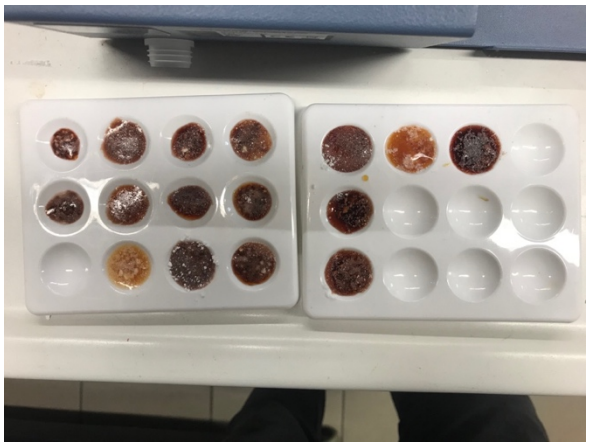


Fig. 9: "Ferric Chloride Test Water Bath Trials" (Candidate, 11/6/2021)

To ensure the impurities present in certain trials were observed, each trial was crushed and mixed using a mortar and pestle. A small sample of from each trial was taken and placed into a spot plate, and $FeCl_3$ solution and recorded, shown in Fig. 9.

6.1 Further Questions

To draw a more conclusive analysis of the purity of the aspirin trials, infrared spectroscopy could be done to all aspirin trials, after which their IR Spectrums would be compared to each other's, commercial aspirin and salicylic acid alongside the melting point analysis that has

already been done. High-performance liquid chromatography could also be used in order to provide more data on the purity of the trials collected.

Furthermore, this investigation would be more medically relevant if all analyses conducted were also conducted on the recrystallized trials of the crude aspirin, which would provide a better and more thorough investigation of the 2 synthesis methods and the effects of the different catalysts on the process.

Appendix 1: “Raw Data for the Results of the Ferric Chloride Test”

Catalyst	Trials	Colour Observed
None	W1	dark red
	W2	dark red
	W3	dark red
	M1	orange
	M2	orange
	M3	orange
H_2SO_4	W1	dark red
	W2	dark red
	W3	
	M1	orange
	M2	dark red
	M3	
HCH3CH2COO	W1	dark red
	W2	dark red
	W3	dark red
	M1	orange
	M2	dark red
	M3	orange
H_3PO_4	W1	dark red
	W2	dark red
	W3	light orange
	M1	orange
	M2	orange
	M3	orange
Al(NO¬3)3¬ ·9H2O	W1	dark red
	W2	dark red
	W3	dark red
	M1	orange
	M2	orange
	M3	orange
Aspirin Tablet	1	light orange
Salicyclic Acid	1	dark red

Appendix 2: “Raw Data for Final Mass of Filter Paper” Source: Candidate, 3/10/21

Catalyst	Trials	Mass Salicylic Acid ±0.01 g	Volume Acetic Anhydride ±0.1 ml	Starting Mass of Filter Paper ±0.01 g
None	W1	1.99	2.0	0.99
	W2	2.04	2.0	0.92
	W3	2.00	2.0	0.91
	M1	2.07	2.0	0.73
	M2	2.08	2.0	0.71
	M3	2.09	2.0	0.82
H_2SO_4	W1	2.04	2.0	0.95
	W2	2.05	2.0	0.97
	W3	2.07	2.0	0.93
	M1	2.03	2.0	0.69
	M2	2.04	2.0	0.81
	M3	2.08	2.0	0.71
HCH3CH2COO	W1	2.08	2.0	0.92
	W2	2.08	2.0	0.93
	W3	2.07	2.0	0.93
	M1	2.02	2.0	0.71
	M2	2.08	2.0	0.79
	M3	2.07	2.0	0.70
H_3PO_4	W1	2.05	2.0	0.93
	W2	2.03	2.0	0.94
	W3	2.03	2.0	0.95
	M1	2.09	2.0	0.71
	M2	1.98	2.0	0.82
	M3	1.98	2.0	0.84
Al(NO¬3)3¬ ·9H2O	W1	2.08	2.0	0.92
	W2	2.03	2.0	0.94
	W3	2.09	2.0	0.92
	M1	2.00	2.0	0.81
	M2	2.01	2.0	0.78
	M3	2.09	2.0	0.71

Appendix 3: “Raw Data for the Results of the Melting Point Analysis” Source: Candidate, 3/10/21

Catalyst	Trials	Start to melt ± 1 °C	Finish Melting ± 1 °C
None	W1	101	119
	W2	102	114
	W3	101	120
	M1	117	123
	M2	117	127
	M3	114	125
H_2SO_4	W1	93	105
	W2	96	120
	W3		
	M1	92	105
	M2		
	M3	95	116
HCH3CH2COO	W1	90	105
	W2	96	110
	W3	99	107
	M1	111	124
	M2	107	118
	M3	105	115
H_3PO_4	W1	95	111
	W2	97	114
	W3	100	120
	M1	114	125
	M2	110	122
	M3	112	122
Al(NO¬3)3¬ ·9H2O	W1	109	125
	W2	112	122
	W3	107	128
	M1	108	117
	M2	110	121
	M3	110	122
Aspirin Tablet	1A	120	130
Salicyclic Acid	1S	143	152

Appendix 4: “Full Table of Melting Point Range and Comparison of Trial and Aspirin Tablet”
Source: Candidate: 9/10/21

Catalyst	Trial	Range ± 2°C	Difference Between Final Melting Points of Trial and Aspirin Tablet ± 2°C
None	W1	18	11
	W2	12	16
	W3	19	10
	M1	6	7
	M2	10	3
	M3	11	5
H_2SO_4	W1	12	25
	W2	24	10
	W3		
	M1	13	25
	M2		
	M3	21	14
HCH3CH2COO	W1	15	25
	W2	14	20
	W3	8	23
	M1	13	6
	M2	11	12
	M3	10	15
H_3PO_4	W1	16	19
	W2	17	16
	W3	20	10
	M1	11	5
	M2	12	8
	M3	10	8
Al(NO¬3)3¬ ·9H2O	W1	16	5
	W2	10	8
	W3	21	2
	M1	9	13
	M2	11	9
	M3	12	8
Aspirin Tablet	1	10	Not Relevant
Salicyclic Acid	1	9	Not Relevant

Appendix 5: “The Masses of Crude Aspirin Produced and % Yield of Each Trial”

Source: Candidate, 3/10/21

Catalyst	Trials	Mass of Aspirin Produced g ±0.02 g	% Yield
None	W1	2.93	112
	W2	1.64	62.9
	W3	2.41	92.3
	M1	2.35	90.0
	M2	2.19	83.9
	M3	2.01	77.0
H_2SO_4	W1	2.33	89.1
	W2	2.00	76.5
	W3		
	M1	2.76	106
	M2		
	M3	3.34	128
HCH3CH2COO	W1	2.51	96.3
	W2	2.54	97.4
	W3	2.66	102
	M1	2.11	80.8
	M2	2.61	100
	M3	1.96	75.1
H_3PO_4	W1	2.42	92.8
	W2	2.85	109
	W3	2.62	100
	M1	2.44	93.5
	M2	2.02	77.4
	M3	2.23	85.4
$Al(NO_3)_3 \cdot 9H_2O$	W1	2.16	82.7
	W2	2.16	82.8
	W3	2.45	93.8
	M1	2.15	82.4
	M2	2.35	90.0
	M3	2.24	85.8

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【評語】030035

Everyone takes aspirin once and this research explore alternative approaches to synthesis aspirin from salicylic acid and acetic anhydride. The student tried to understand how the synthesis works with minimum support from teachers or external resources. Although the results are limited but the enthusiasm toward research is definitely recognized.