**CHE 2060**

**A suite of aspirin and analgesic lab exercises**

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# Introduction

Many of us rely on occasional use of **analgesics** to keep us moving and comfortable. Analgesics are drugs that relieve pain by acting on our peripheral or central nervous systems. Common everyday, over-the-counter (OTC) analgesics include aspirin (acetylsalicylic acid), Motrin (ibuprofen), and Aleve (naproxen) and These three drugs belong to a class of analgesics called **NSIADs, non-steroidal anti-inflammatory drugs**. We now know that NSAIDs work by inhibiting enzymes of the cyclooxygenase family like COX-1 and COX-2 that synthesize prostanioids, small molecules that cause inflammation and constriction of blood vessels. NSAIDs are used to treat pain, fever and inflammation. Tylenol (acetaminophen) is not an NSAID. While it is used to treat pain and fever, acetaminophen does not treat inflammation. Acetaminophen is also thought to work by inhibiting COX enzymes.



While the oldest of these analgesics, acetylsalicylic acid, was synthesized in the 1890s by Felix Hofmann of the Bayer Company in Germany, the use of drugs to treat pain is much, much older. Willow bark was used to treat pain in Asia over 2400 years ago. In the 1840s, organic chemists found that the molecule they named salicin could be isolated from willow bark (*salix*) and meadowsweet (*spirea*) and that it could be used to treat pain. In 1870, a Swiss chemist found that salicin was converted to salicylic acid in the human body; it was used to treat pain but irritated the stomach lining. When Felix Hofmann added a single acetate group to salicylic acid he created acetylsalicylic acid, which reduced stomach irritation but was still effective against pain. Today aspirin is still used for pain, fever and inflammation but is also used to prevent heart disease and may reduce the frequency of some cancers. Over 11,ooo tons of aspirin are made in the US each year. (Lewis et al., 2003)

This suite of lab exercises focuses on aspirin but involves a few other analgesics and related drugs as well. These exercises teach the basic techniques of organic chemistry, including: isolation; recrystallization; melting point determination; testing identity by simple chemical reactions; determination of solubility; thin-layer chromatography; and chemical synthesis.

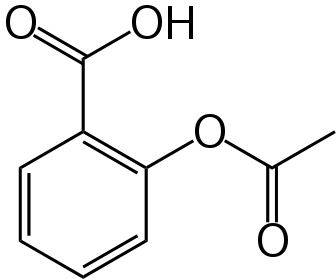
**A note about safety:**

The chemicals used in this suite of labs pose significantly higher health and safety hazards than the chemicals used in CHE 1031. A library of SDS sheets for all chemicals used here is posted at Richmond-hall.weebly.com/library-of-labs.html. Please read the relevant SDS before coming to lab.

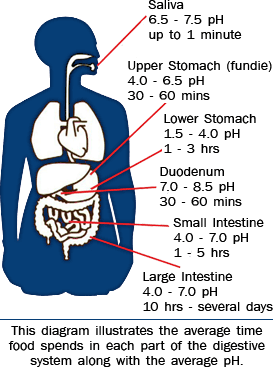
# Part A: Solubility of aspirin determines route of uptake & efficacy

Aspirin is a common anti-inflammatory analgesic (pain killer) used to treat pain and fever. Aspirin’s active ingredient is acetylsalicylic acid, is a derivative of a natural compound that belongs to a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). Other NSAIDs are ibuprofen (Motrin) and naproxen (Aleve).

Most aspirin is taken orally as a tablet, although topical applications (‘Apercreme’) are also used. The rapid action and effectiveness of oral medications like aspirin depend on the ability of the compound to enter our bloodstream. The more **soluble** a compound is, the more rapidly it passes from our digestive system to our bloodstream.

****How soluble is aspirin? At room temperature, acetylsalicylic acid is slightly soluble in water, 3 mg per mL of water. The structure of acetylsalicylic acid clearly demonstrates the acidic nature of the molecule; the hydroxide group can donate a hydrogen atom, acting as an acid.

*acetylsalicylic acid*

**Once aspirin is swallowed it enters the acidic stomach where it is still only slightly soluble and therefore not well absorbed. However, once it reaches the duodenum (aka first section of small intestine) the pH rises to just above neutral and the aspirin releases its acidic hydrogen atom and becomes a negatively charged conjugate base, the acetylsalicylate anion. The anion is very soluble, so aspirin is well absorbed in the duodenum when it becomes a charged and soluble molecule.

In the first of these aspirin lab exercises you will investigate the solubility of aspirin in acidic, neutral and basic aqueous solutions.

Chemicals: Equilibrium:

aspirin tablet mortar & pestle

distilled water Erlenmeyer flasks

sodium hydroxide, 0.0200 M transfer pipette, pipettes & roller

phenol red indicator solution burets and stand

ethanol, ethyl acetate, dichlormethane, funnel and filter paper

isopropanol, methanol, other solvents electronic balance & weigh paper

**Protocol for testing aspirin’s solubility:**

1. Set up shallow hot-water and ice-water baths in beakers. Use a heating stir plate for the former.
2. Crush aspirin tablets with the mortar and pestle.
3. Label twice as many test tubes as you have solvents, including water.
4. Weigh out 0.2 g of aspirin powder and transfer to each of the test tubes.
5. Place one set of tubes in the hot-water bath and the other set in the ice-water bath.
6. Use pipettes to add 2 mL of each solvent to the appropriate test tubes. You should have duplicates of each solvent: one heated and one on ice.
7. Vortex, or finger vortex, the tubes and let them sit at their respective temperatures for 5 minutes.
8. Record your observations using a scale of o to 5 for no change, least and most soluble.
9. Dispose of the contents of the tubes in the waste container provided and wash the tubes with warm water and lab detergent.

**Aspirin titration protocol:**

1. Crush aspirin tablets with the mortar and pestle.
2. Weigh out 0.5 g of aspirin powder and record the mass exactly.
3. Transfer the powder to an Erlenmeyer flask.
4. Using a buret, add exactly 50.0 mL of distilled water to the flask, recoding both Vi (volume initial) and Vf (volume final) on the buret.
5. Swirl for five minutes.
6. Filter into a clean and dry Erlenmeyer flask.
7. Use a 10-mL pipette to transfer 1o-mL of the filtrate to each of three Erlenmeyer flasks.
8. Add four drops of phenol red to each flask.
9. Titrate with 0.200 M NaOH to a very faint peach or terra-cotta color, recording both Vi and Vf on the buret.

**Titration calculations:**

1. Create a balanced chemical equation for the reaction of acetylsalicylic acid and sodium hydroxide.
2. Calculate the moles of NaOH used in the titration using volume and molarity.
3. Calculate the moles of acetylsalicylic acid in 10-mL of filtrate using stoichiometry.
4. Calculate the mass of acetylsalicylic acid in this 10-mL volume of filtrate.

# Part B: Isolation of acetylsalicylic acid (aka aspirin) from tablets

The aspirin tablets you buy at the pharmacy contain aspirin, aka acetylsalicylic acid, and a variety of other ingredients. For example, Bayer aspirin is about 90% acetylsalicylic acid, but also contains carnuba wax, cornstarch, hypromellose, powdered cellulose, and triacetin. The tablet’s acetylsalicylic acid can be purified from the other ingredients using differential solubility and recrystallization. Acetylsalicylic acid is more soluble in ethanol than the tablet’s other ingredients. However, acetylsalicylic acid doesn’t crystalize well when dissolved in ethanol, so recrystallization will use water.

Chemicals: Equipment:

aspirin tablets heating stir plate

absolute ethanol beakers & Erlenmeyer flasks

distilled water mortar & pestle

ice vacuum flask & rubber stopper

Büchner funnels with filter paper

watchglass

scoopula or spatula

**Procedure:**

1. Create a warm water bath by heating a large, half-full beaker of water on a heating stir plate.
2. Weigh ten aspirin tablets and record the mass exactly.
3. Crush the tablets into a fine powder in a mortar and pestle.
4. Transfer the powder to a 250-mL Erlenmeyer flask.
5. Use a graduated cylinder to collect 10 mL of absolute ethanol, pour it into the mortar and pestle, swirl to collect any remaining powder and pour the ethanol into the flask. Repeat the ethanol wash with another 10 mL.
6. Gently rest the Erlenmeyer flask of aspirin and ethanol in the warm water bath to increase the solubility of the acetylsalicylic acid. All of the acetylsalicylic acid should dissolve within five minutes, while the other ingredients will not.
7. Set up a Büchner funnel with filter paper in a filtration flask and connect the flask to a vacuum. Turn the vacuum on.
8. Remove the flask from the warm-water bath, swirl and pour its contents into the Büchner funnel. The filtrate will be acetylsalicylic acid in ethanol, while the other ingredients should remain in the funnel.
9. Remove the ethanol by evaporation under low pressure. Remove the Büchner funnel from the flask and replace it with a rubber stopper.
10. Place the stoppered flask in the warm-water bath.
11. Turn the vacuum on and gently rotate or swirl the flask in the hot water bath.
12. Once all of the ethanol has evaporated, break the vacuum by loosening the stopper, and remove the flask from the vacuum system.
13. Add 100 mL of distilled water to the flask and place it back in the warm-water bath for five minutes. The warmer the water the faster the acetylsalicylic acid dissolves, and a temperature close to boiling works well.
14. If some of the acetylsalicylic acid remains undissolved, add another 10 mL of water.
15. Once all of the acetylsalicylic acid has dissolved, decant it into a clean 250-mL beaker. A filmy substance on the surface of the water is fine.
16. Once the acetylsalicylic acid and water solution has cooled to room temperature, place it in an ice bath for five minutes.
17. Meanwhile, set up another Büchner funnel and filter on the filtration apparatus.
18. Decant the cold, settled acetylsalicylic acid/water mixture into the Büchner funnel, reserving the solids for last.
19. Add 5 ml of cold, deionized water to the beaker, swirl to collect remaining acetylsalicylic acid crystals and add to the Büchner funnel.
20. Repeat the cold-water wash three times.
21. Leave the flask and funnel on filtration to dry the crystals as much as possible, then break the vacuum and remove the funnel.
22. Using a scoopula, carefully transfer the crystals to a dry and weighed watchglass, cover with a Kimwipe and set aside to dry overnight.
23. Weigh the crystals and watchglass and record the mass exactly.
24. Transfer the crystals to a small bottle or test tube, label it and reserve the crystals for an upcoming lab exercise.

**Calculate** the percent yield of your isolation and compare it with the expected mass of acetylsalicylic acid in the tablets.

# Part C: Testing purity of isolated acetylsalicylic acid using melting point

A simple, traditional and low-tech method of testing the purity of compounds is determination of melting point (mp), the temperature at which the compound melts from a solid to a liquid physical state. Pure compounds have sharp or sudden melting points, while impure compounds or mixtures of compounds have broad or wide melting points. Why? A pure compound is a pile of identical molecules. In a solid physical state these identical shapes pack together tightly, allowing them to have large areas of intermolecular contact and thus high intermolecular bonding energy. On the other hand, mixtures may contain a wide variety of molecules. These widely different shapes and sizes do not pack tightly together in a solid physical state; instead, there are gaps between neighboring non-identical molecules. This lowers intermolecular contact and thus intermolecular bonding energies; it’s easier to pull these different molecules apart, or to melt their solid phase. The melting point of acetylsalicylic acid is 138 - 140°C, while the melting point of salicylic acid is 158 - 160°C.

Chemicals: Equipment:

acetylsalicylic acid Mel-temp device

salicylic acid melting point tubes

crushed aspirin powder *[or glass capillary tubes]*

experimentally purified acetylsalicylic acid oven set at 50°C

ethanol

ethyl acetate

**Melting point determination protocol:**

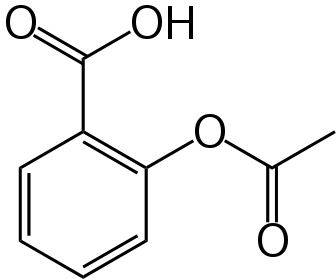
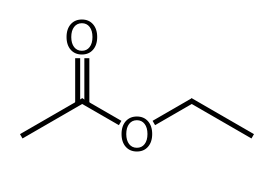
1. Place samples in a low-temperature (50°C) oven overnight so that they are dry for testing.
2. If melting point tubes are not available, heat one end of a capillary tube in a Bunsen burner until the glass fuses to create a sealed end. Be sure the tube does not bend and allow the sealed tube to cool.
3. Tap the open end of the melting point tube into the powdered sample a few times, until there is about 0.5 cm of powder in the tube. (Note that a dab of sharpie color can be used to ‘label’ melting point tubes.)
4. Turn the tube open side up and tap on the bench until the powder settles and packs into the bottom of the tube.
5. Turn on the Mel-temp device and set the temperature control dial to zero. Record the initial temperature.
6. Place the melting point tube into the Mel-temp device and slowly increase the temperature. Slowly increasing temperature is essential to successful determination of mp. Ideally, temperature should increase no more than 2 degrees per minute. You may want to conduct a few trial runs to find a setting with the proper heating rate.
7. Keep careful watch through the eyepiece and record the temperatures at which the sample slumps and the temperature at which it clearly becomes a liquid. Slumping looks like blocks of ice beginning to soften and move a bit.
8. Dispose of tubes in the sharps container.

# Part D: Testing purity & composition using thin-layer chromatography

Chromatography is a technique that uses the relative solubilities of molecules to separate them from a mixture. In many forms of chromatography, samples are spotted onto on end of a support or matrix (often paper or silica supported by glass of sheets of plastic) and the solvent moves up through the samples by capillary action. Molecules that are the most soluble in that solvent move the furthest as the solvent travels up through the matrix; less soluble molecules remain closer to the origin (aka the starting point). The position of molecules is then visualized so that their migrations can be compared.



This lab uses ethyl acetate (aka ethyl ethanoate) as a chromatography solvent. Acetylsalicyclic acid, an organic molecule of moderate polarity, is soluble in this molecule of similar polarity.

** **

*acetylsalicylic acid ethyl acetate*

Once chromatography is complete, the location of molecules must be visualized. Because of their aromatic conjugated ring structures, many of the active molecules in analgesic tablets absorb ultraviolet (uv) light and appear as dark spots. And iodine vapor binds to molecules with aromatic structures or multiple bonds, creating yellow spots. Relative migration is calculate as:

**Rf = distance of sample migration / distance to solvent front.**

Chemicals: Equipment:

acetylsalicylic acid chromatography tanks (glass jars w/ lids)

salicylic acid silica TLC plates

caffeine ruler & pencil

powdered analgesic tablets capillary tubes

soluble sodium or calcium salicylate test tubes

Ethanol pipettes & roller

Ethyl acetate scoopula or spatula

Dichloromethane uv light

Iodine crystals

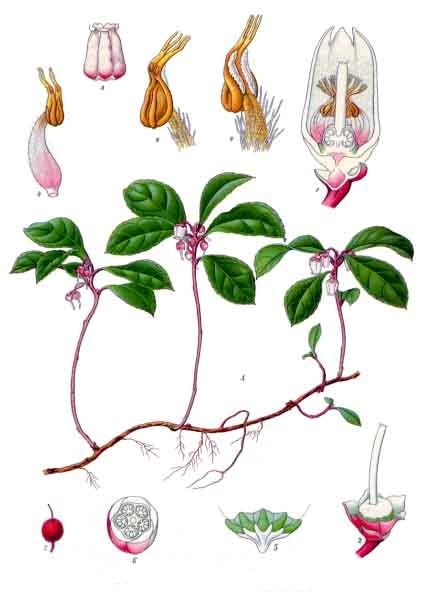
**TLC protocol:**

When handling the TLC plate, be sure not to touch the silica surface with bare hands; your hands will spot human samples everywhere they touch! Instead, pick up the plate by the edges or with tweezers / forceps. Wear gloves for each step of this protocol.

1. Begin by setting up your TLC tank or jar in a chemical fume hood. Place a large piece of filter paper, the height of the tank, upright in the tank. This filter paper will wick up solvent and saturate the tank with solvent vapor.
2. Pour in enough ethyl acetate to create a layer no more than ½ cm deep and close the tank. If using a jar, you may want to place a piece of cling wrap over the jar before screwing on the lid. The tank needs to equilibrate to saturate the atmosphere with solvent.
3. Meanwhile, label one test tube for each of your samples.
4. Working in the fume hood, make up solvent for dissolving your samples by mixing equal volumes of ethanol and dichloromethane in a test tube labeled ‘sample solvent’.
5. Using the tip of a scoopula or spatula, place a small amount of powdered sample in each test tube.
6. In the hood, add 1 mL of sample solvent to each of your powdered samples. Let the samples sit for a moment to allow the samples to dissolve.
7. Meanwhile, use the pencil and ruler to draw a light pencil line 1 cm from the bottom of the plate. This line is called the origin.
8. Use a capillary tube to spot your samples at the origin. Keep your samples spots small and tight by allowing the spot to dry between multiple applications of sample. Keep track of how many times you spot the plate for each sample.
9. Cover your sample tubes with cling wrap or clean marbles while waiting a few moments to let your samples dry on the plate.
10. Carefully transfer the plate to the TLC tank and close the lid.
11. Watch carefully and remove the TLC plate from the tank once the solvent front is within a cm or two of the top of the plate. Mark the solvent front with pencil across the width of the plate.
12. Allow the TLC plate to dry.
13. Meanwhile, set up an iodine visualization tank in a chemical fume hood. Place a scattering or thin layer of iodine crystals in the bottom of the tank and cover the tank tightly. A purple iodine vapor will slowly fill the tank. Avoid this vapor!
14. Take the dry plate into a dark room and illuminate it with a uv light. Use a pencil to circle all spots visible with uv.
15. Transfer the TLC plate to the iodine tank and cover the tank. Watch for the formation of yellow stains. Remove the plate when until spots are clearly visible but the background is still clear. Leave the TLC plate in the hood to allow excess iodine to evaporate.
16. Take a photo of your stained TLC plate and then measure:
17. the distance from the origin to the solvent front; and
18. measure the distance from the origin to each spot, noting whether the spot was visualized with uv light, iodine vapor or both.

**Calculate:** Rf values for each spot of each sample, both knowns and unknowns or mixtures.

# Part E: Synthesis of salicylic acid from oil of wintergreen

American wintergreen or eastern teabury (*Gaultheria procumbens)* is a small evergreen plant rich in an aromatic compound, methyl salicylate, used as a fragrance, flavor, analgesic and rubefacient (a substance that increases circulation and produces redness when applied topically). In plants, methyl salicylate discourages herbivores, recruits beneficial insects and may be used to warn other plants about plant viruses.

Navite Americans used a tea made from wintergreen to treat pain, inflammation and sometimes kidney disease. Today, methyl salicylate is used in liniments, like Bengay, to treat musculoskeletal pain. When applied topically, it appears to act as a counterirritant. Once in the body, methyl salicylate converted into other salicylates, including the NSAID salicylic acid.

In this lab, wintergreen oil is modified to create salicylic acid (aka 2-hydroxybenzoic acid). Wintergreen oil is 98% methyl 2-hydroxybenzoate. You will perform two chemical reactions to convert the methyl 2-hydroxybenzoate to 2-hydroxybenzoic acid.



In the first reaction, sodium hydroxide is added resulting in a substitution reaction that removes a methyl group to create sodium 2-hydroxybenzoate and methanol. In the second reaction, hydrochloric acid is added to create a neutralization reaction producing salicylic acid and sodium chloride. Chemicals: Equipment:

oil of wintergreen (1.17 g/mL) heating stir plate or mantle

2 M NaOH beakers

concentrated HCl reaction flask with a condenser

ice boiling chips

Büchner funnel & filter paper

watchglass

electronic balance

pipettes & roller

ring stand & clamp

pH paper

**Protocol:**

1. Fill a large beaker half full of water, place on the heating stir plate and heat to create a boiling water bath.
2. Set the ring stand and clamp up behind the heating stir plate.
3. Use a pipette to transfer 2 g of wintergreen oil to a reaction flask.
4. Use a graduated cylinder to collect 25 mL of 2 M NaOH and add that to the reaction flask.
5. Add a few boiling chips.
6. Connect the condenser to the top of the flask and clamp the glassware together.
7. Attach the flask & condenser to the ring stand by fixing the ring stand clamp to the condenser.
8. Carefully lower the reaction flask into the hot water bath and be sure it is held there securely.
9. Heat the reaction over the boiling water bath for 3o minutes.
10. Remove the reaction flask & condenser from the water bath and allow it to cool.
11. Pour the cooled mixture into a small beaker and immerse the beaker in an ice-water bath.
12. While stirring, add concentrated HCl to the beaker dropwise until the solution is just acidic. Test pH using pH paper. Crystals should form at an acidic pH and should be fine white of transparent needles.
13. Set up a vacuum filtration device with Büchner funnel & filter paper.
14. Filter the cooled, acidified and crystalized reaction mixture through the Büchner funnel.
15. Wash the crystals with a little ice-cold water.
16. Transfer the crystals to a pre-weighed watch glass and allow them to dry overnight.

**Calculate** the percent yield of the reaction: % yield = 2-hydroxybenzoic acid (g) \* 100

oil of wintergreen (g)

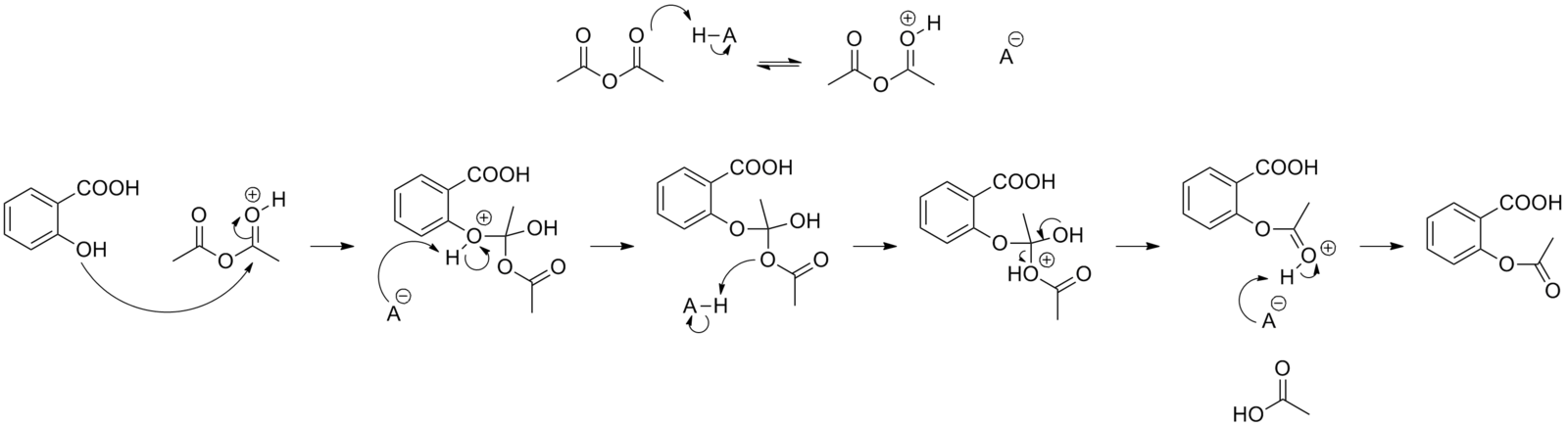
# Part F: Synthesis of acetylsalicylic acid from 2-hdroxybenzoic acid

In this exercise, you will react the salicylic acid (aka 2-hydroxybenzoic acid) created in the last exercise with acetic anhydride to produce acetylsalicylic acid and acetic acid. Because acetic anhydride reacts with water all equipment must be dry to ensure success!



Ideally, this reaction is done with a limiting amount of salicylic acid and excess acetic anhydride so that the product is only contaminated with excess acetic anhydride. How is the contaminating acetic anhydride removed? When the crystals produced by the reaction are washed with cold water, the water reacts with excess acetic anhydride and hydrolyzes (or breaks) it into two molecules of acetic acid. The acetic acid is water-soluble and passes through the filter while acetylsalicylic acid is only slightly soluble in water and remains in the filter.

**Mechanism of synthesis** (from Wikipedia ‘Aspirin’):



*Where: H-A is the phosphoric or sulfuric acid catalyst and acetic acid is a by-product.*

Chemicals: Equipment:

salicylic acid heating stir plate & beaker

acetic anhydride (10.6 M) pear-shaped flask & condenser

concentrated phosphoric acid (14.8 M) beakers

*[or concentrated sulfuric acid]* vacuum flask & set up

ice glass stirring rod

distilled water pipettes & roller

Büchner funnel & filter paper

watch glass

scoopula or spatula

electronic balance & weigh paper

**Aspirin synthesis procedure:**NB: Most of this procedure is done in a chemical fume hood.

1. Set up the heating stir plate in a chemical fume hood and create a hot-water bath.
2. Weigh out 2.o g of 2-hydroxybenzoic acid and record the mass exactly.
3. Transfer the compound to a pear-shaped flask.
4. Working in the hood, use a pipette to collect 2 mL of acetic anhydride and add it to the flask.
5. Still in the hood, add 8 drops of concentrated phosphoric acid.   
   [Note: concentrated sulfuric acid can be substituted for phosphoric acid, though yields will be lower.]
6. Place the condenser on top of the flask and clamp the glassware together.
7. Swirl the flask in the hot-water bath until the solid is dissolved. Heat for another 5 minutes.
8. Use a pipette to carefully add 5 mL of cold water to the flask.
9. Stir vigorously with a glass stir rod and stand the flask in an ice-water bath until precipitation is complete.
10. Isolate the product by filtration through a Büchner funnel and filter paper.
11. Wash with a little ice-cold water.
12. Transfer the wet crystals to a pre-weighed watch glass and dry overnight. Up to 40% of mass may be water.
13. Weigh the dry product in the watch glass.

**Calculate:**

1. Moles of 2-hydroxybenzoic acid
2. Moles of acetic anhydride
3. Limiting reactant
4. Theoretical yield and percent yield of acetylsalicylic acid

* Percent yields of 90% can be obtained.

# Part G: Purifying synthetic acetylsalicylic acid by recrystallization[[1]](#footnote-1)

Synthesized compounds often contain impurities but can be purified by a number of methods. If the solubilities of the target compound and the impurities differ, this physical property can be used to separate them. All of the compounds used in, or formed during, synthesis of acetylsalicylic acid are soluble in ethanol. With the exception of the target molecule, acetylsalicylic acid, most are also soluble in water. So, when water is added to a mixture of these molecules the acetylsalicylic acid will crystalize – come out of solution as a solid – while impurities remain soluble. Filtration can then be used to separate the crystalline acetylsalicylic acid from the soluble impurities. Pure compounds form crystals with regular and characteristic shapes while impure mixtures form irregularly shaped crystals.

Following recrystallization, phenol testing, melting point determination and / or thin-layer chromatography can be used to compare the purity of the crude and recrystallized acetylsalicylic acid.

Chemicals: Equipment:

experimentally synthesized acetylsalicylic acid small Erlenmeyer flask

absolute ethanol heating stir plate

distilled water glass stir rod

ice pipettes & roller

beaker (for ice-water bath)

vacuum filtration setup

Büchner funnel & filter paper

watch glass

**Protocol for recrystalization of acetylsalicylic acid:**

1. Setting aside enough for phenol testing, melting point determination and thin-layer chromatography, weigh the remaining crude experimentally synthesized acetylsalicylic acid, record the mass exactly, and transfer the powder to a small Erlenmeyer flask.
2. Use a pipette to transfer 4 mL of ethanol to the flask.
3. Warm the flask in a h0t-water bath until the solid sample is dissolved.
4. Immediately remove from the heat.
5. Use a pipette to slowly add 13 mL of cold, distilled water.
6. Crystals should begin to form. If they do not, use a glass stir rod to scratch the glass and initiate crystal formation.
7. Rest the flask in an ice-water bath.
8. Once crystal formation seems complete, use a vacuum apparatus, Büchner funnel and filter paper to collect the acetylsalicylic acid crystals. Collect and transfer any stray crystals with ice-cold, distilled water and add them to the funnel.
9. Wash the crystals with 3 mL of ice-cold, distilled water. Repeat.
10. Leave the vacuum on for a few minutes to dry the crystals.
11. Turn off the vacuum and carefully peel up the filter paper and transfer the filter paper and crystals to a pre-weighed watch glass and dry overnight.
12. Weigh the watch glass and acetylsalicylic acid and record the mass exactly.

**Calculate** your percent recovery = mass recovered \* 100

starting mass

# Part H: Testing experimentally synthesized aspirin for purity & integrity

When aspirin (acetylsalicylic acid) is stored for a long time and/or exposed to moisture it tends to degrade. Water hydrolyzes the bond between the acetate group and salicylic acid. The free acetic acid gives old aspirin a distinct vinegar smell. Molecular structures show that salicylic acid has a phenol group (a hydroxide on an aromatic ring) which is absent on acetylsalicylic acid because the hydroxyl component of the phenol has been replaced with an acetate group (O-CO-CH3).

****

The phenol test can be used to determine whether a sample contains phenol groups. Iron (III) ions react with phenolic groups to produce a blue or violet product. In the absence of a phenolic group iron (III) ions will produce a pale yellow color.



Chemicals: Equipment:

salicylic acid test tubes

acetylsalicylic acid pipettes & rollers

experimentally synthesized acetylsalicylic acid mortar & pestle

ibuprofen, naproxen, acetaminophen spatula

Lysol (with phenol) transfer pipette

iron (III) chloride, 1% solution hot-water bath

ethanol

distilled water

**Phenol test protocol:**

1. Use a mortar & pestle to crush a few grams of each sample to be tested.   
   Be sure to thoroughly wash and dry the mortar and pestle with large volumes of water and then distilled water between samples to avoid cross contamination!
2. Label one test tube for each compound to be tested.
3. Add 5 mL of water to each test tube.  
   [Note that a 1:1 mixture of water and ethanol can be used and may be a better solvent for some samples.]
4. Use a spatula to place a small amount of each sample into the appropriately labeled test tube.
5. Vortex the samples to dissolve them.
6. Use a transfer pipette to add 10 drops of 1% iron (III) chloride to each test tube.
7. Vortex and record your observations about color and solubility.
8. Dispose of tested samples in the sink with copious water. Wash your glassware thoroughly with water.

# References:

David Lewis, Colin Osborne, Maria Pack (2003) Aspirin: a curriculum resource for post-16 chemistry and science courses, 2nd edition, Royal Society of Chemisty

http://www.rsc.org/learn-chemistry/content/filerepository/CMP/00/000/045/Aspirin.pdf

Cheli Fossum (2012) Experiment 8 – Synthesis of aspirin, Laney College

http://www.laney.edu/wp/cheli-fossum/files/2012/01/8-Synthesis-of-Aspirin.pdf

UVM’s Chem 32 Lab Manual

Wikipedia is the source of many of the chemical structures shown in this document.

The figure of pH in the human digestive system is borrowed from Allegany Nutrition:

http://www.alleganynutrition.com/index.php?Human%20body%20pic

1. Cheli Fossum (2012) Experiment 8 – Synthesis of aspirin, Laney College [↑](#footnote-ref-1)