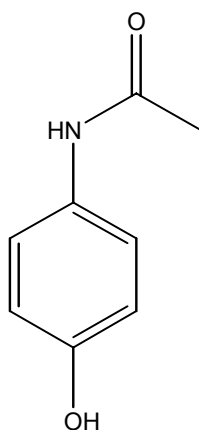


Experiment 11**Separation and Identification of the Major Components of
Common Over-the-Counter Painkilling Drugs****Student Handout****Purposes**

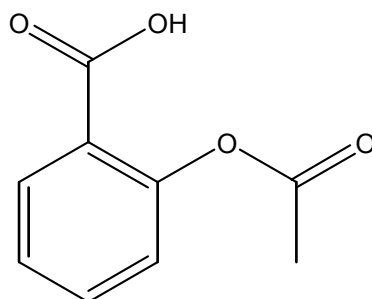
1. To separate the major components of a common over-the-counter painkilling drug.
2. To identify the components.

Background

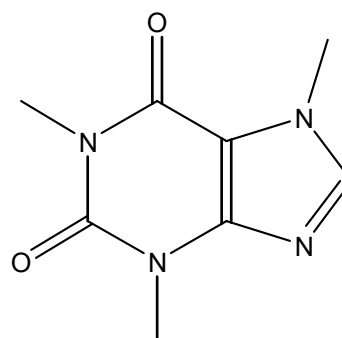
This experiment puts into practice the techniques for separating the components in common painkilling tablets. The common components in painkilling tablets are acetaminophen, aspirin and caffeine, the structures of which are shown below:



Acetaminophen
(*p*-Hydroxyacetanilide)
mp 170 °C



Aspirin
(Acetylsalicylic acid)
mp 135 °C



Caffeine
mp 238 °C

Apart from these components, a binder is usually used to prevent the components from crumbling on storage or while being swallowed. Starch, microcrystalline cellulose and silica gel are the commonly used binders. They are all insoluble in water and common organic solvents.

On the other hand, the solubilities of the three components are different in different solvents. For example, aspirin and caffeine are soluble in dichloromethane while acetaminophen is not. Hence, we can separate acetaminophen (and the binder) from

aspirin and caffeine by dissolving the tablet in dichloromethane followed by filtration. Acetaminophen is found to be soluble in ethanol. Therefore, acetaminophen can be separated from the binder with the same technique.

Inspection of the structures of aspirin and caffeine reveals that they are organic acid and organic base, respectively. The corresponding conjugated base and conjugated acid are soluble in water but not in dichloromethane. Furthermore, water and dichloromethane are immiscible. Therefore, the aspirin and caffeine in the filtrate can be separated by extraction either with acid, which will remove the caffeine as a water-soluble salt, or by extraction with base, which will remove the aspirin as a water-soluble salt. The latter procedure will be used in this experiment.

The products obtained are then identified by melting-point determination and thin-layer chromatography (TLC).

Safety

Handle all chemicals with great care. Avoid direct contact of chemicals with skin. Dispose of chemical waste, broken glassware and excess materials according to your teacher's instruction.

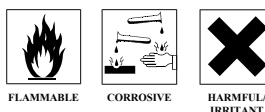
Further information on the chemicals used in the experiment can be found in the Material Safety Data Sheet (MSDS). Consult your teacher for details.



**EYE PROTECTION
MUST BE WORN**

Materials and Apparatus Available

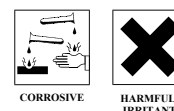
4:1 (v/v) 1-Butyl ethanoate/ethanoic acid



3 M Sodium hydroxide solution



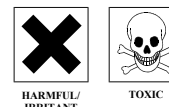
3 M Hydrochloric acid



Iodine



Dichloromethane




Ethanol




Anhydrous MgSO_4


Mortar and pestle	Beakers
Melting-point tubes	TLC plates
Painkilling tablet	pH paper
Test tubes	Conical flasks
TLC Chamber	Separating funnel
Melting-point apparatus	Water condenser (optional)


Experimental Procedure

 Photos of the experiment are available at <http://www.chem.cuhk.edu.hk/ssc.htm>.

- Separation of acetaminophen/binder from aspirin/caffeine*

In a mortar, grind two given tablets to very fine powder. Place this powder in a conical flask. Add about 10 cm³ of dichloromethane. Put the conical flask into a beaker of warm water at about 30 °C briefly. (Caution: the boiling point of dichloromethane is only 40 °C!) Filter the solution. 
- Separation of aspirin and caffeine*

Transfer the filtrate obtained in Part (1) into a separating funnel. Add 8 cm³ of 3 M sodium hydroxide solution and shake the mixture thoroughly. Remove the aqueous layer and extract the organic solution again with 1 cm³ of water. Collect the aqueous layer and combine it with the previously collected aqueous extract. 
- Extraction and isolation of aspirin*


To the aqueous hydroxide extract obtained in Part (2), add 6 - 9 cm³ of 3 M hydrochloric acid drop by drop and test the acidity of the extract with pH paper from time to time until the pH of the extract is ~3. If a suspension is formed, cool the mixture with an ice-bath, filter it and wash the solid with iced water. Then dry the solid completely. Weigh the solid obtained. 
- Extraction and isolation of acetaminophen (optional)*

Transfer the solid residue obtained in Part (1) to a conical flask, add 8 cm³ of ethanol and boil the mixture for 1 - 2 minutes. Filter the mixture. Transfer the filtrate to a beaker and evaporate the solvent from the filtrate completely in a hot water bath. Weigh the solid obtained.
- Extraction and isolation of caffeine (optional)*

Add ~0.5 g of anhydrous MgSO₄ powder into the dichloromethane extract obtained in Part (2) until the drying agent no longer clumps together. Swirl the mixture for ~30 seconds to complete the drying process and filter the mixture. Remove the solvent from the solution completely by simple distillation. Weigh the solid obtained.
- Melting-point determination*

Determine the melting-points of the separated components.

7. *Thin-layer chromatography*

Dissolve the standards and the separated components in methanol in separate test tubes. (Use ~0.05 g of sample and 3 cm³ of methanol for each sample.) Run TLC using the given 1-butyl ethanoate/ethanoic acid mixture as the mobile phase. After the TLC plates has been developed, allow the mobile phase to evaporate and put the TLC plates into an iodine chamber (a TLC chamber with iodine solid inside). 

Questions for Further Thought

1. How can you determine whether a sample is pure or not from melting-point determination?
 2. Although acetaminophen does not contain a carboxylic acid group, it is slightly acidic. Briefly explain why.
 3. Write a chemical equation to show how aspirin can be prepared from salicylic acid.
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Reference

J. C. Gilbert and S. F. Martin, *Experimental Organic Chemistry*, 2nd Ed., Saunders College Publishing, New York, 1998, pp. 135 - 153, 633 - 635.
