Investigations Folio: Regulation of common analgesics

Background Information

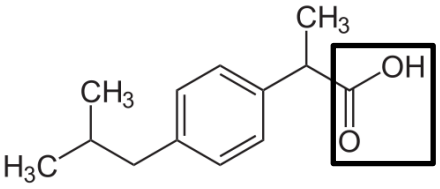
At the turn of the 20th century the discovery and testing of medicines was a largely unregulated process. Many new compounds were given to patients almost immediately after synthesis or discovery. In contrast, the development of modern pharmaceuticals is a long and expensive process typically taking over a decade. Chemistry is used at all stages to develop the synthesis of the pharmaceutical and determine its purity.

Before being administered to potential patients, chemists need to know how the pharmaceutical works, how safe it is, and what dosage is required. How the pharmaceutical works is initially investigated using an isolated enzyme or cellular systems (cell cultures) before being trialled in animal models and ultimately in volunteer patients. Clinical trials are used in the later stages to see if a new pharmaceutical works in one set of patients compared to the effects of a placebo on another group.

Ibuprofen, Aspirin and Paracetamol are commonly available, regulated analgesics.

Ibuprofen

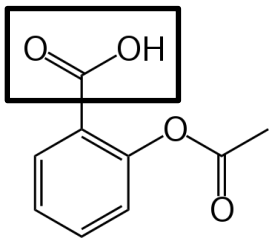
- Ibuprofen is a pharmaceutical of the nonsteroidal anti-inflammatory (NSAID) class, that is used primarily as a medication in the treatment of pain, inflammation, and fever.



- Ibuprofen contains a carboxylic acid functional group that, as a weak acid, is able to neutralise bases such as metal hydroxides.
- The solubility of Ibuprofen in water, can be increased through the addition of propane-1,2,3-triol (glycerol) and by heating the solution to a moderate temperature.
- In Australia Ibuprofen is also administered as Ibuprofen lysine (the lysine salt of Ibuprofen) which offers greater solubility in the aqueous environment encountered in the human body.
- Manufacturers of pharmaceuticals are required to disclose the quantity of Ibuprofen contained in each tablet. In Australia dosage, typically conforms to 200 mg of Ibuprofen per tablet.

Aspirin

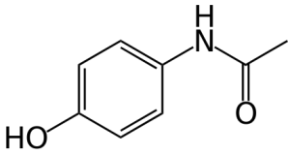
- Aspirin, also known as acetylsalicylic acid (ASA), is a medication used to treat pain, fever, and inflammation.



- Aspirin contains a carboxylic acid functional group that, as a weak acid, is able to neutralise bases such as metal hydroxides.
- Aspirin is also a nonsteroidal anti-inflammatory drug (NSAID) and works in similar ways to Ibuprofen but also suppresses the normal functioning of platelets in the blood.
- In Australia aspirin is typically administered as tablets that are ingested or in combination with a carbonate base to form a solution of carboxylate ions prior to consumption. Greater solubility is offered as a carboxylate salt.
- Manufacturers of pharmaceuticals are required to disclose the quantity of Aspirin contained in each tablet. In Australia dosage, typically conforms to 300 or 500 mg of Aspirin per tablet.

Paracetamol

- Paracetamol, also known as acetaminophen (APAP), is a medication commonly used to treat pain and fever.



- It is classified as an analgesic and is typically used for mild to moderate pain. It is often delivered orally but is also available intravenously.
- Manufacturers of pharmaceuticals are required to disclose the quantity of Paracetamol contained in each tablet. In Australia dosage, typically conforms to 500 mg of Paracetamol per tablet.

- The regulatory body for pharmaceuticals in Australia is the Australian Government, Department of Health, Therapeutic Goods Administration. More information can be found at: https://www.tga.gov.au/

Assessment Conditions

- You will have one 110-minute tutorial session to explore the background chemistry for the investigation and to deconstruct the problem.
- You will have one 110-minute tutorial to trial and develop a procedure based on one of the general procedures that has been supplied or a procedure that has been developed and confirmed by your teacher (note: one procedure may be selected for the entire group to pursue).
- You will have one homework session to finalise the procedure, undertake a risk assessment during the ordering of equipment, and respond to safety requirements for the procedure, apparatus and reagents.
- You will have one 110-minute tutorial to undertake the final developed procedure for the investigation.
- You will be required to use the spaces provided to record annotated evidence of your understanding – **verified during each stage of the investigation under direct supervision.**
- You will then be required to elaborate upon this evidence in the construction of a final formal report. **No new evidence may be introduced.** You will be given an additional week to complete the final report.
- You will work collaboratively during the investigation, but each student must demonstrate evidence of **original thought** in the deconstruction phase and in the construction and submission of an **individual report**.
  *(Word limit for the investigation is **1500** excluding, apparatus and reagents, procedure, safety and results)*

Report Requirements

- Introduction with relevant chemistry concepts, and either a hypothesis and variables, or an investigable question
- Reagents and apparatus
- Identification and management of safety
- Procedure that outlines trials and steps taken
- Results
- Analysis of results, identifying trends, and linking results to concepts
- Evaluation of procedures and data, and identifying sources of uncertainty (errors)
- Conclusion, with justification.

Introduction – Background Chemistry

Key requirements

Communicating knowledge and understanding of concepts

- Construct an *introduction* to the investigation, which explains the chemical and physical properties of the analgesic/s you intend to investigate.

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Investigation

Key requirements

Deconstructing the parts of a problem to determine the most appropriate method for investigation

Formulating investigable questions and hypotheses identifying variables

How do we know what is in the over-the-counter medicines we take?

Investigate the regulation and dosage of common analgesics; Ibuprofen, Aspirin and Paracetamol.

Your investigation could consider:

- the confirmation of synthesis of the active ingredient;
- the mode of delivery in the human body;
- the chemical composition of the medicine;
- or the purity or quantity of active ingredient present in the medicine.

Hypothesis or Investigable Question

- Develop and outline a *hypothesis* or *investigable question* for the investigation.

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- If a *hypothesis* has been developed, identify the *independent* and *dependent* variables in the investigation and describe how they will be altered measured where necessary. Outline the *factors* that will be *held constant*, outline how they will be held constant and why they need to be kept constant.

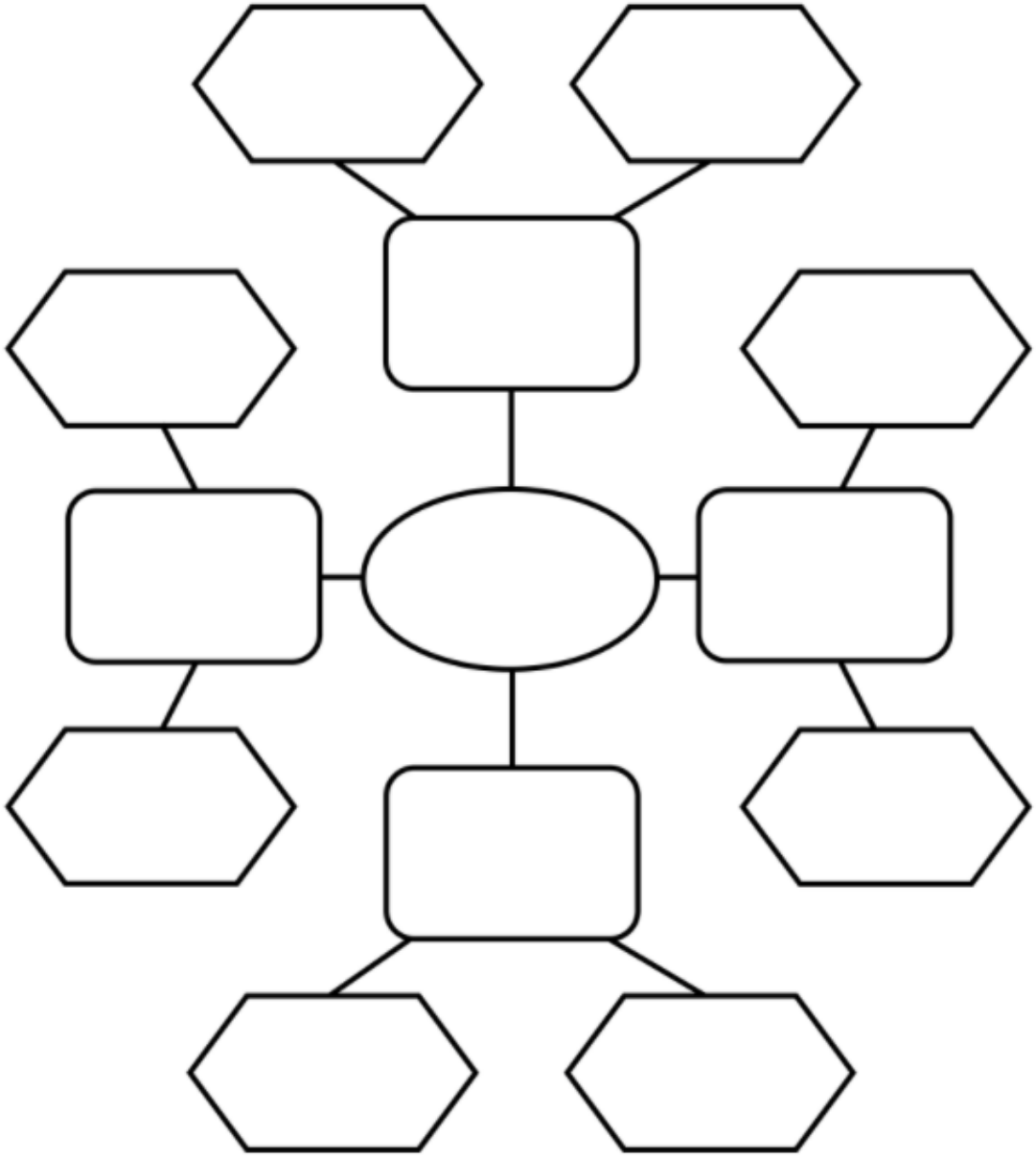
Variable	**How it will be altered or measured**
Independent variable	
Dependent variable	

Factors held constant (controlled variables)	**How it will be controlled**	**Why it is controlled**

Variables that cannot be controlled (Extraneous variables)	

[IAE1]

- If an *investigable question* has been pursued, outline the sub-questions and processes that you may investigate.



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General Procedure ❶ Analysis of Ibuprofen through titration

Apparatus & Reagents

Burette	Beakers	Glass stirring rod
Burette stand	Measuring cylinders	Propane-1,2,3-triol (glycerol)
Wash bottle	Funnel	Tablets (Ibuprofen of differing brands)
Conical flasks	White tile	Phenolphthalein indicator
Heater stirrer	Distilled water	0.100 $molL^{-1}$ NaOH (standardised)
Thermometer		

Safety Notes

Sodium hydroxide may cause irritation to the skin and eyes.

*Wear a **lab coat** and **safety glasses** during this practical. Refer to MSDS supplied for each reagent.*

General Procedure

Neutralising the glycerol

- Rinse and prepare the burette.
- Fill the burette with sodium hydroxide solution.
- Introduce 25 mL of glycerol and 25 mL of warm water (approximately 60°C) to a conical flask.
- Add 2-3 drops of phenolphthalein indicator to the conical flask.
- Introduce the sodium hydroxide dropwise with stirring until the first permanent pink colour appears.

Performing the titration

- Place one tablet into the pink neutralised solution in the conical flask.
- Incorporate the tablet with a glass stirring rod or thermometer (some insoluble components may remain).
- Add an additional 2-3 drops of phenolphthalein indicator to the conical flask.
- Titrate the contents of the flask with the sodium hydroxide from the burette until the first permanent faint pink colour appears. Record the titre and repeat for two further titrations.
- Calculate the mass of ibuprofen present in each tablet.
- Collate results from the other groups present for further analysis.

General Procedure ❷ Analysis of Aspirin through titration

Apparatus & Reagents

Burette	Beakers	Glass stirring rod
Burette stand	Measuring cylinders	Ethanol (50%)
Wash bottle	Funnel	Tablets (Aspirin of differing brands)
Conical flasks	White tile	Phenolphthalein indicator
(Magnetic stirrer)	Distilled water	0.100 $molL^{-1}$ NaOH (standardised)

Safety Notes

Sodium hydroxide may cause irritation to the skin and eyes.

*Wear a **lab coat** and **safety glasses** during this practical. Refer to MSDS supplied for each reagent.*

General Procedure

Dissolving the tablet

- Place the aspirin tablet into a conical flask.
- Add 10 mL of ethanol to the flask and submerge the flask in hot water until the tablet starts to disintegrate.
- Break up any remaining clumps of the tablet with a glass stirring rod (some insoluble components may remain). Ensure to rinse any residue into the flask from the stirring rod.
- Add 20 mL of distilled water to the flask.
- Add 2-3 drops of phenolphthalein indicator to the conical flask.

Performing the titration

- Fill the burette with sodium hydroxide solution.
- Titrate the contents of the flask with the sodium hydroxide from the burette until the first permanent faint pink colour appears. Record the titre and repeat for two further titrations.
- Calculate the mass of Aspirin present in each tablet.
- Collate results from the other groups present for further analysis.

General Procedure ❸ Analysis of analgesics using Thin Layer Chromatography

Over-the-counter analgesics typically contain one or more of the following active ingredients: acetaminophen, aspirin, caffeine, or ibuprofen. Thin layer chromatography (TLC) offers a simple method of analysis for these products.

Apparatus & Reagents

TLC plates	Glass pipettes	Bunsen burner
Mortar and pestle	Pipette bulb	Ethanol
Spatula	100 mL Beaker	Ethanoic (acetic) acid
Test tubes	Watch glass	Ethyl (acetate) ethanoate
Stoppers	Glass capillaries	Various medications (analgesic tablets)

Dissolving solvent – ethanoic acid and ethanol (1:20).

Developing solvent – ethyl ethanoate, ethanoic acid, and ethanol (25:1:1).

Pure samples – caffeine, acetyl salicylic acid, acetaminophen, and ibuprofen.

Safety Notes

*Wear a **lab coat** and **safety glasses** during this practical. Refer to MSDS supplied for each reagent.*

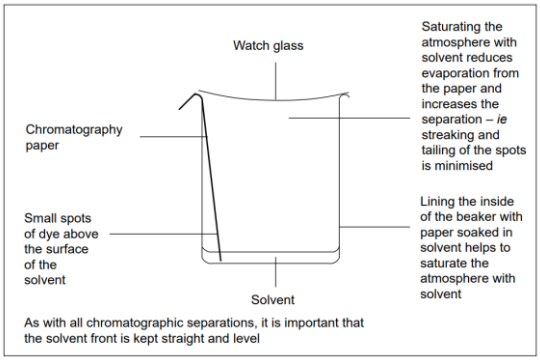
General Procedure

Preparation of the samples

- Push a small wad of cottonwool through the top of a pipette so that it forms a plug at the point where the pipette narrows.
- Crush an analgesic tablet in a mortar and pestle and transfer the tablet to the pipette.
- Fill the pipette with ethanoic (acetic) acid and ethanol (1:20) to dissolve some of the analgesic.
- Force the solution out through the cotton filter into a vial using the pipette bulb.
- Label the vial with the name of the analgesic being tested.
- Repeat the procedure for each of the available tablets.
- Obtain pure samples of the known standards.

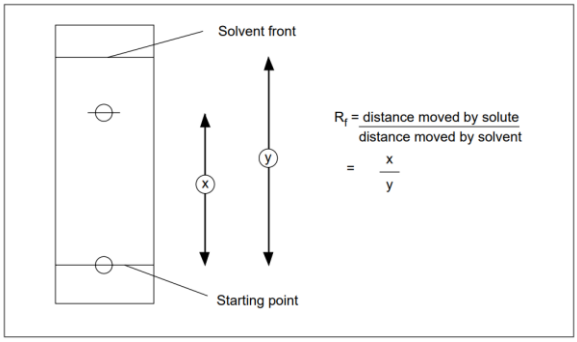
Spotting the samples and standards

- Draw a pencil line 1 cm from the bottom of a TLC plate. Mark, in pencil, the positions and label the samples and standards to be applied to the plate.
- Draw spotters from glass capillaries using a Bunsen burner.
- Immerse the spotter into the sample vial until some of the sample is drawn into the capillary.
- Very gently spot the sample onto the plate at the identified position. Keep the spots small and concentrated by applying the sample at least 3 times and allowing the spot to dry between applications.
- Repeat this procedure for each of the samples and standards available.



Development of the TLC plate

- Prepare a developing chamber by placing the developing solvent (25:1:1 ethyl (acetate) ethanoate, ethanol, and acetic acid) at a level below the origin on the plate in a beaker.
- Place the TLC plates in the chamber and cover the beaker with a watch glass to create a saturated environment. Allow the solvent front to rise to within one cm of the top of the plates.
- Remove the plates, mark the solvent front, and allow them to dry.
- Visualize the spots by illumination under a UV lamp.
- Trace around each spot with a pencil and then measure the distance travelled by each component.
- Calculate the R_f by dividing the distance of the solvent front by the distance of the spot.
- The R_f value is characteristic of each substance and may be used for identification of the substance.



Procedure

Key requirements

Selecting and using appropriate equipment, apparatus, and techniques

- Using the general procedure provided or an investigated procedure, design, construct and describe a final procedure for the investigation, including any necessary reagents and equipment not previously listed.
- Clearly indicate any modifications and improvements that have been made to the original procedure and explain why these changes have been made.
- Complete a Risk Assessment via RiskAssess https://www.riskassess.com.au/ to place an order for any required apparatus and reagents and to evaluate the safety of the design and associated reagents.

[IAE1 , IAE4]

Results

Key requirements
Collecting, representing, *analysing, and interpreting* ***data***

- Construct suitable table/s for the collation of raw and processed data and observations.

[IAE2]

Calculations, Analysis and Discussion

Key requirements

Collecting, representing, ***analysing, and interpreting data***

- Undertake any required calculations.

[AE2]

- Analyse the raw and processed data.

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- Identify sources of *random* and *systematic* error encountered during the investigation, explain their significance, and outline any evidence of the presence of the identified errors in the results obtained.

Key requirements

Evaluating procedures and considering their impact on results

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Evidence for collaboration (Optional)

Teacher's Signature: _____

Skill	Comment	Limited evidence E	Some evidence D	Good evidence C	Strong evidence B	Exemplary evidence A
Contribution to the design and investigation						
Distribution of group roles						
Confirmation of results						
Safety and organisation of the workspace						
Time management						

[IAE1]

- Describe how working collaboratively with your partner during the practical led to greater effectiveness and efficiency. Outline your contribution. Discuss how the collation of results from other groups investigating the tablets, may have increased your understanding of the procedure and confidence in the results obtained.

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Conclusion

Key requirements

Drawing conclusions

- Justify suitable conclusions based on your findings and discuss the limitations of these conclusions.

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	A	B	C	D	E
Investigation, Analysis, and Evaluation	Designs a logical, coherent, and detailed chemistry investigation. Obtains records, and represents data, using appropriate conventions and formats accurately and highly effectively. Systematically analyses and interprets data and evidence to formulate logical conclusions with detailed justification. Critically and logically evaluates procedures and discusses their effect on data.	Designs a well-considered and clear chemistry investigation. Obtains, records, and represents data, using appropriate conventions and formats mostly accurately and effectively. Logically analyses and interprets data and evidence to formulate suitable conclusions with reasonable justification. Logically evaluates procedures and their effect on data.	Designs a considered and generally clear chemistry investigation. Obtains, records, and represents data, using generally appropriate conventions and formats with some errors but generally accurately and effectively. Undertakes some analysis and interpretation of data and evidence to formulate generally appropriate conclusions with some justification. Evaluates procedures and some of their effect on data.	Prepares the outline of a chemistry investigation. Obtains, records, and represents data, using conventions and formats inconsistently, with occasional accuracy and effectiveness. Describes data and undertakes some basic interpretation to formulate a basic conclusion. Attempts to evaluate procedures or suggest an effect on data.	Identifies a simple procedure for a chemistry investigation. Attempts to record and represent some data with limited accuracy or effectiveness. Attempts to describe results and/or interpret data to formulate a basic conclusion. Acknowledges that procedures affect data.
Knowledge and Application	Demonstrates deep and broad knowledge and understanding of a range of chemical concepts. Develops and applies chemical concepts highly effectively in new and familiar contexts. Critically explores and understands in depth the interaction between science and society. Communicates knowledge and understanding of chemistry coherently, with highly effective use of appropriate terms, conventions, and representations.	Demonstrates some depth and breadth of knowledge and understanding of a range of chemical concepts. Develops and applies chemical concepts mostly effectively in new and familiar contexts. Logically explores and understands in some depth the interaction between science and society. Communicates knowledge and understanding of chemistry mostly coherently, with effective use of appropriate terms, conventions, and representations.	Demonstrates knowledge and understanding of a general range of chemical concepts. Develops and applies chemical concepts generally effectively in new or familiar contexts. Explores and understands aspects of the interaction between science and society. Communicates knowledge and understanding of chemistry generally effectively, using some appropriate terms, conventions, and representations.	Demonstrates some basic knowledge and partial understanding of chemical concepts. Develops and applies some chemical concepts in familiar contexts. Partially explores and recognises aspects of the interaction between science and society. Communicates basic chemical information, using some appropriate terms, conventions, and/or representations.	Demonstrates limited recognition and awareness of chemical concepts. Attempts to develop and apply chemical concepts in familiar contexts. Attempts to explore and identify an aspect of the interaction between science and society. Attempts to communicate information about chemistry.