



The pH Effect: How Beverages Impact Ibuprofen and Diphenhydramine Dissolution



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Innovate: IA Project Showcase

Problem Statement: When it comes to drinking a beverage with a medication, there are plenty of options to choose from such as juice, tea, smoothies, and many more. However, there is no designated “worse” or “best” drink for taking medication. The purpose of this study is to determine which beverages one should or should not take when consuming either ibuprofen (Advil) or diphenhydramine (Benadryl).

Abstract

People often take various types of medications, and their beverage of choice is something that comes along with taking the medicine. There are plenty of options to choose from, such as juice, milk, tea, smoothies, protein shakes, soda, and many more. The purpose of this study is to determine which beverages one should or should not take when consuming either ibuprofen (Advil) or diphenhydramine (Benadryl). The significance of this study is associated to its potential to improve medication use safety, specifically when it comes to drug-beverage interactions. By providing insights on beverage choices that can potentially enhance or hinder the effectiveness (or dissolution) of certain medications, specifically ibuprofen and diphenhydramine, this study can help people make informed decisions relating to beverages and medications. To achieve this, a controlled laboratory experiment was conducted. Commonly consumed beverages were tested for their pH levels, and solubility tests were conducted to determine how each beverage impacts the dissolution of both ibuprofen and diphenhydramine. The results revealed that diphenhydramine dissolved most effectively in acidic drinks like Pepsi, while ibuprofen showed higher dissolution rates in neutral or slightly basic drinks like spring and alkaline water. These results align with the chemical properties of the drugs and suggest that beverage pH can influence how quickly and effectively medications begin to absorb.

Background

Over-the-counter medications like ibuprofen and diphenhydramine are consumed often for pain relief and management of allergies, and it is very crucial to understand their interactions with beverages with certain pH levels. Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that is often used to reduce minor aches or pains, while diphenhydramine is an antihistamine drug that helps relieve allergy symptoms, such as sneezing, runny nose, and a cold. Many studies relating to drug-beverage interactions were conducted when it was discovered that citrus juices, such as grapefruit juice and orange juice, can increase the bioavailability or effects of various medications (Bailey et al., 1991). More recent research indicates that Fanta and Pepsi can increase the pH and temperature efficacy of certain medications, which can help to increase their overall effectiveness (Sojinu et al., 2019). Although there is a lot of information regarding how certain beverages can impact the effectiveness of various other types of medications, there is not really a lot of information on the interaction of ibuprofen and diphenhydramine with certain beverages. This study will provide insights into how beverage choices can potentially enhance or hinder the absorption of certain medications, specifically ibuprofen and diphenhydramine. It could potentially help people make informed decisions relating to beverages and medications, which could lead to better health outcomes.

The pKa of ibuprofen varies depending on its type, with an acidic pKa of 4.45 and a general pKa ranging from 4.91 to 5.3. Being an acidic drug, ibuprofen dissolves best in an environment where the pH is higher than the drug's pKa, with research indicating its highest dissolution rates at around the pH 7.2, and significantly lower dissolution at the pH 1.2. In contrast, diphenhydramine, a basic drug with a pKa of 8.98 (or 9.1 for its basic form), dissolves best in more acidic environments where the pH is lower than the drug's pKa. The highest dissolution rates for diphenhydramine occurs at around the pH values of 1 to 4.

Materials

Materials needed for this experimentation include:

- Ibuprofen tablets (200 mg each)
- Diphenhydramine tablets (25 mg each)
- Beakers (1000 mL)
- Magnetic stirrer with temperature control
- Magnetic stir rod
- Thermometer
- Graduated cylinders (600 mL)
- pH meter
- Distilled water
- Dissolution media (various solutions of different pH levels)
- Pipettes (5 mL)
- Stopwatch
- UV-Vis spectrophotometer
- 0.22 μ m syringe filters
- 5 mL tubes

Dissolution medias: Pepsi (regular), Gatorade Fruit Punch, Redbull (regular), Naked Blue Machine, Tropicana Orange Juice, Milos No Calorie Famous Sweet Tea, Evian Water, Waiakea Hawaiian Volcanic Water, Fiji Water, Icelandic Glacial, and Essentia Water

Method and Process Steps

1. Preparation of Dissolution Media:

- Prepare 600 mL of each dissolution medium at different pH levels.
- Measure the pH of each medium using a pH meter.

2. Dissolution Setup:

- Pour 600 mL of one of the prepared dissolution mediums into a beaker.
- Place the beaker on a magnetic stirrer and maintain the temperature at 37°C using a thermometer.

3. Dissolution Test:

- Drop one-two tablets of one of the medications (diphenhydramine or ibuprofen) into the beaker.
- Start the stopwatch immediately.
- At 2, 5, 10, 20, and 30 minutes, withdraw 4 mL of the solution using a pipette.
- Immediately replace the 4 mL withdrawn with 4 mL of the same solution.
- Filter each sample using a 0.22 μ m syringe filter into labeled tubes.

4. Sample Analysis:

- Using a UV-Vis spectrophotometer, dilute each sample 1:10 with the appropriate dissolution medium and measure the absorbance at the aspirin absorption maximum.
- Record and compare the dissolution rates in different pH environments.

5. Data Collection & Analysis:

- Compare dissolution profiles across different pH media.
- Determine if the medication dissolution meets expected trends (e.g., faster dissolution in acidic media).
- Analyze how pH influences diphenhydramine and ibuprofen solubility using the data.

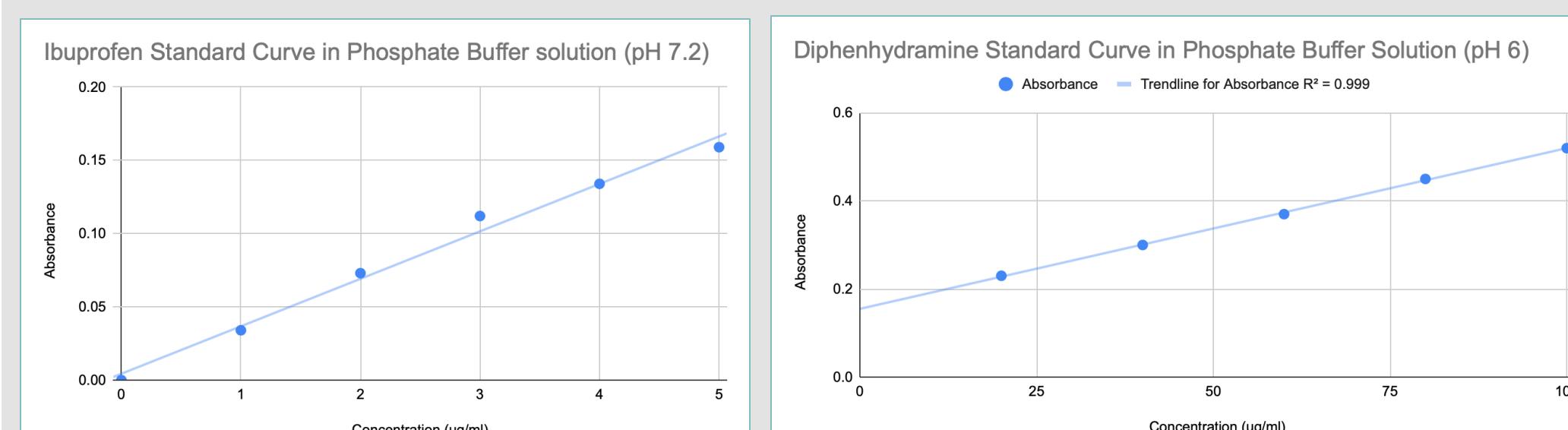


Figure 1 and 2: The two graphs above display the standard curves that were used to measure the concentrations of diphenhydramine and ibuprofen

Research Question: How does the pH level of common beverages affect the absorption of over-the-counter medications, such as ibuprofen and diphenhydramine?

Hypothesis

1. Hypothesis for Diphenhydramine (Benadryl):

The pH level of Pepsi (pH 2.39, independent variable) will significantly affect the dissolution rate of diphenhydramine (dependent variable), leading to a faster dissolution rate due to its highly acidic environment.

- **Criteria for Success:** If diphenhydramine dissolves significantly faster in Pepsi compared to beverages with neutral or alkaline environments, this supports the hypothesis that acidic environments enhance diphenhydramine dissolution (since it is a weak base and it tends to dissolve better in acidic conditions).

2. Hypothesis for Ibuprofen (Advil):

The pH level of Evian water (pH 7.2, independent variable) will significantly affect the dissolution rate of ibuprofen (dependent variable), potentially resulting in a faster dissolution rate due to its near-neutral pH.

- **Criteria for Success:** If ibuprofen dissolves faster in Evian water compared to highly acidic or basic beverages, this supports the hypothesis that beverages with a neutral pH helps to speed up ibuprofen dissolution (since ibuprofen is a weak acid and dissolves better in alkaline environments).

Conclusion

The goal of this experiment was to examine how the pH level of different beverages impacts the dissolution rates of diphenhydramine (Benadryl) and ibuprofen (Advil), based on the hypotheses that the pH of a beverage would significantly affect the dissolution of each drug. For diphenhydramine, the hypothesis suggested that Pepsi, with its highly acidic pH of 2.39, would increase its dissolution due to the acidic environment playing a role in the dissolution of weak bases. The results supported this hypothesis, as diphenhydramine dissolved significantly faster in Pepsi than in beverages with neutral or alkaline pH levels. This suggests that acidic beverages can enhance the dissolution of weak bases, making them potentially more effective when consumed in such environments. However, this also implies that individuals should be cautious of overly acidic drinks, as they might lead to faster absorption, potentially increasing side effects or altering the medication's expected effect. For ibuprofen, the hypothesis predicted that Evian water's near-neutral pH of 7.2 would promote faster dissolution, as ibuprofen is a weak acid that dissolves more efficiently in alkaline conditions. The results confirmed this, with ibuprofen dissolving faster in Evian water compared to acidic or highly basic beverages. This indicates that neutral pH environments, such as those in many types of water bottles, may be the most suitable for enhancing ibuprofen's dissolution. On the other hand, individuals taking ibuprofen should be careful of highly acidic drinks, like citrus juices or sodas, as they may not dissolve ibuprofen as efficiently, and this could potentially delay the onset of the medication's effect. In conclusion, the experiment confirmed both hypotheses and demonstrated how pH can influence the dissolution rate of medications. The findings suggest that when taking diphenhydramine or ibuprofen, individuals should consider avoiding highly acidic beverages, such as soda and citrus juice, to ensure proper dissolution and absorption. Neutral or slightly alkaline beverages, like water, may be the best choice for optimal medication effectiveness, providing a more predictable dissolution rate and minimizing potential variations in absorption.

Results

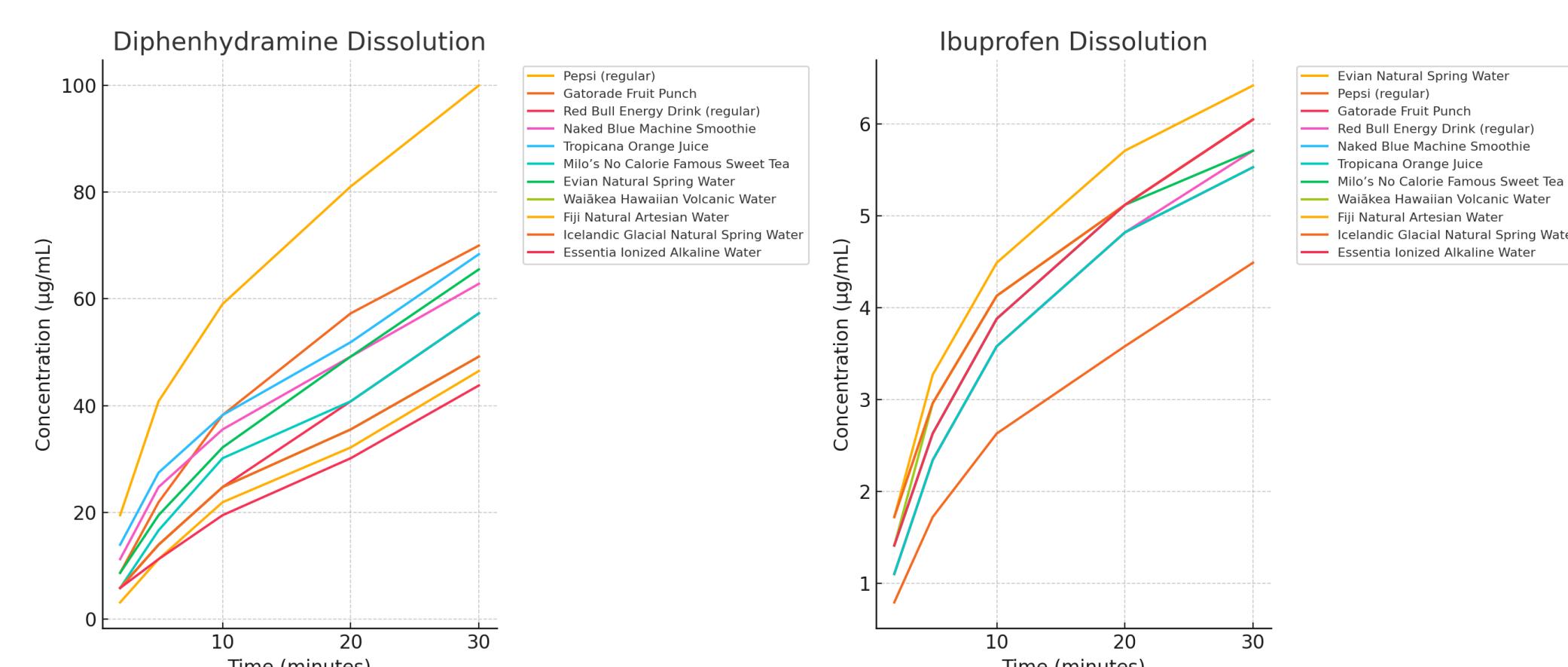


Figure 3: The two graphs above show the dissolution profiles of diphenhydramine and ibuprofen in various beverages over 30 minutes. The left graph shows diphenhydramine concentrations, with Pepsi promoting the fastest and highest dissolution. The right graph shows ibuprofen dissolution, where Evian Natural Spring Water led to the highest concentrations. Beverage composition significantly affects the rate and extent of drug dissolution.

The results of the dissolution experiment support both initial hypotheses regarding the solubility of diphenhydramine and ibuprofen in various beverage environments. Diphenhydramine, a weak base, showed significantly faster and higher dissolution rates in acidic drinks, with Pepsi (pH ~2.39) resulting in the highest concentration across all time points. Other acidic beverages like Gatorade Fruit Punch and Tropicana Orange Juice also facilitated relatively high solubility. In contrast, neutral or alkaline drinks such as Evian, Fiji, and Essentia demonstrated much slower dissolution, indicating that acidic environments enhance the solubility of diphenhydramine. On the other hand, ibuprofen, a weak acid, dissolved most efficiently in Evian Natural Spring Water (pH ~7.2), with other neutral or slightly alkaline waters such as Icelandic Glacial and Waiakea Hawaiian Volcanic Water also promoting faster dissolution. Acidic drinks like Pepsi and Tropicana Orange Juice showed notably lower dissolution for ibuprofen, reinforcing the concept that weak acids dissolve better in neutral or slightly basic conditions. Overall, the data validates the behavior of each drug in relation to pH and highlights how beverage acidity can significantly affect medication solubility.

Next Steps

The next steps for this experiment could include testing a wider variety of beverages to explore how different pH levels impact the dissolution of diphenhydramine and ibuprofen. This could involve adding beverages like tea, milk, or energy drinks, which vary in pH and composition, to see how they influence solubility. Additionally, testing other medications with similar pH-dependent properties could help validate the findings for diphenhydramine and ibuprofen. Another potential direction is developing a digital resource or app for consumers that provides information on which beverages are optimal for dissolving common medications based on pH, helping people make informed choices when taking medications. This could be an invaluable tool for those looking to maximize the effectiveness of their treatments while avoiding drinks that could interfere with dissolution.

Acknowledgements

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