Dissolution Efficacy of Various Advil Pill Forms in Gastric Acid-like Conditions

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Abstract

Pills come in many shapes and sizes, and with various coatings. Some are powder caplets or tablets with thin sugar coatings, while others contain liquid inside a gel (Brookshire, 2017). These alterations may play a role in how quickly a pill is broken down and absorbed into the bloodstream (Brookshire, 2017). Speed is one of the greatest consumer desired benefits for relieving symptoms and many Advil pills claim to have fast and effective pain relief (GSK group, 2017). This experiment examined the dissolving efficacy of four types of Advil pills; Advil tablets, Advil caplets, Advil Liqui-Gels, and Advil Mini-Gels. The time taken to dissolve was examined at pHs 2, 3 and 7 using lemon juice (n=3), orange juice (n=3), and water (n=1), respectively, for each pill type. The acidic pHs were chosen to simulate gastric acid and breakdown in the stomach, while pH 7 served as a control. Our results concluded that Advil Liqui-Gel pills take a significantly longer time to dissolve at all tested pHs in comparison to the three other pill types, which took similar amounts of time.

Introduction

One of the most popular Non-Steroidal Anti-Inflammatory Drugs (NSAID) on the market is Advil. With a large range of pill types and forms they promote quick and easy pain relief. The active ingredient found in all standard Advil pills is ibuprofen (GSK group, 2017). Ibuprofen is an NSAID which provides analgesic and antipyretic relief for people of all ages by blocking COX-1 and COX-2 pain inducing pathways in the body (Timperley Tauh, 2020). Although ibuprofen has helped many, it is also widely known for being a main cause of stomach ulcers prompting strict guidelines on the daily dosage.

Four of the most common Advil pill forms are tablets, caplets, gels and liquid filled. Tablets and caplets both have an outer sucrose sugar coating (Drugs.com, 2000), while Mini-Gels (Drugs.com, 2000) and liquid gels (US National Library of Medicine, 2020) both have an outer gelatin coating with solubilized ibuprofen on the inside. These outer coverings are a determining factor in the dissolution efficacy of the pill form. Constant experimentation on pill forms and coatings is important for both consumers and pharmaceutical companies as every year Americans spend 1.9 billion dollars on analgesics alone, making them the third most bought pain therapy in the United States (Rasu et al. 2014). As it is a competitive market, drugs that can reliably market fast acting relief will be the ones consumers will reach for first, thus benefiting pharmaceutical companies and increasing consumer demand.

This experiment aimed to determine which pill form dissolves the fastest in stomach acid-like conditions. Tablets, caplets, Mini-Gels and liquid-gel Advil pills were dissolved in varying pH. Lemon juice (~ pH 2), orange juice (~ pH 3) and water (~ pH 7) were used and each pill was timed to see how long it took to dissolve in each condition. We hypothesized that in a given acidic medium, if the time it takes the pills to dissolve is dependent on the outer shell coating, then those with similar composition will dissolve in similar times.

Materials & Methods

To simulate an average body temperature, we heated a total of ¾ cups of lemon juice to 100°F (37.7 °C), using a double-boiler method. Double-boiling involves boiling a small amount

of water in a pan over the stovetop, and placing a metal or heat-proof bowl on the pan, and heating the desired liquid via the steam from underneath. Temperature was checked using a thermometer. After heating, ¼ cup of the juice was transferred into 3 clear glass cups using a measuring cup.

One pill of 200 mg Advil was then dropped into each of the three cups, and a stopwatch started immediately. The pills were then observed and data was collected based on how long it took for the pill to break down in the juice. If the pill took longer than 10 minutes to break down, the juice was stirred with a spoon for 15 seconds every 10 minutes until completed. Since 'breakdown' looks different for each pill, the timer was stopped once the pill was no longer a solid structure for the caplets and the tablets. For Mini-Gels, and Liqui-Gels, the timer was stopped once the inside of the pill was released into the solvent.

The methods were then repeated, using Tropicana pulp-free orange juice instead of lemon juice, and one trial of water (per pill-type) was also completed, to act as our control group. All of the above methods were completed using four different kinds of Advil pills; Advil tablets, Advil caplets, Advil Mini-Gels, and Advil Liqui-Gels, all containing 200 mg of ibuprofen were tested. Data was collected in units of minutes. Results were then analyzed with GraphPad Prism software - using a one-way ANOVA test, as well as Tukey Tests, to determine whether there was a statistically significant difference in average break down time between type of pill, and pH of solvent.

Results

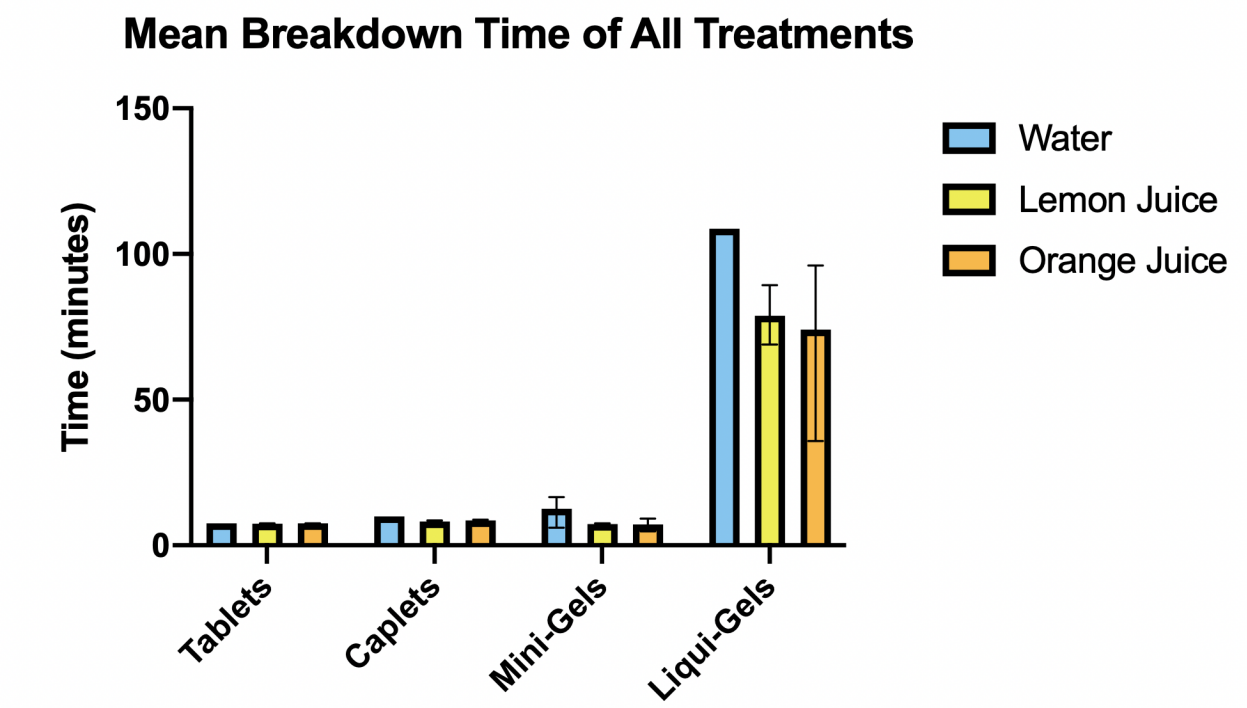

Figure 1: Average time taken for all pills to release ibuprofen interior, in minutes. Vertical bars represent the mean of values collected. Error bars represent the range of values collected. ANOVA test results determined that Liqui-Gel breakdown time was statistically significant compared to all other pill types (ANOVA comparing water treatments $F=81.07$, $p=0.0122$; ANOVA comparing lemon juice treatments $F=145.0$, $p<0.0001$; ANOVA comparing orange juice treatments $F=11.88$, $p=0.0026$). Sample sizes include: lemon juice n=3, orange juice n=3, water n=1 (apart from Mini-Gels where n=3).

Table 1: Tukey Test results that determined a statistically *significant* difference in mean breakdown time

Treatments	**Adjusted p-value**
Tablets+*Water* vs. Liqui-Gels+*Water*	0.0159
Caplets+*Water* vs. Liqui-Gels+*Water*	0.0167
Mini-Gels+*Water* vs. Liqui-Gels+*Water*	0.0119
Tablets+*Lemon* vs. Liqui-Gels+*Lemon*	<0.0001
Caplets+*Lemon* vs. Liqui-Gels+*Lemon*	<0.0001
Mini-Gels+*Lemon* vs. Liqui-Gels+*Lemon*	<0.0001
Tablets+*Orange* vs. Liqui-Gels+*Orange*	0.0053
Caplets+*Orange* vs. Liqui-Gels+*Orange*	0.0058
Mini-Gels+*Orange* vs. Liqui-Gels+*Orange*	0.0051

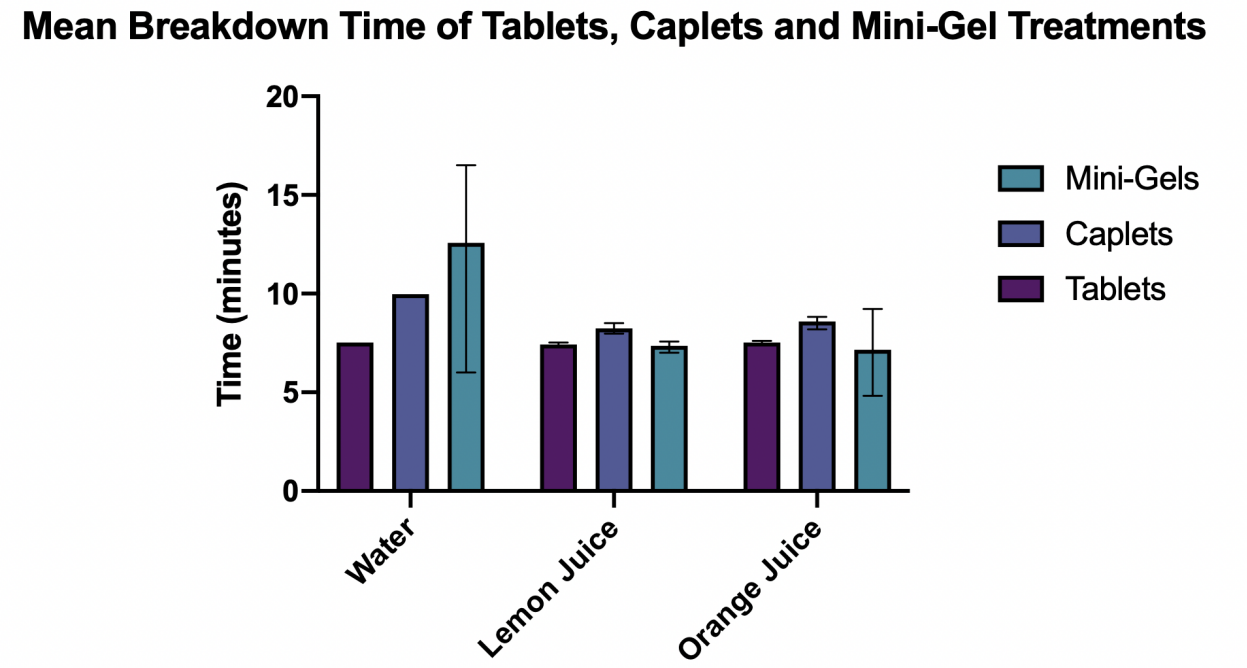

Figure 2: Average time taken for tablets, caplets, and Mini-Gels to release ibuprofen interior, in minutes. Liqui-Gels not included in this figure in order to visualize the results on an appropriate scale. Vertical bars represent the mean of values collected. Error bars represent the range of values collected. Sample sizes include: lemon juice n=3, orange juice n=3, water n=1 apart from Mini-Gels where n=3.

For the different solutions, given the same pill type, the differences in the mean times to dissolve were not revealed to be statistically significant for the tablets, Liqui-Gels, or Mini-Gels (gel capsules). In all three of these cases, there was insufficient evidence (p value > 0.05) to reject the null hypothesis that the different pH solution influenced how fast the pills dissolved. In contrast, for the caplets, the ANOVA did reveal a statistically significant result, as the p-value

(p=0.0204) suggested that there was only a 2.04% change that the difference in the mean dissolution times for the different solutions were due to random chance. Thus, we may conclude that the caplets did dissolve significantly slower in the water treatment (~pH 7) than the more acidic lemon (~pH 2) and orange juice (~pH 3) solutions. This difference is noteworthy, but not of great significance to our analysis as we are primarily focused on determining the differences in the times that the different pills take to dissolve in the same conditions, and not which pH solutions make it dissolve faster. The purpose of implementing different pH treatments was just to simulate a range of acidic conditions somewhat comparable to those of stomach acid, which ranges from 1.5 to 2.5 (Beasley et al., 2015).

Concerning the statistical tests for the different pill types in the same solutions, all three of our solutions yielded similar results. Based on the post-hoc Tukey tests for each of these solutions listed in Table 1, it was revealed that tablets, capsules, and Mini-Gels all dissolved in similar time frames that each differed significantly from that of the liquid-gels - that took considerably longer to dissolve (seen in figure 1). In other words, in all three conditions for tablets, caplets, and Mini-Gels, there was insufficient evidence (p-value >0.05) to reject the null hypothesis that the type of pill influenced the time in which it dissolved. Additionally, there was sufficient evidence (p-value < 0.05) to suggest that the significantly slower dissolution times for the Liqui-Gels compared to the others was not due to random chance.

Discussion

The fact that the tablets and caplets dissolved in similar time frames is consistent with our hypothesis which is based on the similar properties of the outer shells, but this does not explain their respective similarity to the Mini-Gels, nor the distinction between the respective mean times for the Mini-Gels and the Liqui-Gels, which were both identified as having a similar gelatine outer shell.

In order to explain these experimental findings, we turned to the inactive ingredients in each of the different Advil pill types because this is the property that differentiates them. To this end, we determined that it is actually quite difficult to predict which shell coverings are supposed to dissolve faster than the others because although the primary shell ingredients can be identified on the labels, their respective quantities are hardly specified. Ultimately, what we know for sure is only that the gel capsules (present in Liqui-Gels and Mini-Gels) are primarily composed of gelatin and that the tablets and caplets have a thin sugar coating (see introduction). Although the solubility of sugar and gelatin in water can be identified, this comparison would not be representative of the Advil pill shell solubilities because the gel capsules are not entirely composed of gelatin and the sugar coating is not only sugar. However, based on our observations during the dissolution of the pills in the acidic solutions, it was apparent that the sugar layer seemed to be noticeably thinner (paper-like) than that of the gelatin capsules. This could have been a factor that may have contributed to the liquid-gel's significantly longer dissolution time.

To relate this to the respective efficiencies of the pills, despite dissolving considerably slower than the other pill types in our experiment, the literature asserts that Liqui-Gels may in fact be the fastest to be absorbed by the body (Sunrise House, 2019). In short, this is because in this type of pill, the active ingredient (ibuprofen) is already present in liquid form and may be readily absorbed by the body as soon as the capsule is dissolved (Sunrise House, 2019). This is not the case for the tablets and caplets for which the ibuprofen is in solid state. Consequently, the latter must be completely broken down before they can be absorbed, which may take longer (Sunrise House, 2019). The most likely explanation of a longer breakdown time for Liqui-Gels, is its possible reliance on mechanical means of degradation. Our experiment chose to analyze the chemical degradation component, however, in-vivo, mechanical means of breakdown is also a large factor. If this experiment were to be completed again, having a constant form of mixing or disruption would allow the data collected to be of higher quality in-vivo conditions.

There are a couple notable sources of error that may have contributed to some of the inconsistencies in our findings. First, and possibly most significant, is that fact that four different students completed the tests on each of the different pill types. As a result, the data for the different pill types was subject to the methodological error that each student may have differed slightly in their ways of carrying out the experiment and collecting the data (due to differences in equipment and personal judgment), despite using a previously standardized method. Secondly,

throughout the dissolution process, we were not able to keep a constant 100°F temperature. Although each solution may have been heated to 100°F before the insertion of the pills, the rate of cooling of the same solution may have differed considerably based on the ambient conditions where each student carried out their trials. Lastly, to minimize random errors, this experiment could have benefited from a larger sample size, especially for the water control where only one pill for each type was tested. Unfortunately, this issue was due to budgetary restrictions, as some of the pill types are considerably more expensive than the others.

Conclusion

Our results did not support our initial hypothesis that the pills with similar compositions would dissolve at similar times. Advil tablets, Advil caplets, and Advil Mini-Gels all dissolved within a similar time frame and each differed significantly from the longer time taken by Advil Liqui-Gel. Despite both Advil Mini-Gels and Advil Liqui-Gels having a gelatin coating, the difference in dissolving efficacy suggests that other factors, such as the undisclosed quantity of inactive ingredients present, may play a role in the tested conditions. Our findings did not correlate with dissolving efficacy in the body, where liquid gels pills are the fastest.

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Appendix

Table 2: Collected data of breakdown time for each treatment, in minutes. Dashes indicate that there was no data collected in that section.

	Tablets	Caplets	Mini-Gels	Liqui-Gels
Water	7.53	9.97	6.00	108.70
	-	-	15.20	-
	-	-	16.50	-
Lemon Juice	7.33	8.23	7.50	68.97
	7.52	8.51	7.58	78.05
	7.42	7.98	7.70	89.37
Orange Juice	7.42	8.20	7.45	35.83
	7.55	8.75	9.22	90.30
	7.60	8.83	4.82	96.10