Clin Nutr Res. 2024 Apr;13(2):89-95
https://doi.org/10.7762/cnr.2024.13.2.89
pISSN 2287-3732·eISSN 2287-3740

cnr
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Original Article

Effect of Thickened Beverage and Swallowing Aid Jelly Used for Dysphagic Patients on the Disintegration of Orally Administered Tablets

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Received: Feb 16, 2024
Revised: Apr 12, 2024
Accepted: Apr 19, 2024
Published online: Apr 25, 2024

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Conflict of Interest
The authors declare that they have no competing interests.

Author Contributions
Conceptualization: Yoo B, Yoo W; Data curation: Cho W; Formal analysis: Cho W;

ABSTRACT

Thickened beverages or swallowing aid jelly (SAJ), commonly used as tablet-swallowing aids for dysphagic patients, may influence the disintegration of orally administered tablets. With this in mind, we evaluated the disintegration times of therapeutic tablets immersed in thickened beverages or SAJ compared to immersion in ones without them. Thickened beverages and SAJs were prepared with various beverages (water, orange juice, and milk) using food thickeners and SAJ powders marketed in Korea. The tablet disintegration times were the same in thickened beverages and SAJs, and there was no statistically significant difference associated with the thickness levels of the thickened beverages. The disintegration times of Tylenol immersed in orange juice or milk were slightly higher compared to those immersed in water. Moreover, there was no difference in disintegration time when using the thickened beverages and SAJs. The disintegration times of Aspirin were similar in all of the thickened beverages or SAJs, and there were no differences between non-immersed and immersed tablets. These results demonstrate that the disintegration of Tylenol and Aspirin is not greatly affected by immersion in any of the thickened beverages and SAJs.

Keywords: Dysphagia; Tablets; Deglutition

INTRODUCTION

Patients with dysphagia often have difficulty in swallowing food and tablets, and even after swallowing, they experience a foreign body sensation in the throat or chest. Accordingly, it is possible to prevent accidental aspiration using deglutition aids such as a food thickener or swallowing aid jelly (SAJ) to reduce the swallowing speed of foods [1]. Therefore, to help dysphagic patients swallow orally administered pharmaceuticals, a thickened beverage or SAJ is often coadministered with the medication.

Food thickeners are widely used to thicken food and beverages to promote safe food intake for patients with swallowing difficulty. Recently, commercially available xanthan gum (XG)-based thickeners are preferred over starch-based thickeners because of the superior

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Funding acquisition: Yoo B; Investigation: Cho W; Methodology: Cho W; Project administration: Yoo B; Resources: Yoo W; Software: Cho W; Supervision: Yoo B; Validation: Yoo B, Yoo W; Visualization: Cho W; Writing - original draft: Cho W; Writing - review & editing: Yoo B.

thickening characteristics, viscosity stability, and high palatability of the former [2]. SAJs are jellies specifically designed to coat medicine, thereby making it easier to swallow them and prevent them from sticking in the throat or causing choking. Therefore, SAJ products are being used as tablet-swallowing aids for dysphagic patients. However, when the tablets are consumed in thickened beverages or SAJ, the disintegration of the tablets may be inhibited [3]. Recently, Matsuo et al. [4] reported that food thickeners inhibit or delay the disintegration of some medications, thereby reducing the pharmaceutical effects of the medications.

Although the disintegration times of tablets immersed in thickened beverages or SAJ products marketed mainly in Japan have been extensively studied [1,4-6], this is not the case for commercial XG-based food thickeners and SAJ powders marketed in Korea. The commercial thickener and SAJ components have not been disclosed and the disintegration effect of tablets may depend on the type of swallowing aid food in which the tablets have been immersed. In particular, little information is available on the effect of beverage type and thickness level on the disintegration time of tablets immersed in thickened beverages and SAJs. Thus, the objectives of this study are 1) to investigate the effect of thickened beverages and SAJs prepared with a commercial powder-type food thickener and an SAJ marketed in Korea on the disintegration time of tablets (Tylenol and Aspirin), which are widely used in Korea as general pharmaceuticals; and 2) to examine the effect of thickness level and beverage type on the disintegration time of tablets immersed in thickened beverages and SAJ products. These results will provide useful information for dysphagic patients taking orally administered medications with various thickened beverages and SAJs.

MATERIALS AND METHODS

Materials

Tylenol (500 mg; film-coated tablets; Integrated Healthcare Indonesia, East Jakarta, Indonesia) and Aspirin (100 mg; enteric-coated tablet; Bayer Bitterfeld GmbH, Bitterfeld-Wolfen, Germany) tablets, widely consumed in Korea as general pharmaceuticals, were purchased from a local pharmacy. A powder-type XG-based thickener (Visco-up® thickener) and an SAJ (Visco-up® jelly) containing locust bean gum, XG, gellan gum, and carrageenan used for the management of dysphagia were kindly provided by Rheosfood Inc. (Seoul, Korea); these were selected because they are the most well-known swallowing aid products manufactured in Korea. Three beverages marketed in Korea: bottled water (Jeju Special Self-Governing Development Co., Jeju, Korea), orange juice (Coca-Cola Beverage Co., Yangsan, Korea), and whole milk (Namyang Dairy Products Co., Cheonan, Korea) were chosen for the preparation of the thickened beverages and SAJ products.

Preparation of thickened beverages and SAJ products

All thickened beverages and SAJ products were prepared based on the manufacturers' guidelines. Various amounts of the thickener powder were dissolved in water, orange juice, or whole milk while continuously magnetic stirring for 60 minutes at room temperature, followed by standing overnight at 4°C in a refrigerator to hydrate completely. The thickener concentrations (1, 2, and 3% w/w) used in this study were consistent with the manufacturer's guidelines for producing syrup-like (thickness level 1), honey-like (thickness level 2), and pudding-like (thickness level 3) fluids. The SAJ was prepared by dissolving 8 g of the jelly powder in 100 mL of boiling beverage for 1 minute under magnetic stirring, followed by

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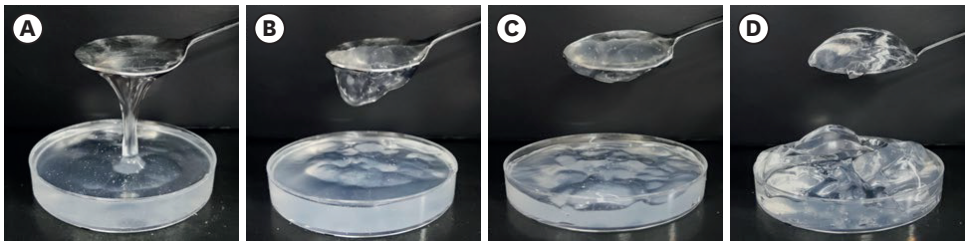

Figure 1. Appearances of thickened water samples with different thickness levels. (A) Level 1, (B) level 2, (C) level 3, and (D) swallowing aid jelly.

cooling down at 4°C in a refrigerator. **Figure 1** shows the appearance of thickened waters with different levels and SAJ prepared with water.

Disintegration test

The disintegration test was performed according to the Korean Pharmacopoeia 12th edition [7] (Ministry of Food and Drug Safety, 2019), which categorizes the disintegration test fluid for each tablet using a disintegration tester (LB-2D; Huanghai Co., Ltd., Shanghai, China). Tylenol (a film-coated tablet) was tested in deionized water. On the other hand, Aspirin (an enteric-coated tablet) was tested in the first test fluid (pH 1.2) and the second test fluid (pH 6.8), which are used to mimic the tablet disintegration in the stomach and small intestine. After immersing the tablets in the thickened beverages with different thickness levels or SAJs for 1 minute, the tablets were transferred to test tubes and tested at 37 ± 1°C with a rotation speed of 31 rpm [4]. The disintegration time of non-immersed tablets was used as the control. Based on the National Institute of Food and Drug Safety Evaluation standard, the disintegration time was defined as the time when tablets lost their original shape by the naked eye during the test. The disintegration time was visually assessed when no solid residue was left inside the chamber. When the tablets had not disintegrated within 120 minutes, the disintegration time was defined as 120 minutes. All measurements were performed nine times for each tablet.

Statistical analysis

The results are reported as the mean ± standard deviation. The experimental results were analyzed through one-way analysis of variance using SPSS (version 27.0; SPSS Institute Inc., Chicago, IL, USA) with the significance level set at $p < 0.05$.

RESULTS

The disintegration times of non-immersed Tylenol were compared to those in thickened beverages and SAJs prepared with different beverages (**Figure 2A**). Tylenol disintegrated within 31.6–32.4 seconds after being immersed in both thickened water or SAJ with water (**Table 1**). In contrast, Tylenol immersed in thickened beverages or SAJs with orange juice and milk disintegrated within approximately 34.9–36.1 seconds, indicating that these beverages delayed the disintegration of Tylenol. However, there are no significant differences in disintegration times between the tablets immersed in the swallowing aids and non-immersed tablets in the same dispersing medium. In particular, there are no significant differences between the thickened beverages with different thickness levels. This indicates that the tablet disintegration time was not influenced by the type of swallowing aid and the thickness level in the thickened beverage system.

https://doi.org/10.7762/cnr.2024.13.2.89

Table 1. Disintegration times (seconds) of Tylenol tablets immersed in thickened beverages at different thickness levels or the SAJ products

Beverage type	Non-immersion	Thickness level 1	Thickness level 2	Thickness level 3	SAJ
Water	$30.9 \pm 1.2^{A,b}$	$31.9 \pm 2.0^{A,b}$	$32.0 \pm 1.8^{A,b}$	$32.4 \pm 1.9^{A,b}$	$31.6 \pm 1.7^{A,b}$
Orange juice	$36.5 \pm 1.7^{A,a}$	$35.3 \pm 2.9^{A,a}$	$36.0 \pm 2.2^{A,a}$	$35.8 \pm 1.8^{A,a}$	$35.8 \pm 1.3^{A,a}$
Whole milk	$35.3 \pm 1.4^{A,a}$	$36.0 \pm 1.5^{A,a}$	$35.8 \pm 1.5^{A,a}$	$36.1 \pm 2.1^{A,a}$	$34.9 \pm 1.7^{A,a}$

Values are reported as the mean ± standard deviation. Mean values with uppercase letter (A) within the same row are not statistically significantly different ($p < 0.05$). Mean values with different lowercase letters (a or b) within the same column are statistically significantly different ($p < 0.05$).
SAJ, swallowing aid jelly.

The disintegration times of Aspirin immersed in thickened beverages with different thickness levels or the SAJ assessed using the first (pH 1.2) and second (pH 6.8) test fluids are reported in **Table 2**, respectively. In all cases, the Aspirin tablets had not disintegrated in the first

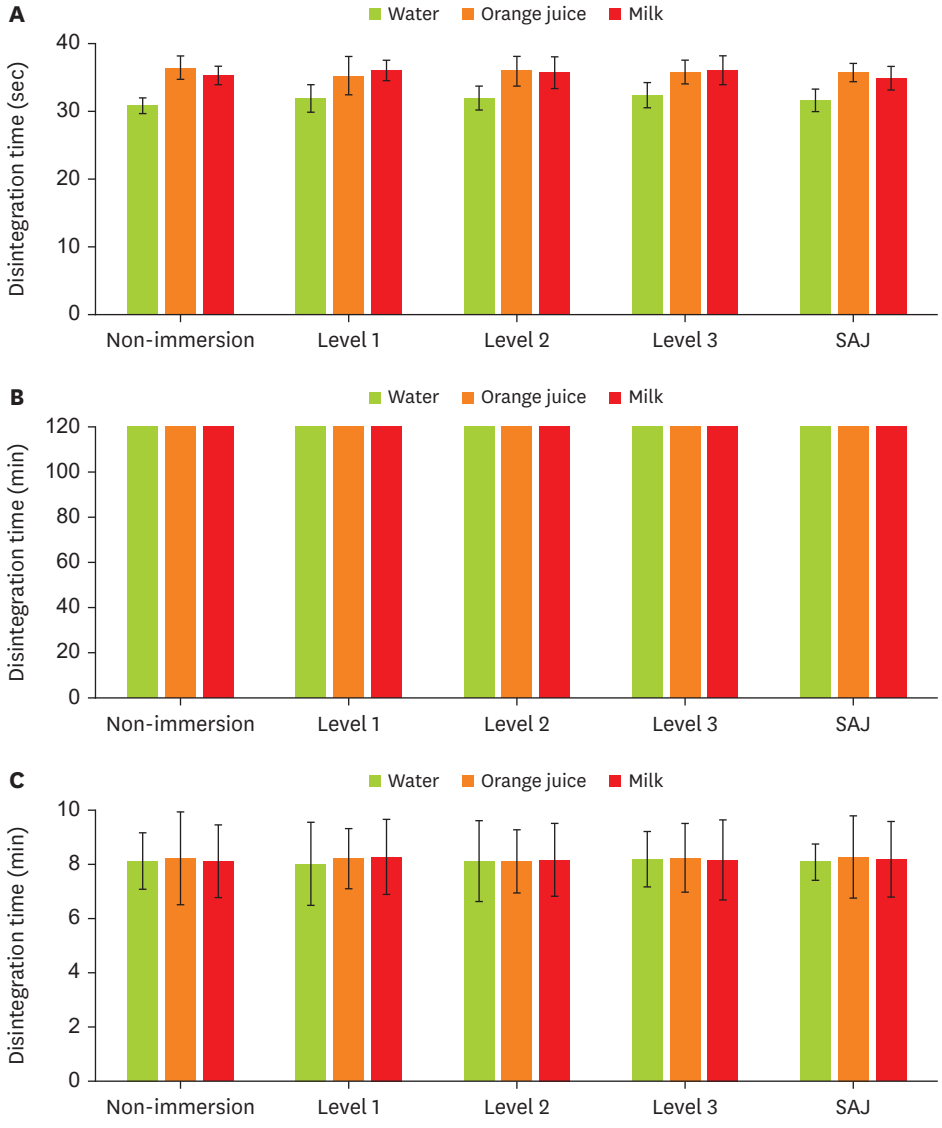

Figure 2. Tablet disintegration times of Tylenol (A) and Aspirin (B and C) immersed in different thickened beverages with different thickness levels (non-immersion, 1, 2, and 3) or swallowing aid jelly. Aspirin disintegration test was performed in (B) the first (pH 1.2) and (C) second fluids (pH 6.8). Error bars indicate standard deviation.

https://doi.org/10.7762/cnr.2024.13.2.89

Table 2. Disintegration times (minutes) of Aspirin immersed in thickened beverages with different thickness levels or SAJ products evaluated in the first (pH 1.2) and second test fluids (pH 6.8)

Test fluid	Beverage type	Non-immersion	Thickness level 1	Thickness level 2	Thickness level 3	SAJ
First fluid (pH 1.2)	Water	> 120	> 120	> 120	> 120	> 120
	Orange juice	> 120	> 120	> 120	> 120	> 120
	Whole milk	> 120	> 120	> 120	> 120	> 120
Second fluid (pH 6.8)	Water	$8.12 \pm 1.07^{A,a}$	$8.01 \pm 1.54^{A,a}$	$8.12 \pm 1.50^{A,a}$	$8.19 \pm 1.02^{A,a}$	$8.10 \pm 0.66^{A,a}$
	Orange juice	$8.22 \pm 1.73^{A,a}$	$8.21 \pm 1.11^{A,a}$	$8.11 \pm 1.16^{A,a}$	$8.25 \pm 1.28^{A,a}$	$8.29 \pm 1.52^{A,a}$
	Whole milk	$8.11 \pm 1.33^{A,a}$	$8.27 \pm 1.39^{A,a}$	$8.17 \pm 1.35^{A,a}$	$8.17 \pm 1.47^{A,a}$	$8.19 \pm 1.39^{A,a}$

Values are reported as the mean ± standard deviation. Mean values with uppercase letter (A) within the same row are not statistically significantly different ($p < 0.05$). Mean values with lowercase letter (a) within the same column are not statistically significantly different ($p < 0.05$).
SAJ, swallowing aid jelly.

test fluid even after 120 minutes (**Figure 2B**) but had fully done so after approximately 8 minutes in the second test fluid (**Figure 2C**). The results indicate that the disintegration time of Aspirin was similar among all the thickened beverages and SAJs, and there were no significant differences between immersed tablets and non-immersed tablets.

DISCUSSION

The number of patients with dysphagia, who may have difficulty swallowing orally administered medications, is increasing daily. Accordingly, the use of swallowing aid foods, such as food thickeners and SAJs, is increasing to improve the swallowing process and safety. Commercially available XG- or starch-based food thickeners vary depending on their composition. In this study, we used a commercially available XG-based food thickener marketed in Korea due to its excellent viscosity, stability, and solubility, and its popularity is high due to its soft texture and high palatability [8]. In general, thickened beverages are classified into several different thickness levels to provide the desirable thickness level for each dysphagic patient. To this end, the guidelines of the National Dysphagia Diet (NDD) characterize the thickness levels of beverages based on the viscosity at a shear rate of 50 $second^{-1}$ [9]. The NDD defines thickened beverages as thin (1–50 mPa·s), nectar-thick (51–350 mPa·s), honey-thick (351–1,750 mPa·s), and pudding-thick (> 1,750 mPa·s). According to the manufacturers' guidelines, each thickened beverage is classified as level 1 (nectar-thick), level 2 (honey-thick), and level 3 (pudding-thick).

In this study, Tylenol and Aspirin, which are widely consumed in Korea as general pharmaceuticals, were used to investigate the effects of thickened beverages and SAJs prepared with water, orange juice, or milk on the disintegration times of orally administered tablets. It is known that Aspirin, an enteric-coated tablet, can cause gastrointestinal problems, so it should be effective by melting in the intestine without melting in the stomach [10]. It consists of various components such as methacrylic acid copolymers that protect drug stability from acidic environments and maintain drug efficacy. As a result, this allows Aspirin to reach the intestine without disintegrating in the stomach at pH 1.2 and dissolve in the intestine at pH 6.8. Therefore, two test fluids at pH 1.2 and 6.8 should be used to mimic the disintegration of Aspirin in our gastrointestinal tract. The disintegration times of Tylenol were 3–6 seconds faster in water than in orange juice or milk in the thickened beverage or SAJ systems (**Table 1**, **Figure 2A**), suggesting that the disintegration time is influenced by the beverage rather than the presence of the food thickener or SAJ. The most relevant mechanism in the disintegration process is known to be the swelling of the tablet due to the liquid penetrating its pores due to capillary action [11]. In addition, it can be assumed that

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pulp or emulsion particles suspended from each beverage can interfere with the penetration of the pores of Tylenol. Therefore, orange juice and milk were unable to penetrate the pores of Tylenol as easily as water. Importantly, the disintegration times of Tylenol in the same beverages or SAJs were not statistically significantly different. This means that neither the food thickener nor the SAJ affected the disintegration time of Tylenol in the beverage. In particular, SAJ, which contains stronger gel-like solids than thickened beverages, did not cause a delay in tablet disintegration. It is known that when the solids of the SAJ attach to the tablets, voids of SAJ solids around the tablets are formed and water can easily invade the voids [12]. In addition, there were no significant differences in the tablet disintegration times of the beverages with different thickness levels, indicating that the tablet disintegration time is not influenced by the thickness level in the thickened beverage system.

Aspirin did not disintegrate within 120 minutes in the first test fluid for all of the samples (**Table 2**, **Figure 2B**). In the second test fluid, the tablet disintegrated in all of the samples with or without the thickener or SAJ within approximately 8 minutes, with no statistically significant differences among them (**Table 2**, **Figure 2C**). This means that neither the food thickener nor the SAJ affected the disintegration time of Aspirin. Similar results have been reported by Matsuo et al. [4], who also examined the effect of thickened beverages on the disintegration time of Aspirin. In addition, the type of beverage affected the disintegration time of Tylenol (**Table 1**) but not Aspirin, indicating that the disintegration time of tablets could be dependent on the type of beverage because Tylenol and Aspirin are different formulations, which explains the differences in the methods and results of the studies. Therefore, the effect of thickeners and SAJs on the disintegration time of other types of therapeutic tablets needs to be studied in the future.

In conclusion, the thickened beverages and SAJs evaluated in this study could be useful as information indicating alternatives that could potentially be used to help patients with dysphagia take orally administered medication. Our findings suggest that ingestion of Tylenol and Aspirin with thickened beverages and SAJs, which are prepared with Visco-up® food thickener or SAJ powder marketed in Korea does not affect the tablet disintegration time and is therefore safe for use by patients with dysphagia. Our study provides valuable information for pharmacists and clinicians to determine the most appropriate delivery method for tablets to patients with dysphagia. However, in the present study, as only film- and enteric-coated tablets were employed, additional studies to evaluate the influence of thickened beverages and SAJs on the disintegration time of other types of tablets are needed.

ACKNOWLEDGEMENTS

We would like to thank Rheosfood Inc. for providing free food thickener and swallowing aid jelly powder (Visco-up®) samples.

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