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Study on the Characteristics of Zolpidem Orally Disintegrating Tablets from Different Formulations

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Abstract

Objective: The aim of this study was to examine zolpidem (ZLP) orally disintegrating tablets (ODTs) from different formulations in order to characterize their physicochemical properties and thus, provide the necessary prescribing and dispensing information on those preparations.

Methods: Five 5-mg-ZLP ODTs from five different formulations were used in this study. These tablets were subjected to weight and content uniformity tests as indicators of quality. In addition, they were subjected to dissolution, wetting time, hardness, and disintegration tests.

Results: The content uniformity test ensured that preparations contained a uniform quantity of the active ingredient. The weight of each preparation was the same as that listed on the package insert. In the dissolution test, all the preparations had dissolved by at least 85% after 15 min. The hardness test showed that, on average, all the preparations had a hardness of at least 30 N. Results of the wetting time and disintegration tests indicated that the five preparations have different mechanisms of disintegration.

Conclusion: Our results revealed differences in the physicochemical properties between the five formulations. We concluded from this study that formulation differences could affect the disintegration, dissolution, and absorption of ODTs. In order to provide better medical care for each individual patient, it is necessary for the pharmacist to pursue information regarding the pharmaceutical properties of medications.

Keywords: Orally Disintegrating Tablets; Physicochemical Properties; Disintegration; Zolpidem

Introduction

Over the past few years, aging of the Japanese population has become associated with psychological problems like depression, stress, and insomnia [1,2]. Insomnia might be the result of a certain lifestyle, environmental conditions, or a mental/physical illness. It might also occur as an adverse reaction to a medication. Usually, insomnia is not caused by a single factor or disease but by several overlapping factors. Insomnia is common among the elderly, but recently, its prevalence has been rising among young people too.

A wide range of brand-name and generic drugs are prescribed to treat insomnia. A generic contains the same amount of the active pharmaceutical ingredient (API) as a brand-name drug. If the Ministry of Health, Labour, and Welfare certifies a generic as having the same efficacy and action as a brand-name drug, it permits the manufacture and sale of this generic. Generally, a generic uses the same API as a brand-name drug, making it less expensive to develop (since the API has already been identified) and thus less expensive in the market. In other words, the spread of generics is believed to reduce medical expenses borne by patients and curb government expenditures on medical insurance without lowering the quality of medical care. However, in 2015, generics accounted for only 56.2% of the pharmaceuticals in Japan, and this is a low percentage compared to that in foreign countries [3,4]. One of the reasons for this might be the concern of medical personnel about the quality of generics and the consistent supply of information on those drugs. In light of these circumstances, the Ministry of Health, Labour, and Welfare has devised a road map to promote the use of generics.

Conventional oral dosage forms require attention when taken by patients who find difficulty in swallowing, like the elderly, to avoid aspiration. In addition, for water deprivation patients due to disease, it is necessary to take into consideration the amount of water used when taking. To address these problems, a new dosage form known as orally disintegrating tablets (ODTs) has been developed. This dosage form consists of tablets that rapidly disintegrate and dissolve in the saliva and are thus easy to swallow without the need for water [5]. In addition, patients suffering from dysphagia, motion sickness, repeated emesis, or a mental disorder prefer ODTs since they cannot swallow large quantities of water [6]. Moreover, it is a suitable dosage form for drugs that are readily absorbed via the oral mucosa or have immediate pharmacological action. ODTs are classified into three types based on their method of formulation: Rapidly disintegrating tablets [7], molded tablets [8], and typical ODTs [9]. These three different types differ in the types of disintegrants, types of additives, and methods of manufacture, which presumably affects the tablets' disintegration.

Benzodiazepines were considered the treatment of choice for insomnia for several years until the advent of newer benzodiazepine-like drugs termed non benzodiazepines like zolpidem. Zolpidem (ZLP) is an imidazopyridine compound that enhances $GABA_A$ receptor function by binding to the omega (ω)-1 receptor subtype. ZLP is widely used in clinical practice because it exerts only a weak effect on the ω-2 receptor, which is responsible for muscle relaxation, and because patients are less likely to develop tolerance or dependence upon ZLP usage even when it is repeatedly administered [10].

Zolpidem is classified as BCS Class I. In Japan, only five companies sell generic forms of ZLP ODTs that are evaluated in accordance with the guidelines for Bioequivalence Testing of Generic Drugs. Since ZLP ODTs can be taken without water, the tablets can be taken immediately before bed time. However, different ZLP ODTs contain different additives that would presumably result in differences in their disintegration time and solubility. It is important to examine the characteristics of ZLP ODTs from different formulations in order to provide suitable prescribing and dispensing information on those preparations. However, the characteristics of different ZLP ODTs have not yet been examined.

Therefore, in the current study, we examined ZLP ODTs from five different formulations, and checked the tablet shape, weight uniformity, and content uniformity as indicators of quality. In addition, we subjected the ODTs to a dissolution test, wetting time test, hardness test, and disintegration test in order to evaluate the characteristics of the five preparations.

Materials and Methods

Materials

ZLP tartrate ODTs (5 mg) from five different formulations were used in the present study. The used formulations were: A: Sawai Pharmaceutical Co., Ltd., B: Kobayashi Kako Co., Ltd., C: TOWA PHARMACEUTICAL Co., Ltd., D: ELMED EISAI Co., Ltd., E: Nichi-Iko Pharmaceutical Co., Ltd. ZLP crystals were donated from Sawai Pharmaceutical Co., Ltd. Other reagents were of special commercial grade (Wako Pure Chemical Industries Co., Ltd.) (Table 1).

OD-tablets	Product company	OD-tablets' additive
A	Sawai Pharmaceutical Co. ,Ltd.	Microcrystalline cellulose, Magnesium Oxide, Red Ferric Oxide, Sucralose, Magnesium Stearate, Vanillin, Hydroxypropylcellulose, D-mannitol, Magnesium Aluminometasilicate, Flavor
B	Kobayashi Kako Co., Ltd.	D-Mannitol, Microcrystalline Cellulose, Low Substituted Hydroxypropylcellulose, Precipitated Calcium Carbonate, Tartaric Acid, Magnesium Hydroxide, Sucralose, Yellow Ferric Oxide, Red Ferric Oxide, Flavor, Magnesium Stearate
C	TOWA PHARMACEUTICAL Co., Ltd.	D-Mannitol, Talc, Yellow Ferric Oxide, l- Menthol, Aspartame (L-Phenylalanine Compound), Light Anhydrous Silicic Acid, Magnesium Stearate, Flavor, Other three components
D	ELMED EISAI Co., Ltd.	Yellow Ferric Oxide, Microcrystalline Cellulose, Flavor, Red Ferric Oxide, Tartaric Acid, Magnesium Hydroxide, Sucralose, Magnesium Stearate, Precipitated Calcium Carbonate, Low Substituted Hydroxypropylcellulose, D- Mannitol
E	Nichi-Iko Pharmaceutical Co., Ltd.	D- Mannitol, Cellulose, Magnesium Oxide, Hydroxypropylcellulose, Aspartame (L- Phenylalanine Compound), Yellow Ferric Oxide, Red Ferric Oxide, Magnesium Stearate, Flavor

Table 1: List of additives in ODTs

Methods

Examination of the appearance: The diameter and thickness of the ODTs were measured using a digital vernier caliper (Shinwa Rules Co., Ltd.).

Weight uniformity test: All formulations were subjected to a uniformity-of-weight test. Weights were measured using an electronic balance (GH-252, A&D Co., Ltd.).

Content uniformity test: A content uniformity test was conducted in accordance with the 17th edition of the Japanese Pharmacopoeia (JP). A sample solution was prepared using ODTs of each formulation and a standard solution was prepared using a standard sample of ZLP tartrate. High-performance liquid chromatography (HPLC) was used to calculate the ZLP tartrate content in proportion to the indicated amount of ZLP tartrate in the formulation. Content was ascertained by determining the acceptance value as described in the 17th edition of the JP. According to the JP, the acceptance value should be 15% or lower, i.e., if the acceptance value of a certain formulation does not exceed 15%, this formulation complies with the JP.

HPLC analysis: HPLC was performed in accordance with a dissolution test for ZLP tartrate tablets specified in the first section of the JP using a high-performance liquid chromatograph (HPLC, SPD-20A SHIMADZU Corp.). Assay conditions were as follows: Inertsil® ODS-3 column (4×150 mm, 5 μm); a column temperature of 35°C; a mobile phase consisting of a mixture of phosphoric acid, methanol, and acetonitrile (11:5:4); a detection wavelength of 254 nm; and a sample injection volume of 40 μL. ZLP tartrate retention time was set so that the flow rate would be 1.7 mL/min. The quantitation and detection limits (QL and DL) achieved were 0.0000022 mg/mL and 0.00000072 mg/mL, respectively. A standard curve was prepared using concentrations of 0.006306, 0.012613, 0.025225, 0.0509, 0.1018, and 0.2036 mg/mL.

Dissolution test: A dissolution test was conducted in accordance with the paddle method in the 17th edition of the JP and the guidelines for Bioequivalence Testing of Generic Drugs [11]. The dissolution test was performed using a dissolution apparatus (NTR-593, Toyama Sangyo Co., Ltd.) at a temperature of 37 ± 0.5°C, stirred at 50 rpm in 900 mL of distilled water or artificial saliva [12-14] (Artificial saliva composition: component's concentration (g/L), pH 4.8, 0.4 g NaCl, 0.4 g KCl, 0.795 g $CaCl_2.2H_2O$, 0.78 g $NaH_2PO_4.2H_2O$, 0.005 g $Na_2S.9H_2O$, and 1.0 g $CO(NH_2)_2$ (Urea) in 1000 mL). Ten milliliters of each sample solution were collected after 0, 5, 10, 15, and 30 min. Regarding distilled water, the sample solution was filtered through a 0.45-μm membrane filter. Then, 5 mL of the filtered sample was diluted to 25 mL with 20 mL of methanol to serve as the sample solution. The content in each sample solution was determined using UV-Vis spectrophotometers (UV-2500PC, SHIMADZU Corp.).

Detection wavelengths of 246 and 238.5 nm were used for distilled water and artificial saliva, respectively.

Wetting time test [15]: This experiment mimics the action of saliva in contact with ODTs. A Whatman filter paper disk folded once diametrically was placed in a 90-mm-petri dish and immersed in 10 mL distilled water or artificial saliva. The tablet was carefully placed on the filter paper over the dividing line (t=0) and the time for complete wetting was measured.

Hardness test: The hardness of each formulation was measured in the direction of the diameter using a Monsanto tablet hardness tester (Minato Medical Co., Ltd.).

Disintegration test: In order to measure the disintegration time for each formulation, the disintegration test was performed using a disintegration tester (ODT-101, Toyama Sangyo Co., Ltd.) [16]. This apparatus allows

automatic adjustment of the level of the test medium. A 20-g-ODT sample was placed on a stainless-steel porous plate at 37 ± 0.5°Cand stirred at 50 rpm in 900 mL of distilled water.

Statistical analysis: Results are presented as the mean ± standard deviation. Statistical significance was evaluated by Tukey-Kramer test.

Results and Discussion

Examination of the appearance

The diameters and shapes of the five types of tablets were examined (Table 2). Preparation A had a diameter of6.52 ± 0.02 mm, preparation B had a diameter of 6.59 ± 0.03 mm, preparation C had a diameter of 7.13 ± 0.03 mm, preparation D had a diameter of 6.58 ± 0.01 mm, and preparation E had a diameter of 6.57 ± 0.04 mm. Preparation A had a thickness of 2.65 ± 0.25 mm, preparation B had a thickness of 2.74 ± 0.01 mm, preparation C had a thickness of 3.42 ± 0.02 mm, preparation D had a thickness of 2.75 ± 0.02 mm, and preparation E had a thickness of 2.57 ± 0.02 mm. All preparations were scored on one side.

Weight uniformity test

Preparation A had an average weight of 90.3 ± 0.5 mg, preparation B had an average weight of 96.1 ± 0.5 mg, preparation C had an average weight of 137.1 ± 0.5 mg, preparation D had an average weight of 96.1 ± 0.5 mg, and preparation E had an average weight of 90.6 ± 0.7 mg (Table 2). The weight of each preparation was the same as that listed on the package insert.

Content uniformity test

This test is done to ensure that all preparations within a batch contain equal quantities of the API. Preparation A had an average content of 103.3 ± 2.7 mg, preparation B had an average content of 102.9 ± 2.0 mg, preparation C had an average content of 101.7 ± 3.1 mg, preparation D had an average content of 101.7 ± 3.1 mg, and preparation E had an average content of 102.36 ± 1.6 mg (Table 2). The ZLP content in all the preparations was about 100%. Preparation A had an acceptance value of 9.7%, preparation B had an acceptance value of 7.8%, preparation C had an acceptance value of 9.0%, preparation D had an acceptance value of 6.1%, and preparation E had an acceptance value of 6.1%. All preparations had acceptance value slower than 15%, thus, according to the JP, all the preparations passed. These results showed that the API content was equivalent in all the preparations.

Dissolution test

A dissolution test was conducted to determine the bioequivalence of the preparations. Results of the dissolution test conducted in purified water are shown in Figure 1.The results show that after 15 min, all the preparations had dissolved by at least 85%. After 5 min, preparations A, B, D, and E had dissolved by 80%, and only preparation C had dissolved by 70%, i.e., preparation C dissolved at a significantly lower rate than the other preparations. The dissolution test was repeated with artificial saliva instead of purified water in order to determine whether saliva would help the disintegration of ODTs. Results of the dissolution test conducted in artificial saliva are shown in Figure 2. The results show that after 15 min, all the preparations had dissolved by at least 85%. However, unlike the purified water test, all the preparations in this test had dissolved by about 90% after 5 min. Only preparation C had dissolved to a significantly lower extent than the other preparations after 15 and 30 min. Both preparations A and E contained approximately 90 mg of hydroxypropyl cellulose (HPC) as an additive, and both preparations B and D contained approximately 96 mg of low-substituted hydroxyl propyl cellulose (L-HPC), i.e., preparations A and E contained the same additive and preparations B and D contained the same additive and thus, each set of preparations is predicted to have similar characteristics. Based on the current findings, there were differences in additives such as binders, disintegrants, and solubilizers between the preparations, which resulted in certain tablets dissolving more readily than others. This explains the differences in the dissolution profiles between the preparations.

Wetting time test

The dissolution test results showed that only preparation C had a different dissolution profile than the other preparations. Thus, we can conclude that preparation C presumably disintegrates in a different manner, for example, water may enter it in a different manner. Attention was focused on this difference, so a wetting time (water absorption) test was conducted. Results of this test showed that preparation A absorbed purified water in 45.8 ± 4.7 s, preparation B absorbed purified water in 12.0 ± 3.0 s, preparation C absorbed purified water in 17.1 ± 1.6s, preparation D absorbed purified water in 12.1 ± 3.1 s, and preparation E absorbed purified water in 52.8 ± 2.8s. Preparations B and D took nearly the same time to absorb water in (Figure 3), while preparations A, C, and E took significantly longer times. ODTs typically disintegrate by one of the following four mechanisms: 1) Moisture enters the tablet even if a small amount of saliva is present, and the whole tablet abruptly disintegrates. 2) When a sufficient amount of water is present, the surface of the tablet gradually disintegrates as the tablet absorbs water, and moisture enters until it reaches the core of the tablet. Then, the core abruptly disintegrates. 3) The surface of the tablet becomes pliable. Disintegration of the tablet is initially delayed, but once moisture reaches the core of the tablet, it abruptly disintegrates. 4) The entire tablet gradually disintegrates from its surface to its core at the same speed. These mechanisms of disintegration presumably lead to differences in water absorption rates. Preparations A and E gradually absorbed water starting at the surface of the tablet, where a thick layer of solution was formed, hampering the entry of water to the center of the tablet, while preparations B, C, and D allowed water to

OD-tablets	A	B	C	D	E
Appearance of formulations					
Diameter* (mm)	6.52 ± 0.02	6.59 ± 0.03	7.13 ± 0.03	6.58 ± 0.01	6.57 ± 0.04
Thickness* (mm)	2.65 ± 0.25	2.74 ± 0.01	3.42 ± 0.02	2.75 ± 0.02	2.57 ± 0.02
Weight* (mg)	90.3 ± 0.5	96.1 ± 0.5	137.1 ± 0.5	96.1 ± 0.5	90.6 ± 0.7
Zolpidem tartrate content (%)	103.3 ± 2.7	102.9 ± 2.0	101.7 ± 3.1	103.9 ± 0.9	102.3 ± 1.6
Acceptance value	9.7	7.8	9.0	6.1	6.1

Table 2: Shape, weight, and content uniformity of ODTs

*Each value represents the mean ± S.D. (n=10).

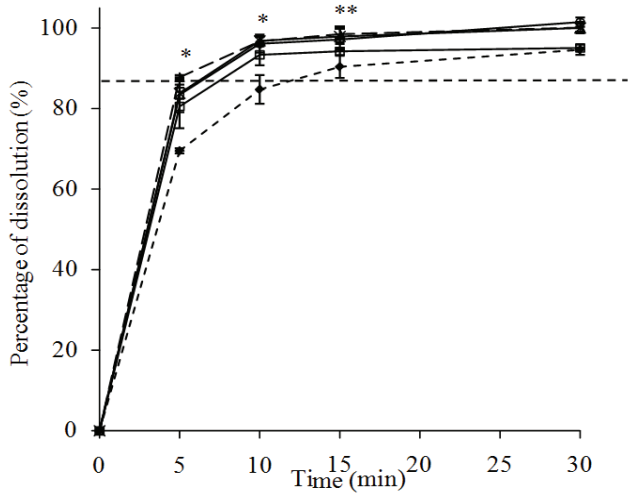

Figure 1: Dissolution rate-time profiles of zolpidem tartrate ODTs
Each point represents the mean ± S.D. (n=3)
Symbols are represented as follows; A: ○, B: △, C: ◆, D: ×, E: □.
Tukey test was performed for official approval (p<0.05).
*Significant differences were observed between A and C, B and C, and C and D, after 5 and 10min (p<0.05 for each). No differences were observed between A and B, A and D, A and E, B and D, B and E, C and E, or D and E.
**Significant differences were observed between A and C, A and E, B and C, B and E, C and D, and D and E after 30min (p<0.05 for each). No differences were observed between A and B, A and D, B and D, or C and E.

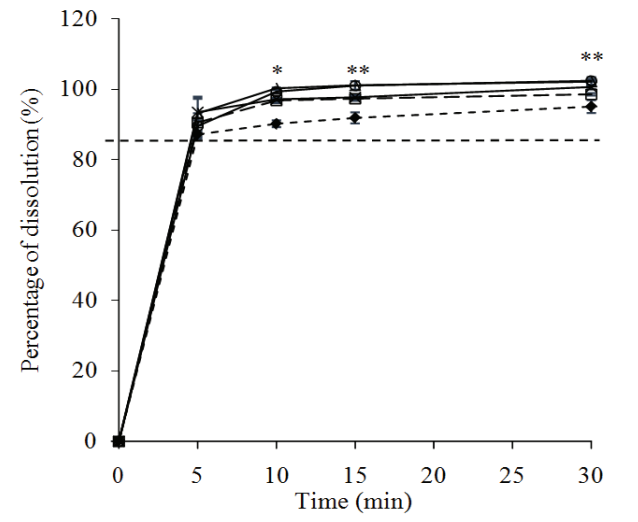

Figure 2: Dissolution rate-time profiles of zolpidem tartrate ODTs in artificial saliva
Each point represents the mean ± S.D. (n=3)
Symbols are represented as follows; A: ○, B: △, C: ◆, D: ×, E: □.
Tukey test was performed for official approval (p<0.05).
*Significant differences were observed between A and C, A and E, B and C, B and D, B and E, C and D, and C and E after 10min (p<0.05 for each). No differences were observed between A and B, A and D, or D and E.
**Significant differences were observed between A and C, B and C, C and D, and C and E after 15 and 30 min (p<0.05 for each). No differences were observed between A and B, A and D, A and E, B and D, B and E, or D and E.

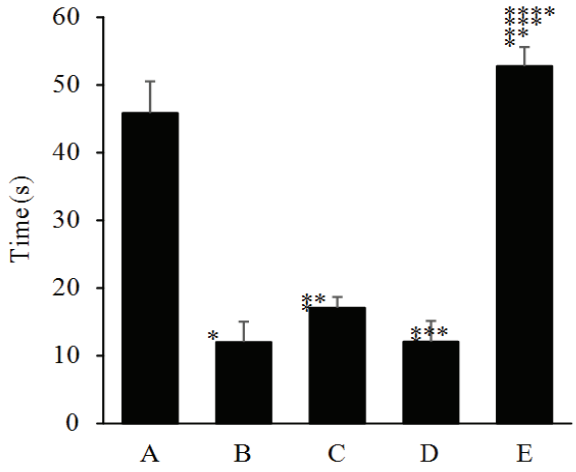

Figure 3-1: Water absorption of Zolpidem tartrate OD-tablets
Tukey test was given to official approval (p<0.05).
*Significant differences were seen between A and B, A and C, A and D, A and E (p<0.05 for each).
**Significant differences were seen between B and C, B and E (p<0.05 for each).
***Significant differences were seen between C and D, C and E (p<0.05 for each).
****Significant differences were seen between D and E (p<0.05 for each).

pass through the surface of their tablets. Preparations A and E contain the binder HPC, which is a cellulose derivative in which hydroxyl groups have been substituted by hydroxylpropyl groups. HPC readily dissolves in water. However, preparations B and D contain L-HPC, which has fewer hydroxypropyl groups and is thus less water-soluble than HPC. This explains why water absorption by these preparations differed. When examining water absorption by an ODT, the test solution used should be similar to saliva in order to mimic the buccal environment. Thus, a water absorption test using artificial saliva was conducted. The test results showed that preparation A absorbed water in 34.0 ± 3.1 s, preparation B absorbed water in 8.8 ± 1.1 s, preparation C absorbed water in 16.6 ± 1.7s, preparation D absorbed water in 7.5 ± 0.9 s, and preparation E absorbed water in 46.1 ± 3.9 s. Preparations A, B, D, and E absorbed moisture from artificial saliva in a shorter time than they did from purified water. Only preparation C took nearly the same time to absorb water and moisture from saliva. HPC is a nonionic additive that is exceptionally compatible with different salts and drugs, so a preparation containing HPC will presumably absorb moisture from artificial saliva faster than purified water. Based on the previous results, we can conclude that preparations A and E disintegrate as follows: The tablet absorbs water, swells, and then disintegrates, while preparations B, C, and D have a porous structure, so they absorb water via capillarity and then disintegrate.

Hardness test

Not only do tablet additives affect its water absorption rate, but also does its hardness. Thus, each preparation was subjected to a hardness test (Figure 4). Results of the hardness test showed that preparation A had a hardness of 30.6 ± 2.8 N, preparation B had a hardness of 34.3 ± 1.8 N, preparation C had a hardness of 43.7 ± 2.4 N, preparation D had a hardness of 30.8 ± 1.2 N, and preparation E had a hardness of 41.7 ± 2.0 N. On average, all preparations had a hardness of at least 30 N. Typically, a hardness level of 30 N or greater means that a tablet can tolerate an impact during the manufacturing process or transport [17], which means that the preparations had appropriate hardness. Preparations C and E were

OD-tablets		A	B	C	D	E
Wetting time* (s)	Water	45.8 ± 4.7	12.0 ± 3.0	17.1 ± 1.6	12.1 ± 3.1	52.8 ± 2.8
	Artificial saliva	34.0 ± 3.1	8.8 ± 1.1	16.6 ± 1.7	7.5 ± 0.9	46.1 ± 3.9
Hardness** (N)		30.6 ± 2.8	34.3 ± 1.8	43.7 ± 2.4	30.8 ± 1.2	46.1 ± 2.0
Disintegration time*** (s)		24.6 ± 1.9	29.7 ± 2.0	22.6 ± 1.2	23.0 ± 2.9	42.4 ± 2.0

Table 3: Wetting time, hardness, and disintegration time of ODTs.

*Each value represents the mean ± S.D. (n=10). Tukey test was performed for official approval ($p<0.05$). Significant differences were observed between A and B, A and C, A and D, A and E, B and C, B and E, C and D, C and E, and D and E. ($p<0.05$ for each). No differences were observed between B and D.

**Each value represents the mean ± S.D. (n=11). Tukey test was performed for official approval ($p<0.05$). Significant differences were observed between A and B, A and C, A and E, B and C, B and D, B and E, C and D, and D and E. ($p<0.05$ for each). No differences were observed between A and D or C and D.

***Each value represents the mean ± S.D. (n=11). Tukey test was performed for official approval ($p<0.05$). Significant differences were observed between A and B, A and E, B and C, B and D, B and E, C and E, and D and E. ($p<0.05$ for each). No differences were observed between A and C, A and D, or C and D.

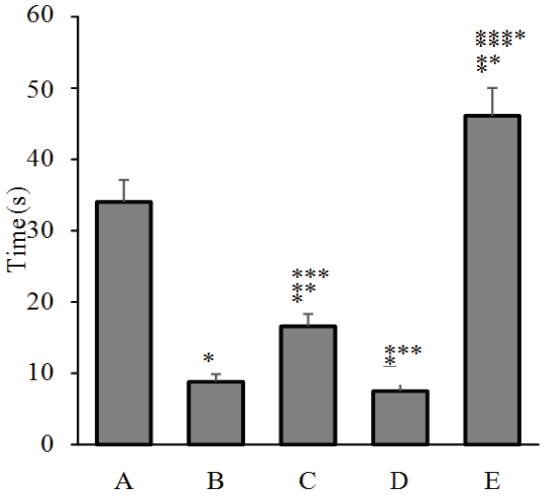

Figure 3-2: Artificial saliva absorption of Zolpidem tartrate OD-tablets
Tukey test was given to official approval ($p<0.05$).
*Significant differences were seen between A and B, A and C, A and D, A and E ($p<0.05$ for each).
**Significant differences were seen between B and C, B and E ($p<0.05$ for each).
***Significant differences were seen between C and D, C and E ($p<0.05$ for each).
****Significant differences were seen between D and E ($p<0.05$ for each)

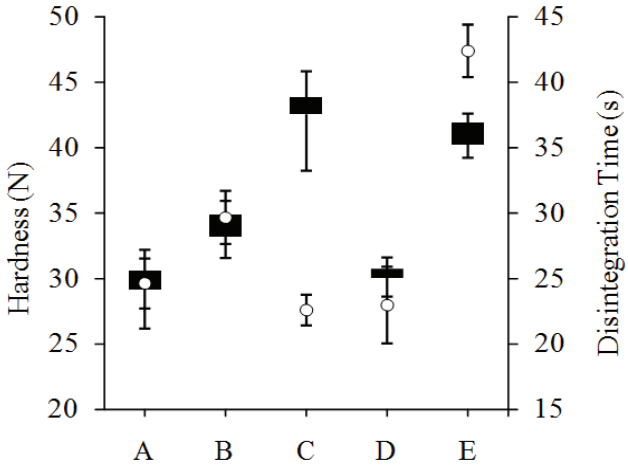

Figure 4: Correlation between hardness and disintegration time
Hardness: ■, Disintegration time: ○

significantly harder than the other preparations. Given this finding, the hardness of preparation C presumably played a role in its low extent of dissolution within 5 min. Even though preparations A and E contained the same additive, their hardness levels differed. This could be the result of differences in the amount of the additive or in the tableting procedures (method of formulation).

Disintegration test

Upon administration, ODTs disintegrate in the mouth. A disintegration test was conducted in order to determine the extent to which water absorption and hardness affected tablet disintegration. Results of the disintegration test showed that preparation A disintegrated in 24.6 ± 1.9 s, preparation B disintegrated in 29.7 ± 2.0 s, preparation C disintegrated in 22.6 ± 1.2 s, preparation D disintegrated in 23.0 ± 2.9 s, and preparation E disintegrated in 42.4 ± 2.0 s (Figure 4). Preparations A, B, C, and D took around 25s to disintegrate, while preparation E took 42s, i.e., it took significantly longer time than other preparations to disintegrate. The US Pharmacopeia (USP) recommends a disintegration time of 30 s for ODTs [18]. The hardness test showed that preparation E is hard, which hampers water from entering the tablet, and the water absorption test showed that a thick layer of solution is formed on the tablet surface, which delays its disintegration. Like preparation E, preparation A also contains HPC, but preparation A is softer, which allows the water to enter the tablet more easily. In addition, HPC allowed the tablet to disintegrate before a thick layer of solution is formed. Although preparation C is hard, it disintegrated in a short time. Preparation C contained some additives that were not found in the other preparations, for example, it contained talc, colloidal silicon dioxide, and magnesium stearate as lubricants. These three lubricants are presumably the reasons why preparation C took less time to disintegrate despite its hardness. It disintegrated when water entered the tablet, but its ingredients delayed dissolution (Table 3).

Conclusion

In this study, five different formulations of ZLP ODTs were subjected to a water absorption test, a hardness test, and a disintegration test. Our results indicate that the five preparations have different mechanisms of disintegration; preparations A and E gradually disintegrated at a constant speed starting from the surface of the tablet, preparations B and D rapidly disintegrated from the inside once water entered the tablet, and preparation C disintegrated once moisture reached the core of the tablet.

Our results showed that preparations A, B, C, and D disintegrated within about 30 s. Thus, these preparations could be taken without water at bedtime and they will facilitate sleep without discomfort. In addition, they are beneficial for patients suffering from dysphagia, who are susceptible to choking when taking medications with water. In conclusion, those four preparations are convenient and simple to use. In contrast, preparation E took 42 s to disintegrate, and this long time could cause patients to feel discomfort. The current results were obtained by examining tablets from a single lot; therefore, other lots need to be examined as well. A pharmacist needs to talk to a patient face-to-face and ascertain a patient's status in order to recommend him a generic that meets his needs. In the future, when pharmacists provide information to patients, they should be responsible for recommending the suitable medication in light of the patient's adherence and compliance. Taking this into consideration, pharmacists need to have a basic understanding of the pharmaceutical properties of medications and they need to update their information on regular basis to be able to provide patients with better medical care.

Acknowledgement

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Conflict of Interest

This study was conducted fairly and impartially and ethical considerations were taken into account. The authors have no relationships with any companies or other commercial entities mentioned in this paper.

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