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ORIGINAL ARTICLE

The practical approach to the evaluation of methods used to determine the disintegration time of orally disintegrating tablets (ODTs)

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Abstract Even that orodispersible tablets (ODTs) have been successfully used in therapy for more than 20 years, there is still no compendial method of their disintegration time evaluation other than the pharmacopoeial disintegration test conducted in 800–900 mL of distilled water. Therefore, several alternative tests more relevant to in vivo conditions were described by different researchers. The aim of this study was to compare these methods and correlate them with in vivo results. Six series of ODTs were prepared by direct compression. Their mechanical properties and disintegration times were measured with pharmacopoeial and alternative methods and compared with the in vivo results. The highest correlation with oral disintegration time was found in the case of own-construction apparatus with additional weight and the employment of the method proposed by Narazaki et al. The correlation coefficients were 0.9994 ($p < 0.001$), and 0.9907 ($p < 0.001$) respectively. The pharmacopoeial method correlated with the in vivo data much worse ($r = 0.8925$, $p < 0.05$). These results have shown that development of novel biorelevant methods of ODT's disintegration time determination is eligible and scientifically justified.

1. Introduction

Orodispersible tablets (orally disintegrating tablets – ODT) were developed in late 80s and introduced to the market in early 90s. Since then, they have become well known solution to overcome difficulties in swallowing solid oral dosage forms commonly encountered in geriatric or pediatric populations (Bandari et al., 2008; Bhowmik et al., 2009). They were introduced to the European Pharmacopoeia for the first time in 2004, and are described as an uncoated tablets intended to be placed in the mouth where they disperse rapidly before

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being swallowed (The European Pharmacopoeia 7th Edition, 2010). The usually applied methods of quality assessment of ODTs include evaluation of their mechanical properties, disintegration time measurement, dissolution studies, taste masking efficiency and stability tests. According to the Eur. Pharm. 7.0 orodispersible tablets should disintegrate in less than 3 min. Food and Drug Administration in Guidance for Industry recommends that this time should not exceeded 30 s (US Department of Health and Human Services, 2008). However, up to now, the compendial method used to measure the disintegration time of ODTs is the same as for uncoated tablets, and there is no other method uniquely designed for ODT disintegration evaluation accepted by the official authorities. The pharmacopoeial test is conducted in a one liter beaker with approximately 800–900 mL of distilled water, which completely does not reflect the conditions in the human mouth, and was previously reported by many researchers (Abdelbary et al., 2005; Bi et al., 1996; Brniak et al., 2013; Harada et al., 2006, 2010; Kakutani et al., 2010; Szakonyi and Zelkó, 2013). Even if it can be valuable in the quality assessment of tablets, it is rather useless for the prediction of real in vivo disintegration time on the development stage. Therefore, there are alternative methods proposed by many authors that reflect to a greater degree the disintegration process in the human oral cavity (Abdelbary et al., 2005; Bi et al., 1996; Brniak et al., 2013; Harada et al., 2006, 2010; Kakutani et al., 2010; Szakonyi and Zelkó, 2013; Morita et al., 2002; Rawas-Qalaji et al., 2009; Narazaki et al., 2004; Sunada and Bi, 2002). The simplest methods include disintegration of tablets placed in a small volume of water in a test-tube or a petri dish (Rawas-Qalaji et al., 2009). Another approach is to use a wire cloth or a sieve (Bandari et al., 2008; Motohiro et al., 2001). The tablets placed on the wire cloth are wetted by a water dropping from a syringe or they are immersed in a disintegration medium when put on the metal sieve. The more complex methods involve using texture analyzers with many different probes that are usually individually designed for ODTs (Abdelbary et al., 2005; Szakonyi and Zelkó, 2013). There are also several testing apparatus constructed to reflect the conditions of human mouth in order to predict in vivo disintegration time (Brniak et al., 2013; Harada et al., 2006, 2010; Kakutani et al., 2010; Rawas-Qalaji et al., 2009; Narazaki et al., 2004). Another analytical approach is to use high speed image registration tools such as CCD camera to record the changes of the tablet shape and its surface during disintegration (Morita et al., 2002). Magnetic resonance imaging technique was also used to analyze the disintegration behavior of wetted orodispersible tablets (Brniak et al., 2013).

The apparatus used for disintegration time measurement can work in static or dynamic conditions, i.e. the disintegration process can be caused only by the water capillary action or some additional forces caused by the apparatus movement such as shearing, grinding or pressure put on the tablet. The authors of alternative methods have demonstrated the higher correlation of their results with in vivo disintegration time in comparison to the compendial test, which proved the superiority of their approaches. However, all tests were performed with different tablets and in different laboratories, thus it can be confusing when trying to compare the results.

Therefore, the aim of this study was to compare different methods used for evaluation of orodispersible tablets on the same series of orally disintegrating tablets and analyze their correlation with disintegration time measured in vivo.

2. Materials and methods

2.1. Materials

The ready to use co-processed excipient designed for ODT direct compression, i.e. F-MELT® type C (Fuji Chemical Industry, Japan) was kindly provided by Harke Pharma GmbH. Kollidon CL (BASF, Germany) was used as a superdisintegrant, microcrystalline cellulose – Avicel PH-101 (FMC Biopolymer) as a filler, and magnesium stearate (POCh, Poland) as a lubricant.

2.2. Preparation of tablets

Two kinds of model placebo tablets were prepared (Table 1). The first ones contained microcrystalline cellulose (Avicel PH-101) and 5% of superdisintegrant Kollidon CL. The second ones were composed of co-processed excipient F-MELT type C. Magnesium stearate in amount of 1% was used for both formulations as a lubricant. Tablets with a diameter of 6 mm and a mass of 130 ± 10 mg were directly compressed with a rotary tablet press (Erweka TRB10). Three different compression forces were used for every composition in order to differentiate the tablets' mechanical properties.

2.3. Tablets' mechanical properties

In order to determine the uniformity of mass, 20 undusted tablets were individually weighted. Their average masses and percent deviations were calculated according to the method described in the European Pharmacopoeia 7.0.

The thickness and hardness of six tablets from every batch was measured with a VK200 tablet tester (Vankel, USA). Their tensile strength (MPa) was calculated from the equation:

$$Ts = 2F/\pi Dh,$$

Table 1 Composition of tablets.

Ingredients (%)	Formulation name					
	K_a	K_b	K_c	F_a	F_b	F_c
Avicel PH-101	94.0			–		
Kollidon CL	5.0			–		
F-MELT type C	–			99.0		
Magnesium stearate	1.0			1.0		

a – the low compression force, b – the medium compression force, c – the high compression force.

where F is the tablet hardness (N), D its diameter (m) and h its thickness (m).

The friability of all prepared formulations was measured according to the Eur. Pharm 7.0 (3). Twenty undusted tablets were weighted, put into the Roche friabilator for 100 cycles, undusted and weighted again. The percentage loss of their initial mass was calculated.

2.4. Fineness of dispersion

The fineness of dispersion test according to the Eur. Pharm. 7.0 was performed in the following manner. Two tablets were placed in a beaker with 100 mL of distilled water, and stirred until completely dispersed. Dispersion was poured through a sieve screen 0.7 mm. If all the parts passed through the sieve, the tablets passed the test. If there were any remaining particles they did not.

2.5. Tablets disintegration in vitro

The test described in European Pharmacopoeia 7.0 as well as six other different methods (Table 2) were used to measure disintegration time of prepared ODTs (Bi et al., 1996; Brniak et al., 2013; Harada et al., 2006, 2010; Rawas-Qalaji et al., 2009; Narazaki et al., 2004). The experiments on tablets of all batches were performed six times with every method and the average values of disintegration time and standard deviations were calculated.

2.5.1. Pharmacopoeial method

The test was performed with disintegration tester ED-2 (Electrolab, India) according to the monograph published in the European Pharmacopoeia 7.0 (Chapter 2.9.1. Disintegration of tablets and capsules). Distilled water in a volume of approximately 900 mL was used as a disintegration medium. Six tablets were placed into the tubes of the disintegration apparatus and the test was started. The disintegration time was measured semi-automatically.

A modification to the pharmacopoeial test proposed by Watanabe et al. (1995) was also performed. Instead of one plastic disk, every tablet was covered with five of them, and only one tablet was tested during one trial. In opposition to the pharmacopoeial test, after the apparatus was lowered immersing the tablet into the medium, it was kept in a still position without any further movement. All other conditions remained the same. Six tablets of each formulation were tested.

2.5.2. Modified paddle apparatus

The method was proposed by Bi et al. (1996). A dissolution paddle apparatus with a wire basket attached at one side of beaker was used. The medium was mixed by the paddle at 50 rpm.

2.5.3. Test-tube method

According to the method described by Rawas-Qalaji et al. (2009), the tablet was placed into the test-tube with 2 mL of distilled water, and its disintegration time was measured with a stopwatch.

2.5.4. Sieve method

Two different sieve methods were used. According to Motohiro et al. (2001) the tablet was placed on the stainless steel sieve (2 mm aperture), and distilled water was dropped on its upper surface with constant speed of 4 mL/min.

Table 2 Main parameters of performed disintegration tests.

Method	Medium volume (mL)	Temperature of medium (°C)	Forces acting on the tablet
Pharmacopoeial	900.0	37.0	–Water wicking –Mechanical destructive force caused by the movement of the basket
Pharmacopoeial – modified	900.0	37.0	–Water wicking –Pressure acting on the tablet by the five plastic disks weight
Modified paddle apparatus	900.0	37.0	–Water wicking –Rotating paddle causes water stirring leading to the tablet erosion
Test-tube method	2.0	Ambient	–Water wicking
Sieve method	4 mL/min	Ambient	–Water wicking
Sieve method with shaker	3.0	37.0	–Water wicking –Water agitation caused by reciprocating shaker
Rotating shaft apparatus	450.0	37.0	–Water wicking –Tablet grinding between rotating shaft and metal plate –Pressure caused by the load of a rotating shaft acting on the tablet
Own construction apparatus	5.0	37.0	–Water wicking –Tablet grinding between rotating shaft and metal plate –Pressure caused by the load of a rotating shaft acting on the tablet
Wetting test	7.0	Ambient	–Water wicking

2.5.5. Sieve method with shaker

In the second sieve method reported by Bhowmik et al. (2009), a glass tube with a sieve on its bottom was used. It was immersed in distilled water about 1 mm deep. The tablet was dropped on the sieve, and the time measurement was started. The tube was constantly shaken with a reciprocating bath shaker (150 rpm).

2.5.6. Rotating shaft apparatus

An apparatus was constructed according to the proposition of Narazaki et al. (Harada et al., 2006, 2010; Narazaki et al., 2004). The examined tablet was placed on a wire gauze, slightly immersed in water, and pressed by the rotary shaft toward the gauze. Then it was grinded by the rotary motion of the shaft until it disintegrated completely. Disintegration time was registered automatically, when the shaft touched the wire gauze.

2.5.7. BJKSN-13 apparatus

The own-construction apparatus, named briefly as the "BJKSN-13" (abbreviation of the first letters of the authors' names and the year of the publication) was based on the idea of Narazaki et al. (2004) and Harada et al. (2006, 2010), but contained a lot of important modifications as previously described in details (Brniak et al., 2013). Briefly, the volume of medium was reduced to 5 mL, the motion of the shaft was different, and the registration mechanism was based on a magnetic sensor instead of an electric circuit. Real time changes in tablet thickness during disintegration were measured and recorded by computer software. The results were presented as disintegration profiles (tablet thickness vs. time) and registered as graphic files. The disintegration time was calculated from the profile using plot digitalizing software. Two forms of the test were performed: the same as described in the previous work (Brniak et al., 2013) and with additional weight applied to the shaft imitating the pressure of the tongue acting on the tablet (named "BJKSN-14").

2.6. Wetting test

The wetting test described by Bi et al. (1996) was conducted for 6 tablets of each formulation. A tablet weighed prior to the test was placed in a Petri dish with a red dye solution, and the time of wetting the whole surface of the tablet was measured. The wetted tablet was weighed and the amount of water absorbed by the tablet was calculated. The results are expressed as a percent (w/w) of the initial tablet weight.

2.7. Tablets disintegration in the oral cavity

The test was performed six times with every kind of prepared placebo tablets. Six healthy volunteers were informed about the study protocol and signed the written informed consent. Prior to the test, they rinsed their oral cavities with 200 mL of water. The tablet was placed on the tongue and the time until it disintegrated completely was measured. It was prohibited to bite or chew the tablet. Only a gentle tongue movement was allowed (Kakutani et al., 2010). Due to the safety reason, even that tablets contained no active substance, all remaining parts of disintegrated tablet were spit out immediately after the test, and volunteers rinsed their mouth again with at least 200 mL of water.

2.8. In vitro/in vivo correlation of disintegration time

In vitro results measured with every method were compared to the in vivo disintegration time. The Pearson's correlation coefficients were calculated with Microsoft Office 2010 Excel analysis ToolPak. Their significance was tested with Student's *t*-test on the significance level 0.001, 0.01 and 0.05.

3. Results

3.1. Mechanical properties of tablets

The tablets' mechanical properties are summarized in Table 3. All prepared tablets were of excellent mechanical properties. Friability values ranged from 0.18% to 0.36% for tablets with Kollidon CL, and from 0.22% to 0.28% for those with F-MELT. Also, the pharmacopoeial requirement of mass uniformity was fulfilled by every formulation. The maximum mass deviation was 6.2% while the value allowed by Eur. Pharm 7.0 is 7.5%. Tensile strength ranged from 0.71 MPa for the tablet compressed with the lowest compression force and up to 8.25 MPa for tablets compressed with the highest force. Tablets with F-MELT passed the fineness of dispersion test while the ones composed of Avicel and Kollidon CL did not, i.e. after pouring the dispersion through the test sieve some particles still remained on the mesh.

3.2. Disintegration studies

In the presented studies, three different types of in vitro methods of tablet disintegration were used: those where the only factor leading to the disintegration was water wicking into

Table 3 Properties of prepared tablets.

Parameters	Formulation name					
	K_a	K_b	K_c	F_a	F_b	F_c
Average mass (mg)	139.9	132.3	138.7	126.6	132.8	135.4
Maximum mass deviation (%)	5.0	5.1	6.2	3.6	2.4	2.7
Tensile strength (MPa)	0.76	2.25	8.25	0.71	2.24	3.42
Thickness (mm)	4.1	3.3	2.6	3.1	2.8	2.7
Friability (%)	0.36	0.22	0.18	0.28	0.19	0.22
Fineness of dispersion	Do not comply with the pharmacopoeial requirement			Comply with the requirement		

the matrix of the tablet, the tests with water agitation or stirring, and the methods where direct destructive forces were put on the tested tablet, such as grinding or pressing with additional weight (Table 2). Therefore, disintegration tests showed great variability in the data measured with different methods (Table 4). The shortest registered disintegration time was 2.3 s, while the longest greatly exceeded 3 min. The values of disintegration time measured with one method were even more than 60 times lower than with another (e.g. results for formulation K_a measured with a rotating shaft apparatus vs. the sieve method with shaker or a modified paddle apparatus).

Moreover, the differences between in vitro and in vivo results were also tremendous. The only similar result for all performed tests was the elongation of disintegration time caused by the increase in compression force during the tableting process. The same behavior was observed for the wetting time (Table 5). On the other hand, the water absorption ratio was inversely proportional to the compression force used during tablet preparation. Moreover, in every case, the values of this parameter were higher for tablets with Kollidon CL than with F-MELT. In the case of formulations K_a–K_c, the value of this parameter ranged from 116.6% to 178.3% while for F_a–F_c it reached only 32.1–107.1%.

The comparison of disintegration times measured with different methods with in vivo results showed the best correlation in case of own-construction apparatus with additional weight applied to the rotating shaft (Table 6). The value of Pearson's correlation coefficient for this test was 0.9994 ($p < 0.001$). Slightly lower values were found for the rotary shaft apparatus constructed according to Narazaki et al. ($r = 0.9907$ with

Table 4 Disintegration time of tablets (mean values and standard deviations).

Disintegration method	Disintegration time (s)					
	Formulation name					
	K_a	K_b	K_c	F_a	F_b	F_c
Tests with water wicking only						
Test-tube method	11.9 ± 0.3	17.3 ± 1.6	101.6 ± 1.9	5.0 ± 0.6	21.4 ± 2.1	> 3 min
Sieve method	106.4 ± 10.8	> 3 min	> 3 min	18.2 ± 2.1	29.7 ± 6.7	> 3 min
Tests with water movement						
Modified paddle apparatus	> 3 min	> 3 min	> 3 min	7.6 ± 2.1	19.0 ± 6.7	148.3 ± 6.6
Sieve method with shaker	> 3 min	> 3 min	> 3 min	23.1	> 3 min	> 3 min
Tests with other forces (grinding, pressing)						
Pharmacopoeial	10.1 ± 1.0	11.8 ± 1.4	64.3 ± 7.8	7.3 ± 0.9	29.3 ± 17.7	171.6 ± 38.1
Pharmacopoeial – modified	9.3 ± 0.5	13.3 ± 1.5	59.3 ± 7.6	8.3 ± 0.8	29.3 ± 10.4	160.2 ± 9.7
Rotating shaft apparatus	3.3 ± 0.4	5.3 ± 1.2	67.2 ± 7.9	2.3 ± 0.4	25.7 ± 13.5	96.7 ± 15.4
Own construction apparatus	10.3 ± 1.6	19.1 ± 4.9	> 3 min	11.2 ± 1.9	39.5 ± 11.5	> 3 min
Own construction apparatus with additional weight	9.3 ± 1.3	10.1 ± 1.8	97.5 ± 11.2	7.3 ± 1.2	34.4 ± 16.4	> 3 min
Disintegration time measured in vivo						
	8.8 ± 3.0	11.7 ± 6.8	89.9 ± 6.2	7.5 ± 0.9	34.4 ± 11.0	103.7 ± 16.9

Table 5 Wetting time and water absorption ratio of tablets.

Parameters	Formulation name					
	K_a	K_b	K_c	F_a	F_b	F_c
Wetting time (s)	4.6 ± 1.6	5.2 ± 1.9	40.7 ± 8.1	4.0 ± 1.1	17.9 ± 1.7	64.5 ± 9.9
Water absorption ratio (%)	178.3 ± 15.4	160.3 ± 17.5	116.6 ± 24.2	107.1 ± 10.5	80.2 ± 6.2	32.1 ± 11.1

Table 6 Correlation of in vitro results with in vivo disintegration time.

Method	Pearson's correlation coefficient
Own construction apparatus with additional weight (BJKSN 2014)	0.9994 ($p < 0.001$)
Rotating shaft apparatus	0.9907 ($p < 0.001$)
Own construction apparatus (BJKSN 2013)	0.9846 ($p < 0.05$)
Test-tube method	0.9766 ($p < 0.01$)
Pharmacopoeial	0.8925 ($p < 0.05$)
Pharmacopoeial – modified	0.8882 ($p < 0.05$)
Modified paddle apparatus	0.9798 (not significant)
Sieve method	−0.3528 (not significant)
Sieve method with shaker	Calculation impossible

$p < 0.001$). It is noticeable that also the simplest method with the test-tube correlated very well with in vivo results ($r = 0.9766$, $p < 0.01$).

The application of own-construction apparatus allowed the registration of disintegration profiles of analyzed tablets. They are registered with a magnetic sensor based on Hall's effect and show changes in the thickness of a tablet in the function of time – as described in details in our previous work (Brniak et al., 2013). The examples of such profiles are presented in Figs. 1 and 2. The different behavior of tablets during the disintegration process can be observed, which is dependent on the kind of excipients used as well as the compression force during tableting. Disintegration profiles of tablets compressed with lower forces (K_a and F_a) are very similar. Tablets swelled a little and disintegrated very rapidly, i.e. in less than 10 s. However, tablets compressed with higher forces disintegrated in a different way. If Kollidon and MCC were present in the matrices they swelled prior to immediate disintegration (Fig. 1). The thickness of the tablets K_c increased by about 25% before rapid disintegration, which is visible on the plot as a green line going up. Otherwise, tablets with F-MELT disintegrated gradually without any significant swelling reported (Fig 2).

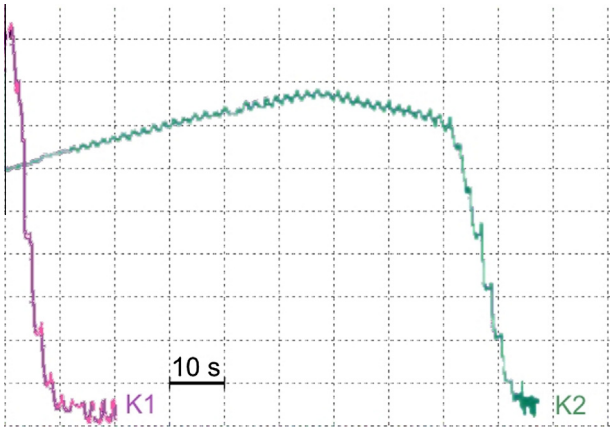

Figure 1 Disintegration profiles (tablets thickness vs. time) registered with BJKSN-14 apparatus for tablets with Kollidon.

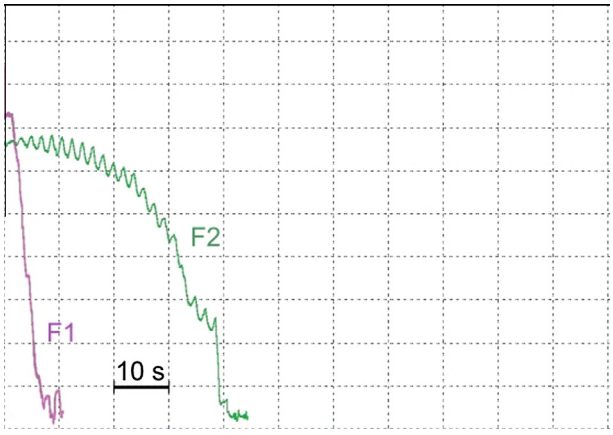

Figure 2 Disintegration profiles (tablets thickness vs. time) registered with BJKSN-14 apparatus for tablets with F-MELT.

4. Discussion

It was previously reported in several studies that the pharmacopoeial method used to measure disintegration time of orally disintegrating tablets cannot be effectively used for prediction of this parameter in vivo (Abdelbary et al., 2005; Brniak et al., 2013). It is rather used only as a quality control parameter. Therefore, other alternative tests reflecting more or less in vivo conditions of ODTs disintegration in the human mouth were proposed. In this study, we compared some of these methods with the results achieved with our own-construction apparatus as well as in vivo disintegration time. The applied methods could be divided into three groups in regard to the forces acting on the tablets during the tests.

Disintegration of tablets in the human mouth is caused by several factors. Water from saliva causes swelling and deformation of the tablet mass through the capillary action. The pressure of the tongue causes squeezing and grinding of the tablet between the surface of the tongue and the upper palate. The tablet mass can also be partially or completely dissolved in the saliva depending on the excipients and pharmaceutical substance used. It mainly occurs in the case of lyophilized formulations containing water soluble drug substances, and causes their disintegration in a matter of seconds. On the other hand, ODTs prepared by the direct compression method usually contain at least some excipients poorly soluble in water, and the dissolution is less important in the mechanism of their disintegration.

The results of our study showed the highest correlation of in vitro data with disintegration time measured in vivo in the case of methods featuring additional force applied to the tablets such as grinding, shearing or pressing of the pulped wetted tablet mass. This indicated that imitation of the tongue acting on the tablet is important in reflecting the in vivo condition. Therefore, tests performed without any other force acting on the tablet other than water wicking into its matrix revealed in most cases a longer disintegration time, and their correlation with the in vivo results was lower. For example, the tablet disintegration time measured with the simple sieve method was usually longer than the required 3 min even for formulations disintegrating as fast as 12 s in the human mouth. The only static method (i.e. without agitation or shearing) with good in vivo correlation was a simple test-tube disintegration test with Pearson's correlation coefficient reaching a value of 0.9766 ($p < 0.01$).

During the studies, two different modifications of our own novel method of disintegration time measurement were tested. The tests were conducted in the same way as described previously (Brniak et al., 2013) as well as with additional weight applied to the rotating shaft. The idea of this modification came from the results of human tongue pressure measurement. As reported in literature, the maximum isometric pressure can vary greatly with age, and ranges from 18.5 kPa in 3 year old children to as much as 78 kPa in adult men (Utanohara et al., 2008; Potter and Short, 2009; Youmans et al., 2009). It is also strongly dependent on the type of measuring equipment used. The study of Utanohara et al. (2008) performed on a group of 853 healthy subjects of both genders in the ages 20–79 reported the range of maximal tongue pressure acting on the upper palate as 32–42 kPa. This was the value of maximal pressure during the 7 s compression of a balloon type probe

placed in the subjects' mouth. There is no available report in the literature showing the pressure acting on the ODT tablet during disintegration in human mouth. It is rather obvious, that the value of that pressure has to be lower than the MIP. Therefore, the value of the pressure affected by the rotating shaft in our original study protocol (i.e. 13.5 kPa) seems to be reasonable. However, in the present study also the experiments with additional weight attached to the shaft were performed. It increased pressure to as much as 42.9 kPa, which was the similar value as MIP reported by Utanohara et al. (2008). The modification resulted in an even higher correlation with the in vivo results – Pearson's correlation coefficient increased from 0.9846 to 0.9994 with $p < 0.001$.

Another aspect of the presented studies was to compare the ready to use co-processed excipient F-MELT with Kollidon CL and MCC. Tablets with superdisintegrant and filler were harder than those with a co-processed substance, and their disintegration times were usually shorter. In order to compare the mouthfeel of tablets containing those different excipients, the fineness of dispersion test according to the European Pharmacopoeia 7.0 was performed. This test is required for dispersible tablets. If they do not pass the test, it indicates that the particles of the suspension created after dispersion of a tablet in water are too big and can give a rough and sandy feel in the mouth. If a tablet passes the test, it means that the particles are fine enough to be palatable for the patient. All tablets with F-MELT passed this test which suggested that their mouthfeel could be acceptable (Table 3). On the other hand, none of the tablets with Kollidon CL and MCC passed the test, i.e. they are not suitable for orodispersible tablets. The wetting test revealed greater water absorption ratio for formulations K_a–K_c that was caused by the high water absorbing properties of microcrystalline cellulose, which was the main component of those tablets. It was also easily visible on the disintegration profiles that tablets containing Kollidon CL and MCC swelled much more than those with F-MELT (Figs. 1 and 2). The excessive swelling can cause an unpleasant mouthfeel and is rather not desirable in orodispersible tablets.

5. Conclusion

This research has shown that development of novel methods of ODT's disintegration time measurement is eligible and scientifically justified. Particularly, it is important to develop methods that better reflect conditions in the oral cavity than the pharmacopoeial method. The volume of medium, its temperature, and the type of forces acting on the tablet during a disintegration test are all important factors affecting the disintegration process. In order to mimic in vivo conditions, all these aspects should be taken into consideration during the novel methods development process.

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References

Abdelbary, G., Eouani, C., Prinderre, P., Joachim, J., Reynier, J., Piccerelle, P., 2005. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int. J. Pharm. 292, 29–41.
Bandari, S., Mittapalli, R.K., Gannu, R., Rao, Y.M., 2008. Orodispersible tablets: an overview. AJP 1, 1–11.
Bhowmik, D., Chiranjib, B., Krishnakanth, Pankaj, Chandira, R.M., 2009. Fast dissolving tablet: an overview. J. Chem. Pharm. Res. 1, 163–177.
Bi, Y., Sunada, H., Yonezawa, Y., Danjo, K., Otsuka, A., Iida, K., 1996. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem. Pharm. Bull. 44, 2121–2127.
Brniak, W., Jachowicz, R., Krupa, A., Skórka, T., Niwiński, K., 2013. Evaluation of co-processed excipients used for direct compression of orally disintegrating tablets (ODT) using novel disintegration apparatus. Pharm. Dev. Technol. 18, 464–474.
Harada, T., Narazaki, R., Nagira, S., Ohwaki, T., Aoki, S., Iwamoto, K., 2006. Evaluation of the disintegration properties of commercial famotidine 20 mg orally disintegrating tablets using a simple new test and human sensory test. Chem. Pharm. Bull. 54, 1072–1075.
Harada, T., Uchida, T., Yoshida, M., Kobayashi, Y., Narazaki, R., Ohwaki, T., 2010. A new method for evaluating the bitterness of medicines in development using a taste sensor and a disintegration testing apparatus. Chem. Pharm. Bull. 58, 1009–1014.
Kakutani, R., Muro, H., Makino, T., 2010. Development of a new disintegration method for orally disintegrating tablets. Chem. Pharm. Bull. 58, 885–890.
Morita, Y., Tsushima, Y., Yasui, M., Termoz, R., Ajioka, J., Takayama, K., 2002. Evaluation of the disintegration time of rapidly disintegrating tablets via a novel method utilizing a CCD camera. Chem. Pharm. Bull. 50, 1181–1186.
Motohiro, O., Hayakawa, E., Ito, K., Tokuno, M., Morimoto, K., Watanabe, K., 2001. US Patent Application 20010014340 (Aug 16).
Narazaki, R., Harada, T., Takami, N., Kato, Y., Ohwaki, T., 2004. A new method for disintegration studies of rapid disintegrating tablet. Chem. Pharm. Bull. 52, 704–707.
Potter, N.L., Short, R., 2009. Maximal tongue strength in typically developing children and adolescents. Dysphagia 24, 391–397.
Rawas-Qalaji, M.M., Simons, F.E.R., Simons, K.J., 2009. Fast disintegrating sublingual tablets effect of epinephrine load on tablet characteristics. AAPS PharmSciTech, 7.
Sunada, H., Bi, Y., 2002. Preparation, evaluation and optimization of rapidly disintegrating tablets. Powder Technol. 122, 188–198.
Szakonyi, G., Zelkó, R., 2013. Prediction of oral disintegration time of fast disintegrating tablets using texture analyzer and computational optimization. Int. J. Pharm. 448, 346–353.
The Council of Europe: The European Pharmacopoeia, 7th Edition, Strasbourg, France, 2010.
US Department of Health and Human Services, 2008. Guidance for Industry: Orally disintegrating tablets, FDA, CDER, Chemistry.
Utanohara, Y., Hayashi, R., Yoshikawa, M., Yoshida, M., Kazuhiro, T., Akagawa, Y., 2008. Standard values of maximum tongue pressure taken using newly developed disposable tongue pressure measurement device. Dysphagia 23, 286–290.
Watanabe, Y., Koizumi, K., Zama, Y., Kiriyama, M., Matsumoto, Y., Matsumoto, M., 1995. New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a disintegrant. Biol. Pharm. Bull. 18, 1308–1310.
Youmans, S.R., Youmans, G.L., Stierwalt, J.A.G., 2009. Differences in tongue strength across age and gender: is there a diminished strength reserve? Dysphagia 24, 57–65.