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A new formulation for orally disintegrating tablets using a suspension spray-coating method

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ABSTRACT

The aim of this study was to design a new orally disintegrating tablet (ODT) that has high tablet hardness and a fast oral disintegration rate using a new preparation method. To obtain rapid disintegration granules (RDGs), a saccharide, such as trehalose, mannitol, or lactose, was spray-coated with a suspension of corn starch using a fluidized-bed granulator (suspension method). As an additional disintegrant, crospovidone, light anhydrous silicic acid, or hydroxypropyl starch was also included in the suspension. The RDGs obtained possessed extremely large surface areas, narrow particle size distribution, and numerous micro-pores. When tabletting these RDGs, it was found that the RDGs increased tablet hardness by decreasing plastic deformation and increasing the contact frequency between granules. In all tablets, a linear relationship was observed between tablet hardness and oral disintegration time. From each linear correlation line, a slope (D/H value) and an intercept (D/H_0 value) were calculated. Tablets with small D/H and D/H_0 values could disintegrate immediately in the oral cavity regardless of the tablet hardness and were considered to be appropriate for ODTs. Therefore, these values were used as key parameters to select better ODTs. Of all the RDGs prepared in this study, mannitol spray-coated with a suspension of corn starch and crospovidone (2.5:1 w/w ratio) showed most appropriate properties for ODTs; fast *in vivo* oral disintegration time, and high tablet hardness. In conclusion, this simple method to prepare superior formulations for new ODTs was established by spray-coating mannitol with a suspension of appropriate disintegrants.

1. Introduction

The development of an appropriate dosage form for older people, children, and bedridden patients has been widely desired because it can be difficult for these patients to swallow conventional tablets or capsules. In these patients, medication compliance and therapeutic effect could be improved by taking orally disintegrating tablets (ODTs) that can rapidly and easily disintegrate in the oral cavity without water (FDA, Rockville, MD, 2008; William and Tapash, 2005). ODTs were defined as a solid dosage form containing medicinal substances that disintegrate within a matter of seconds when placed upon the tongue (CDER, 1992). In the European Pharmacopoeia, ODTs were defined as *Orodisperse* that can be placed in the mouth where it disperses rapidly before swallowing (EP, 2008). As a requirement in these regulations, the relative bioavailability (BA) of ODTs should be the same as that of conventional dosage forms after administering with or without water.

Recently, ODTs are becoming increasingly popular around the world. Based on requests from patients to enhance their quality of life (QOL), new types of ODTs have been developed and then released globally by many pharmaceutical companies. In addition, numerous reports have been published regarding the technologies to prepare ODTs (Watanabe et al., 1995a,b; Bi et al., 1999a,b,c; Chang et al., 2000; Ishikawa et al., 2001; Schiermeier and Schmidt, 2002).

ODTs can be classified into three generations according to differences in the preparation method. In the first-generation, ODTs were prepared by a freeze-drying method. This method was developed and commercialized by Cardinal Health as Zydis® (Seager, 1998). This ODT was prepared by freeze-drying drug suspensions with specific additives, which was filled into the pockets of the press-through packing (PTP). Although the ODTs of this first-generation showed very rapid disintegration, their handling was difficult for patients because the tablets were very friable and highly sensitive to moisture. In addition, these ODTs had a disadvantage that this method could not be applied along with taste-masking compounds for bitter-tasting drugs or for high-dose drugs. In the second-generation, the ODTs were prepared by drying the drug and additives after tabletting their wet mass. This preparation method

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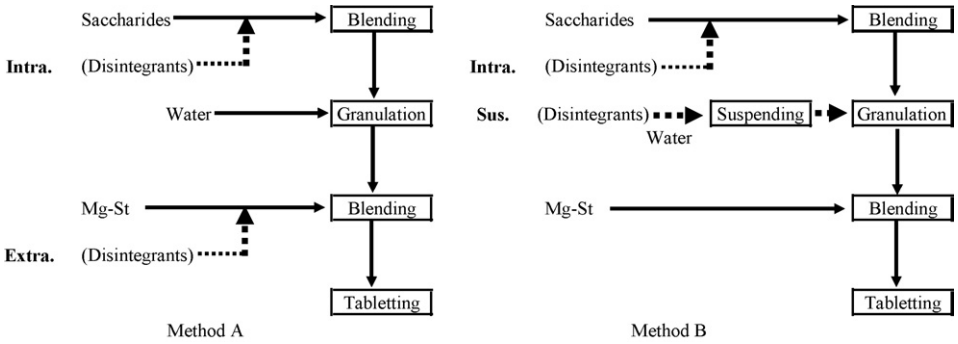

Fig. 1. Manufacturing process for orally disintegrating tablets (method B) and conventional tablets (method A) using fluidized-bed granulator. Method A is divided into the following three methods: Intra., Extra., and no adding. Method B is divided into two methods: Intra./Sus. and Sus.

was developed by Tushima (2001) and commercialized as EPM® tablets. Third-generation ODTs were developed where dry mass including the drug and saccharides were tabletted. This method has been modified by many researchers, and many different types of ODTs have been generated using this approach. For example, WOWTAB-DRY® was completed by applying the crystalline transition of amorphous sucrose after tabletting (Mizumoto, 2005; Sugimoto et al., 2005, 2001, 2006a,b). OraSolv® was prepared by low-pressure compression with foaming agents (Wehling et al., 1991), and Flashtab® was prepared by low-pressure compression of dry powder granules containing the drug, disintegrants, and microcrystalline cellulose (Cousin et al., 1995).

However, the ODTs developed as the first to third generations have disadvantages because all these ODTs have high porosity, low density, and low hardness, in order to achieve their rapid disintegration rates. Because these properties resulted in extremely brittle tablets, they are difficult for pharmacists and patients to handle in the hospital and at home. Furthermore, special equipment, such as a freeze-dryer for wet mass filled into PTP packaging, a tabletting machine for wet mass methods, and drying and wetting chambers for the crystalline transition of amorphous sucrose, are required to prepare these ODTs.

To overcome the above problems, the tablet hardness of ODTs should be improved while retaining their rapid disintegration rate. As a preparation method, the usefulness of direct compression has been reported, in which high compressible disintegrants, such as microcrystalline cellulose or low substituted hydroxypropyl cellulose, were used (Watanabe et al., 1995a,b; Bi et al., 1999a,b,c). However, ODTs prepared by direct compression methods were reported to show incomplete dissolution and swelling of including additives that resulted in a rough feeling on the tongue and delayed disintegration rate in the mouth (Bi et al., 1996; Ishikawa et al., 2001).

In this study, to improve all of the issues for these ODTs, a new ODT, which had high tablet hardness and a fast disintegration rate, was designed using a simple preparation method. The new ODTs were composed of rapid disintegration granules spray-coated with a suspension of appropriate additives using a fluidized-bed granulator. The appropriate additives for the rapid disintegration granules were chosen from several saccharides and disintegrants, and then the physical properties of the new ODTs were evaluated in comparison with those of the first to third-generation ODTs.

2. Materials and methods

2.1. Materials

As saccharides, trehalose (Asahi Kasei Co., Ltd., Japan), D-mannitol (Merck Co., Ltd., Japan), and lactose (Borcuro Co., Ltd., Japan) were used. As disintegrants, corn starch (Nippon Shokuhin Kako Co., Ltd., Japan), crospovidone (ISP Co., Ltd., Japan), hydroxypropyl starch (Freund Industries, Japan) were used. All other materials used in the study were of Japanese Pharmacopoeia (JP) grade.

2.2. Methods

2.2.1. Preparation of orally disintegrating tablets (ODTs)

Fig. 1 shows the manufacturing process for ODTs (method B) and conventional tablets (method A) using a fluidized-bed granulation. Method A was divided into the following three methods: intra method; adding the disintegrant before granulating, extra method; adding the disintegrant after granulating, no adding method; disintegrants were not added. Method B was also divided into the following two methods: an intra/suspension method, adding disintegrant before granulating with a suspension of disintegrant/water; and a suspension method, granulating only with suspension of disintegrant/water. To study the effect of the preparation method using corn starch as the disintegrant on the physicochemical properties of ODTs, the prototype tablets were prepared based on formulas and the method presented in Table 1. In this study, granulating was performed using a fluidized-bed granulator (MP-01, Powrex, Japan) at 500 g scale. After magnesium stearate was blended with the granules by shaking in a plastic bag, the 250 mg prototype tablets were compressed using a rotary tabletting machine (VIRG, Kikusui Seisakusho, Japan).

2.3. Evaluation of granules and tablets

2.3.1. Particle size

The mean particle size (D_{50}) of the granules prepared by fluidized-bed granulation was measured using a laser particle counter (LA-920, HORIBA Corporation, Japan).

2.3.2. Particle properties and scanning electron microscopy (SEM)

The aspect ratio and circularity of the granules were measured using a particle shape image analyzer (PITA-1, Seishine Corporation, Japan). Scanning electron microscopy (SEM) of the granules was performed using a scanning electron microscope (VE-7800S; KEYENCE, Japan).

2.3.3. True density

The true density of the granules prepared by fluidized-bed granulation was measured using a gas pycnometer (Ultra Pycnometer 1000; YUASA-Ionics Corporation, Japan).

2.3.4. Specific surface area

The specific surface area of the granules prepared by fluidized-bed granulation was measured using a specific surface area and pore diameter (NOVA 4200e; Quantachrome Corporation, USA).

Table 1
Formulation of orally disintegrating tablets (250 mg/tablet).

Material	(Conditions)	Formula.No									
		TrD-1	TrD-2	TrD-3	TrD-4	TrD-5	LcD	MaD	CPD	HSD	LSD
Trehalose		247.5	177.5	177.5	177.5	177.5					
Mannitol								177.5	237.5	177.5	235
Lactose							177.5				
Corn starch	(Sus.)				20	70	70	70			
Corn starch	(Intra.)			70	50						
Corn starch	(Extra.)		70								
Crospovidone	(Sus.)								10		
Hydroxypropyl starch	(Sus.)									70	
Light anhydrous silicic acid	(Sus.)										12.5
Magnesium stearate		←					2.5				→
Manufacturing process		A	A	A	B	B	B	B	B	B	B

2.3.5. Tablet hardness

The hardness of the tablets was measured using a tablet hardness tester (KHT-20N, FUJIWARA Corporation, Japan).

2.3.6. Disintegration time in the oral cavity

The complete disintegration time of the tablets in the oral cavity was evaluated in five healthy volunteers. The end point for the disintegration in the mouth was the time when the tablet placed on the tongue had disintegrated until no lumps remained. The volunteers rinsed out their mouth with water before the test. The protocol and experimental design for all disintegration tests in the oral cavity was approved by the Ethical Committee of TOWA Pharmaceutical Co., Ltd.

3. Results and discussion

3.1. Development of a new method to prepare orally disintegrating tablets

Saccharides have been used widely as a filler for conventional tablets because of their low-price, high-solubility, sweet taste, and high compressibility, in which the saccharide particles undergo plastic deformation during tabletting. For the design of orally disintegrating tablets (ODTs), saccharides can be utilized as appropriate additives. However, their high compressibility might be a disadvantage because it will induce a delay in disintegration. In this study, to improve this property of saccharides, their surface was modified using corn starch. It is well known that corn starch can act as a filler, binder, disintegrant, and glidant (Oladapa, 2006). As shown in Table 2, the mean particle size of corn starch was small enough (10–20 μm) to perform as the best wicking agent to improve the saccharide surface.

In order to select an optimum method to modify the surface of saccharide with corn starch, five different ODTs from formulations TrD-1 to 5 were prepared. In these formulations, trehalose was used as the saccharide. The total amount of corn starch was fixed to 70 mg/tablet (28% of total weight) for TrD-2 to 5 because the ratio of corn starch around 30% is recommended for the general formulation of tablets in Japan (Sunada et al., 1998). For formulation TrD-1, trehalose was granulated with purified water using the fluidized-bed granulator and then was tabletted as an ODT. In the case of formulation TrD-2, corn starch was added after the granulation of trehalose and then compressed. For formulation TrD-3, the mixture of trehalose and corn starch was granulated with purified water using the fluidized-bed granulator and then compressed. The formulations TrD-4 and TrD-5 were prepared after improving the surface properties of trehalose. For formulation TrD-5, corn starch was completely spray-coated as a suspension onto the trehalose surface. On the other hand, in formulation TrD-4, part of the corn starch was spray-coated as a suspension and then the residual corn starch was added to the intra phase.

The relationship between the hardness and compression force of five ODTs is shown in Figs. 2 and 3 also shows the relationship between the hardness of tablets compressed with varying forces

Table 2
Physical properties of the materials used.

Material	Particle size, D_{50} (μm)	Solubility, (g/100 mL water)	True density (g/cm^3)	Melting point (°C)
Trehalose	75.1[a]	77.5[b]	1.53[b]	97[b]
Mannitol	64.3[a]	16.7[b]	1.48[b]	188–189[b]
Lactose	58.2[a]	20[b]	1.52[b]	219[b]
Corn starch	19.9[a]	–	1.48[b]	–
Crospovidone	16.1[a]	–	1.22[c]	–
Hydroxypropyl starch	12.9[b]	–	–	–

[a] Measured by laser particle counter (LA-920, HORIBA).
[b] Cited from production catalogues.
[c] Measured by gas pycnometer (Ultra Pycnometer 1000, Yuasa-Ionics Co., Ltd).

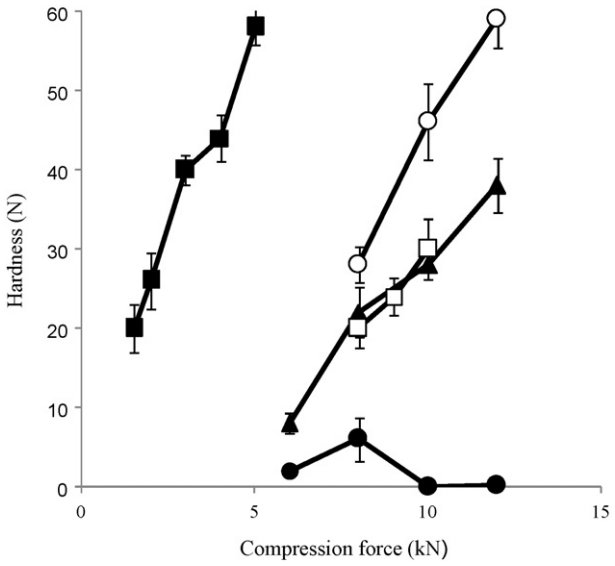

Fig. 2. Relationship between compression force and tablet hardness by various preparation methods. TrD-1 (■), TrD-2 (●), TrD-3 (▲), TrD-4 (□), and TrD-5 (○).

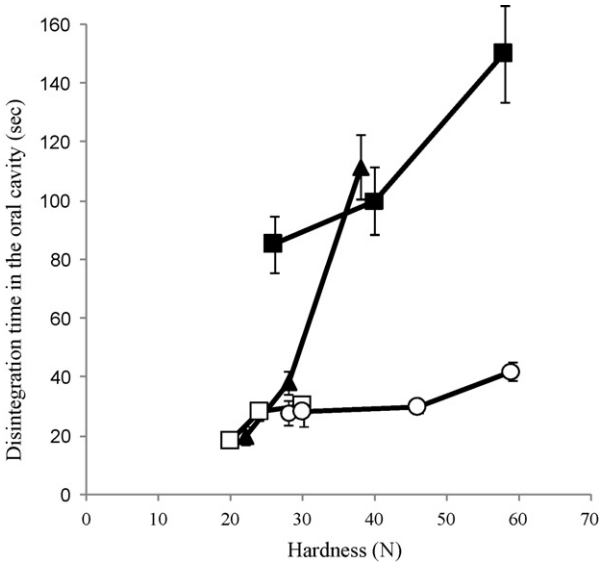

Fig. 3. Relationship between tablet hardness and disintegration time in the oral cavity by various preparation methods. TrD-1 (■), TrD-3 (▲), TrD-4 (□), and TrD-5 (○).

and their disintegration time in the oral cavity (oral disintegration time). TrD-1 showed high compressibility at a low compression force of 1.5 kN, while this tablet showed prolonged oral disintegration time because corn starch was not added. TrD-2 showed low compressibility and capping at a compression force of 10–12 kN. In addition, the fluidity of granules blended with corn starch was low. These findings clearly suggested the inadequacy of formulation TrD-2 for ODTs. Although TrD-3 had high tablet hardness (over 30 N), this tablet also showed prolonged oral disintegration time, indicating the plastic deformation of trehalose because of compression. On the other hand, the tablet hardness of both TrD-4 and 5 was higher with increasing tablet compression force, whereas the oral disintegration time of these tablets was much shorter than those of other formulations even at high compression force.

Generally, the compression process for tabletting was divided into three stages: particle rearrangement, compression, and depression (Otsuka et al., 1997). After these processes, plastic deformation of granules in the tablet occurs (Shu et al., 2002). Therefore, the results in Figs. 2 and 3 implied that the compression process lead to the plastic deformation of trehalose granules, which could be avoided by spray-coating with corn starch in TrD-4 and 5. In addition, spray-coated corn starch increased the contact frequency between the granules.

Fig. 4 shows scanning electron micrographs (SEM) of the physical mixture of trehalose and corn starch (a: physical mixture), the granules of trehalose and corn starch prepared by conventional granulation (b: conventional method), and granules of trehalose spray-coated using the corn starch suspension (c: suspension method). From these pictures, it was revealed that the surface of granules prepared by the suspension method was completely coated by corn starch particles.

Although the suspension method was considered to be the most appropriate for the surface modification of saccharides with corn starch, significant differences between formulations TrD-4 and 5 were not detected in Fig. 3. In order to investigate the role of intra phase corn starch, ODTs were prepared using granules of varying ratios of intra corn starch amounts, and then the relationship between tablet hardness and oral disintegration time was evaluated (Fig. 5). In Fig. 5, good correlations between the tablet hardness and oral disintegration time were observed in all ODTs. From each linear correlation line, a slope and an intercept were calculated by the curve fitting method. The slope (D/H value) means the oral disintegration time in unit tablet hardness. The intercept (D/H_0 value) represents the oral disintegration time when tablet hardness reaches zero, meaning an intrinsic potency of granules for disintegration (disintegratability). Because ODTs with small D/H and D/H_0 values could disintegrate immediately in the oral cavity regardless of the tablet hardness; these values are considered to be key parameters to select better ODTs. In the following studies, these parameters were used for screening to select the best formulation of ODTs.

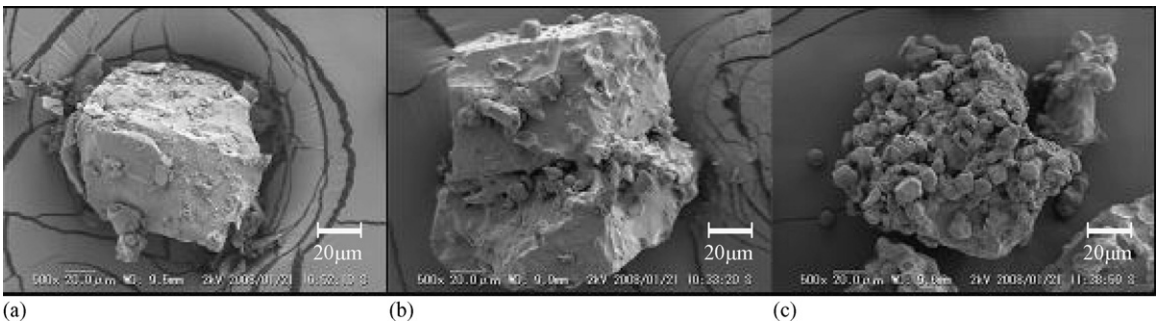

Fig. 4. Scanning electron micrographs of surface-modified trehalose by conventional and suspension method. (a) Physical mix; (b) conventional method; (c) suspension method.

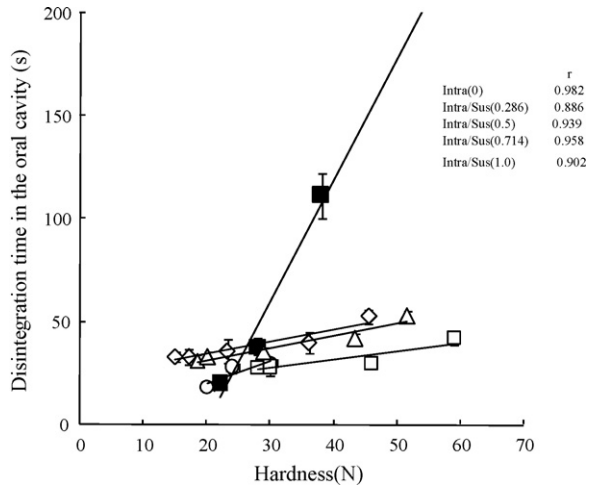

Fig. 5. Relationship between tablet hardness and disintegration time in the oral cavity by suspension method. Intra. (■), Intra./Sus.: (0.286) (○), Intra./Sus.: (0.5) (◊), Intra./Sus.: (0.714) (Δ), and Intra./Sus.: (1.0) (□).

In Fig. 6, the D/H values from all ODTs are plotted against the ratio of intra and spray-coated corn starch. The D/H value decreased with the increasing spray-coating ratio of corn starch. In particular, in the case of ODTs with a spray-coating ratio of more than 30%, the D/H value of ODTs was small and did not depend on the tablet hardness. These results clearly suggested that appropriate ODTs could be prepared using the suspension method.

3.2. Selection of appropriate a saccharide for orally disintegrating tablets

Because the suspension method was found to be useful to prepare ODTs using trehalose and corn starch, the influence of different saccharides on ODTs properties was investigated. First, as alternate saccharides, mannitol and lactose were chosen instead of trehalose, and tablets were prepared with each saccharide spray-coated with corn starch using the suspension method. Tablets prepared with trehalose were used as the reference. In Fig. 7, the relationship is compared between tablet hardness and the oral disintegration time of each tablet. Among the three saccharides, mannitol gave the smallest D/H value. The difference in D/H value depended on the magnitude of compactability of saccharides. On the other hand, D/H_0 was lowest for lactose followed by mannitol < trehalose. This

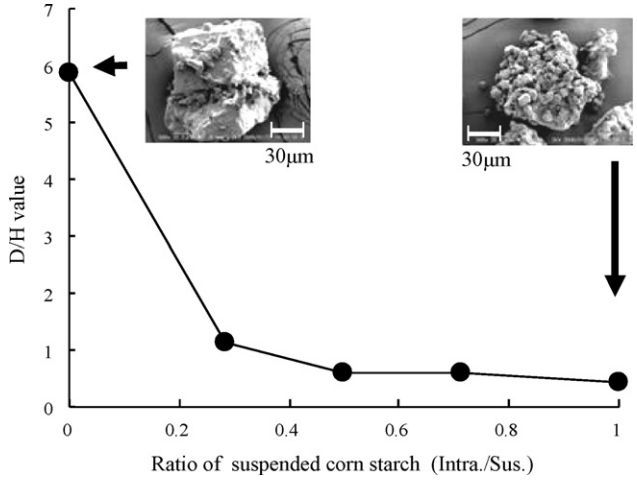

Fig. 6. Relationship between the ratio of suspended corn starch (Intra./Sus.) and D/H value.

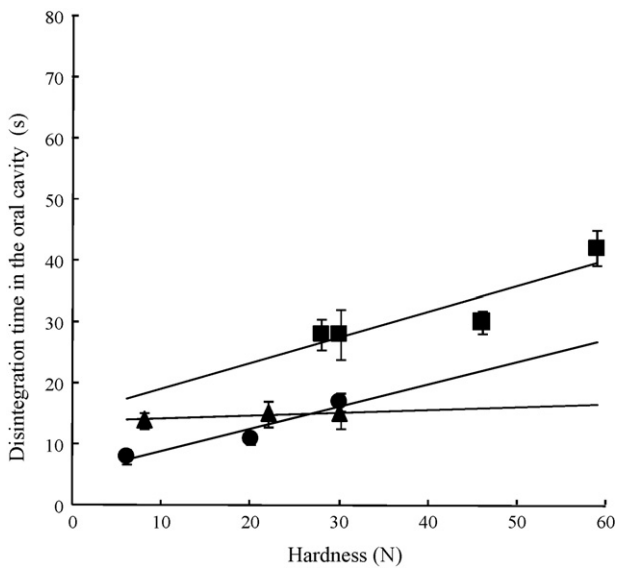

Fig. 7. Relationship between tablet hardness and disintegration time in the oral cavity when tabletted using various compression forces (6–12 kN). Trehalose (■), lactose (●), and mannitol (▲).

rank order could relate to the magnitude of the binding force of saccharides, which correlates with their melting point, as shown in Table 2. In addition, it was revealed that the D/H value of ODTs was reduced remarkably by spray-coating with corn starch regardless of the saccharides used. From the results in Fig. 7 and Table 2, mannitol was chosen as the most appropriate saccharide for ODTs and was used in the following studies.

3.3. Selection of appropriate disintegrants for orally disintegrating tablets

Corn starch showed appropriate properties as a disintegrant for ODT when spray-coating the surface of saccharides by the suspension method. However, as shown in Fig. 7, the hardness of tablets reached to a plateau around 30 N at a compression force of 8 kN. Because this tablet hardness was too low to use clinically, mannitol was spray-coated with other additives mixed with corn starch to improve its usability. As other additives, three different disintegrants were chosen (crospovidone, hydroxypropyl starch, and light anhydrous silicic acid).

At first, ODTs were prepared from granules, in which mannitol was spray-coated with suspension of the three disintegrants without corn starch (Table 1, CPD, HSD, and LSD). Fig. 8 shows the relationship between the hardness of tablets (when compressed by various tabletting pressures) and their oral disintegration times. In the case of crospovidone and light anhydrous silicic acid, because the viscosity of suspension solution (28%) was too high to use for spray-coating, the percentage of these disintegrants in the formulation was decreased to 4% and 5%, respectively.

The D/H value was largest when light anhydrous silicic acid was used as a disintegrant followed by hydroxypropyl starch > crospovidone. Because crospovidone showed the lowest D/H value up to about 70 N, it was suggested that the plasticity of the tablets with this additive was very small. On the other hand, the D/H_0 value showed the following rank order: hydroxypropyl starch > crospovidone > light anhydrous silicic acid. This might relate to the micro-pore ratio among these additives, because light anhydrous silicic acid is well known as a porous compound. The D/H and D/H_0 values, which were calculated from Figs. 7 and 8, are summarized in Table 3. Among these three disintegrants, crospovidone showed the lowest D/H value with similar low D/H_0

Table 3
D/*H* value of ODTs with various combination of excipients and disintegrants.

Excipients	Disintegrants	*D*/*H* value (slope)	DT-lim (intercept)
Trehalose	Corn starch[a]	5.8520	ND
Trehalose	Corn starch[b]	0.4305	15.03
Mannitol	Corn starch[b]	0.0484	13.70
Lactose	Corn starch[b]	0.3647	5.19
Mannitol	Crospovidone[b]	0.1346	11.46
Mannitol	Hydroxypropyl starch[b]	0.5204	23.67
Mannitol	Light anhydrous silicic acid[b]	2.4150	2.81

[a] Conventional method.
[b] Suspension method.

values. It was considered that (1) crospovidone can minimize the plastic deformation by compression because it forms hard particles and (2) crospovidone can keep the air spaces between the particles after tabletting. Crospovidone is provided as an amorphous form that generates spherical particles with a large specific surface area. In addition, crospovidone is reported to be a powder with excellent fluidity and compression compactability (Bolhuis et al., 1984; Shu et al., 2002; Van Kamp et al., 1987). From the present results and its previously reported properties, crospovidone was selected as an appropriate disintegrant to attract corn starch for ODTs.

As the next step, to determine an appropriate composition ratio of corn starch and crospovidone, three different ODTs were prepared, in which the ratio of corn starch and crospovidone were set to 13:1, 6:1, and 2.5:1 (w/w ratio). Fig. 9(a) shows the relationship between compression force (up to 14 kN) and tablet hardness. The hardness increased with increasing compression force and the amount of crospovidone. In the case of ODT with a 2.5:1 ratio, the tablet hardness could be enhanced higher than 70 N, whereas that of tablet with a 13:1 ratio decreased when the compression force was increased to 14 kN. Although ODT with a 2.5:1 ratio showed higher D/H and D/H_0 values than other ODTs in Fig. 9(b), the ratio of corn starch and crospovidone was set to 2.5:1 to obtain enough hardness for tablets for clinical use. This newly developed ODT was named RACTAB as the trade name for commercial release.

The oral disintegration time of RACTAB was compared with those of other commercially available ODTs. Fig. 10 shows the relationship between tablets hardness and oral disintegration time of all ODTs. The oral disintegration time of RACTAB was constant and was shortest at high tablet hardness, while that of commercial ODTs gradually increased with increasing tablet hardness. This result clearly indicated that RACTAB possessed superior properties as an ODT compared with other tablets.

3.4. Disintegration mechanism of new orally disintegrating tablets

To clarify the disintegration mechanism of RACTAB, pharmaceutical and geometrical properties of the rapid disintegration granules (RDGs) in which mannitol was spray-coated with the suspension of corn starch and crospovidone using the fluidized-bed granula-

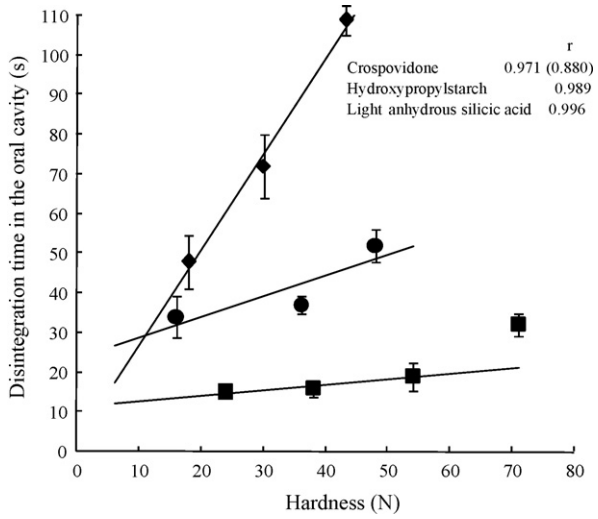

Fig. 8. Relationship between tablet hardness and disintegration time in the oral cavity, when tabletted using various compression forces. Crospovidone (■), hydroxypropyl starch (●), and light anhydrous silicic acid (♦).

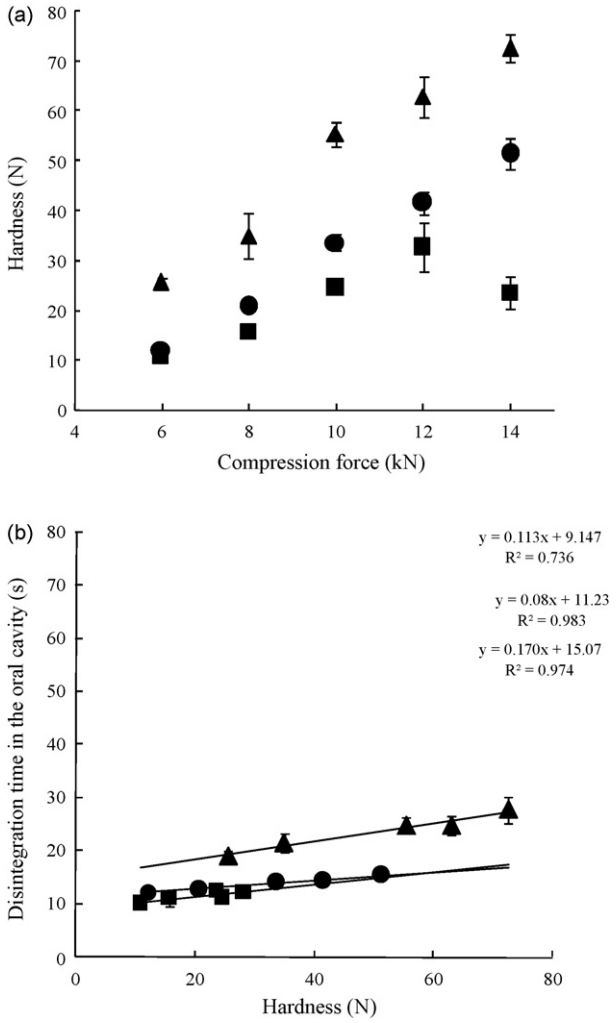

Fig. 9. The effect of the combination of corn starch and crospovidone on the properties of ODTs, by suspension method. (a) Relationship between compression force and tablet hardness. (b) Relationship between tablet hardness and disintegration time in the oral cavity. Ratio of corn starch/crospovidone; 13:1 (■), 6:1 (●), and 2.5:1 (▲).

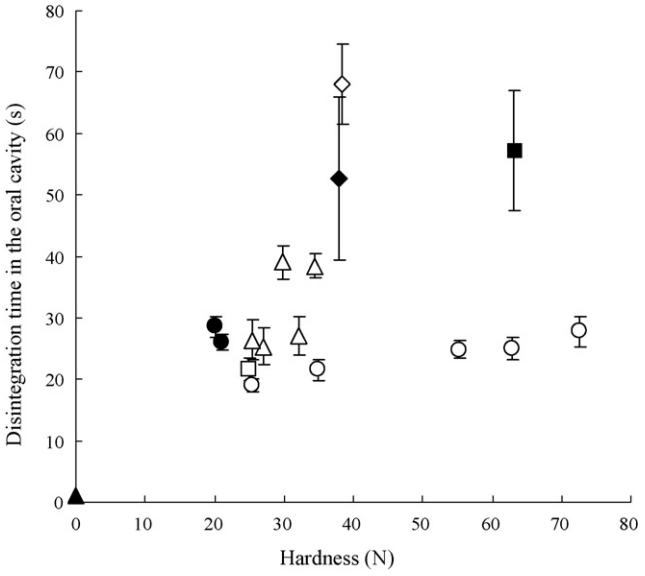

Fig. 10. Relationship between tablet hardness and disintegration time in the oral cavity of ODTs prepared by the suspension method (○) and the conventional method (●, □, ■, ♦, ◊, ▲, △).

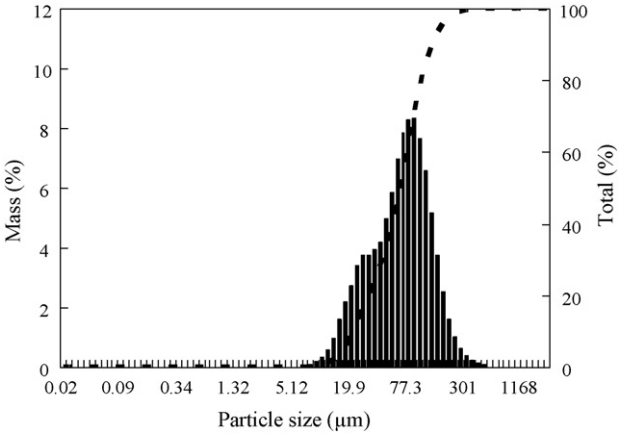

Fig. 11. Particle distribution of rapidly disintegrating particles.

tor were evaluated using particle distribution and gas absorption methods. The particle size distribution and SEM of the actual granules are shown in Figs. 11 and 12. As shown in Fig. 12, mannitol in the granule was completely coated with corn starch and crospovidone. The mean particle size (D_{50}) of the granules was about 70 μm. This D_{50} value was almost the same as that with mannitol, suggesting that the spray-coating with corn starch and crospovidone only slightly increased the particle size of granules. Fig. 13 illustrates the imaged structure of the RDGs.

Material parameters of the granules, which were evaluated using a powder properties tester and gas absorption tester, are summarized in Table 4. It was confirmed that the RDGs possessed quite a large surface area and good fluidity in spite of their small size (about 24 μm for the Heywood diameter). Moreover, the aspect ratio of the granules was lower than that of mannitol, indicating that mannitol was completely coated with corn starch and crospovidone. From these findings, it was confirmed that in RACTAB, the interacting particle diameter was decreased by the existence of small particles of corn starch and crospovidone on the surface of granules, and that this lead to a decrease in the binding force between granules. Therefore, the granules possessed high fluidity, but the hardness of the RACTAB was kept high by the close-packed structure of granules during the tabletting process. RACTAB showed a rapid disintegration rate because this physical structure was maintained even after tabletting.

The specific properties of RDGs prepared in this study are summarized as follows:

- Large specific surface area and small micro-pore (4.42 nm as an average radius)
- High circularity measure and high fluidity
- Low plastic deformation
- Small particle size

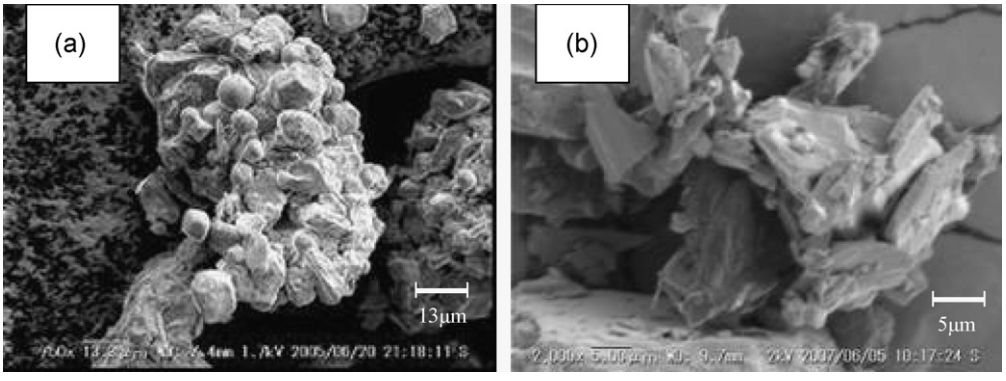

Fig. 12. Scanning electron micrographs of (a) rapidly disintegrating particles by suspension method and (b) intact mannitol.

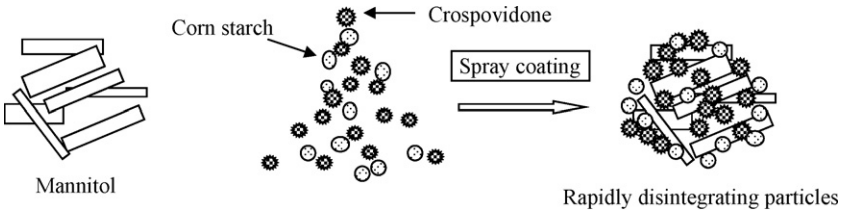

Fig. 13. Schematic representation of the structure of rapidly disintegrating particles.

Table 4
Comparison of particle characteristics of rapidly disintegrating particles and these materials tested.

Material	Heywood diameter[a] (μm)	Angle of repose (°)	True density (g/cm^3)	Surface area (m^2/g)		Aspect ratio (L/D)	Circularity measure	V_{total}[b] (cm^3/g)	R_{ave}[c] (nm)	D[d]
				Laser	BET					
Rapidly disintegrating particles	23.7 ± 17.2	37	1.475	0.0911	1.120	1.557	0.782	0.0025	4.42	3.2
Mannitol	24.1 ± 12.9	42	1.480	–	–	1.695	0.742	–	–	–
Corn starch	12.9 ± 7.4	40	1.478	0.410	1.201	1.429	0.684	0.0026	4.34	3.1
Crospovidone	8.5 ± 4.4	42	1.216	0.368	1.836	1.580	0.695	0.0050	5.41	2.9

[a] Mean ± S.D.; n = 3000.
[b] Total pore volume.
[c] Average pore diameter.
[d] Fractal dimension.

These properties are essential for RDGs to prepare ODTs that show high compressibility, high tablet hardness, rapid disintegration in the oral cavity, and better mouth feeling.

4. Conclusion

The newly developed ODT was found to have superior properties as an ODT, comparatively high hardness of tablet, and fast oral disintegration rate. Because the method to prepare this ODT (suspension method) is simple and does not requires the special equipment, this technology is expected to provide better ODTs for many kinds of drugs that can improve the quality of life of patients.

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