NEW COMPRESSED TABLET RAPIDLY DISINTEGRATING IN SALIVA IN THE MOUTH USING CRYSTALLINE CELLULOSE AND A DISINTTEGRANT

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We formulated a new compressed tablet which is rapidly disintegrated and dissolved in the mouth without the need to drink water. The crushing strength increased with increasing compression force and maximum values (8-18 kgf) for the formulations comprising crystalline cellulose and low-substituted hydroxypropylcellulose (L-HPC) were obtained at the compression force of 300 kgf. Rapid disintegration (within 30 s) was obtained in vitro using various compounding ratios of crystalline cellulose to L-HPC. Tablets prepared with crystalline cellulose and L-HPC rapidly disintegrated in saliva (small amount of water) in the mouth of humans.

KEY WORDS rapidly disintegrating tablet; crystalline cellulose; low-substituted hydroxypropylcellulose; disintegration time; crushing strength; porosity

Drinking water plays an important role in the swallowing of oral dosage forms. Oftentimes we experience inconvenience in swallowing conventional dosage forms such as tablets when water is not available in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold and bronchitis. Particularly, elderly patients encounter difficulties in taking oral solid dosage forms such as tablets and capsules. However, tablets remain popular as a solid dosage form because of the advantages afforded in convenience to patients (e.g., accurate dosage, compactness, portability, blandness of taste and so on). Therefore, it is necessary to develop a new type of tablet having the characteristics of rapid disintegration and dissolution in saliva. The aim of this study was to develop a new compressed tablet which is rapidly disintegrated and dissolved in saliva in the mouth without the need to drink water.

MATERIALS AND METHODS Crystalline cellulose (Avicel PH-102 (mean particle diameter, 120 μm) and PH-301 (mean particle diameter, 40 μm)) and low-substituted hydroxypropylcellulose (L-HPC11 (mean particle diameter, 50 μm) and L-HPC21 (mean particle diameter, 40 μm)) were obtained from Asahi Kasei Kogyo, Tokyo, and Shin-etsu Kagaku Kogyo, Tokyo, Japan, respectively. A model drug of meclizine (HCl salt, powder), a potent antihistamic (antidinic) agent, was purchased from Nihon Baroku Yakuhin, Osaka, Japan. For tabletting experiments, a tablet-hitting pressure displacement measuring system (Sratt Press, Model N-20E, Okada-Seiko Co., Tokyo, Japan) equipped with punches (diameter, 8 mm; concave shape, 10R) was employed as a single-punch tabletting machine. To prepare 200-mg tablets, mixtures of crystalline cellulose and L-HPC in

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various compounding ratios and 1% magnesium stearate (MS) were subjected to various compression force. The crushing strength (force required to break a tablet by compression) was measured in kilograms of force using a Tablet Hardness Tester (Model TS-50N, Okada-Seiko Co.). Density of tablets was measured with a multi-volume pycnometer (Model AccuPyc 1330, Shimadzu Seishakusho Co.) and the porosity of 10 tablets of each compounding ratio was determined by measuring their weight, diameter and thickness, based on the density of each of the 10 tablets.

It was impossible to determine the tablet disintegration time by the method described in JP XII since the prepared tablets disintegrated very rapidly. Therefore, we determined the in vitro disintegration time of the tablets by a modified method using a JP XII disintegration apparatus (Toyama Sangyo, Osaka, Japan) described as follows. One tablet was placed in each of the tubes of the basket, and five lightweight disks were added to each tube. Then the bottom surface of the basket which is made of stainless-steel screen (10 mesh) was immersed in water maintained at 37±2°C as the immersion fluid. The time (s) required for complete disintegration of the tablet in each tube of the basket was determined using a stopwatch. A conventional uncoated tablet (weight, 220 mg; diameter, 8 mm) which is commercially available (the disintegration time by the method described in JP XII is approximately 10 min) did not disintegrate even after 1 h using this method. The sensory test in human subjects reported by Kimura et al.1) was applied with a slight modification. Six healthy volunteers, from whom informed consent was obtained, randomly took one tablet and the time (s) required for complete disintegration of the tablet in the mouth was measured.

RESULTS AND DISCUSSION

Figure 1 illustrates the relationship between the compression force on tabletting and the crushing strength (A) or the in vitro disintegration time (B). The crushing strength increased with increasing compression force and the maximum values (8 kg for the formulation of PH-301 with L-HPC11 and 18 kg for the formulation of PH-102 with L-HPC11) were obtained at the compression force of 300 kgf. The crushing strength for the PH-301:L-HPC system (smaller particle size) was lower than that for the PH-102:L-HPC system (larger particle size). It seems that the prepared tablets have sufficient strength for practical use. Very rapid disintegration (within 5s) was achieved in the case of the PH-301: L-HPC11 system (compounding ratio, 9:1). In the case of the PH-102: L-HPC11 system, the in vitro disintegration time increased with increasing compression force. However, the prepared tablet completely disintegrated at approx. 30 s. When meclazine powder (10%) was added to the mixture of PH-102 and L-HPC, the disintegration time of tablets with meclazine tended to decrease (more disintegrable) in comparison with those without meclazine.

![Graphs](https://via.placeholder.com/150)
The porosity value of the prepared tablets in this study decreased from 45% to approximately 30% when the compression force was increased from 100 kgf to 300 kgf (Fig. 2(A)). However, the prepared tablets have higher porosity values. In general, the disintegration occurs via capillary action rather than swelling; disintegrating materials such as the crystalline cellulose: L-HPC system increase the porosity of tablets, thus promoting capillary action. Rapid disintegration (Fig. 2(B)) of the tablets in a small amount of water may be related to ease of penetration of water into the tablet due to the presence of hydrophilic pores, because the prepared tablets have high porosity values.

Concerning the effect of the difference in the compounding ratio of PH-301 to two types of L-HPC on the crushing strength and the in vitro disintegration time of tablets, the crushing strength tended to decrease from 8 kg to 6 kg when the amount of L-HPC was increased from 10% to 30%. In contrast, the disintegration time tended to increase; however, this increase in the disintegration time is not practically significant (all tablets disintegrated within 30 s). When the amount of L-HPC exceeded 30%, it was difficult to obtain good-quality tablets because of the decreased fluidity of powders.

In the sensory test, we found that tablets prepared using crystalline cellulose (PH-102 and PH-301) and L-HPC were rapidly disintegrated in saliva in the mouth. The disintegration times (within 30 s) obtained in vivo (Fig. 3(B)) show good agreement with those observed in vitro (Fig. 3(A)). Further investigation should be directed toward optimization of formulations containing other drugs.

Fig. 2. Relationships between Porosity and Crushing Strength (A) or In Vitro Disintegration Time (B) of Prepared Tablets

- ○, PH-102 : L-HPC 11 : 9 : 1
- Δ, PH-301 : L-HPC 11 : 9 : 1

Fig. 3. Disintegration Times of Tablets Prepared Using Crystalline Cellulose and L-HPC In Vitro (A) and in the Mouth of Human Subjects (B) Each value represents the mean ± S.D. of three (A) and six (B) experiments.

- I, PH-102 and L-HPC 11 (9 : 1)
- II, PH-301 and L-HPC 11 (9 : 1)

REFERENCES

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