Disintegration and Dissolution Characteristics of Compressed Tablets Consisting of Hydroxypropyl Cellulose and Carboxyvinyl Polymer[1)]

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The disintegration and dissolution characteristics of tablets consisting of hydroxypropyl cellulose (HPC) and carboxyvinyl polymer (CP), were studied, considering the interpolymer complex formation between HPC and CP in the tablet. Brilliant blue FCF (BBL) was used as a model compound of a water-soluble drug. A rapid disintegration was observed when the tablet was prepared with the HPC–CP solid complex. In the case of the physical mixture of HPC and CP, the tablet maintained its original shape during the disintegration test (0—24 h). The slowest dissolution of BBL was observed in water when the tablet was prepared with the physical mixture, and approximately 30% of BBL remained in the solid form in the tablet at 24 h. Although the dissolution of BBL from the tablet prepared with the physical mixture was affected by the pH value of the dissolution medium, other factors, such as the stirring rate of the dissolution medium and the compression pressure of tablet, did not affect the dissolution of BBL from the tablet.

Keywords disintegration; dissolution; compressed tablet; hydroxypropyl cellulose; carboxyvinyl polymer; interpolymer complex; physical mixture

In previous papers,[2,3)] we investigated factors affecting the bioadhesion property of compressed tablets consisting of hydroxypropyl cellulose (HPC) and carboxyvinyl polymer (CP). These polymers have been reported as effective excipients for tablets designed to adhere to the mucous membrane.[2-6)] It has been found that the bioadhesion force of the tablet is greatly affected by interpolymer complex formation between HPC and CP.[2)] The lowest adhesion force was observed when the tablet was prepared with a physical mixture of these polymers in a weight ratio of 3 : 2 (HPC : CP). Interestingly, this was the stoichiometric ratio of the solid complex, which was examined by turbidity and viscosity measurements, and Fourier-transform infrared (IR) spectroscopy.[2)]

Besides the bioadhesion property to the mucous membrane, the characteristics of drug release from the tablet are important for the further development of mucosal adhesive dosage forms. The purpose of the present study was to study the effect of interpolymer complex formation of HPC and CP on the drug release from the tablet. Brilliant blue FCF (BBL) was employed as a model compound of a water-soluble drug.

Experimental

Materials HPC marketed as Hydroxypropyl cellulose-M was purchased from Nippon Soda Co., Ltd. The viscosity of 2% HPC aqueous solution was 240 cP at 20 °C as determined by a Tokyo Keiki BL type viscometer. CP marketed as Carbopol 934 was purchased from B. F. Goodrich Co. The viscosity of 0.2% aqueous solution (at pH 7.0) was 4510 cP at 20 °C as determined by the same apparatus as described above. BBL of extra pure reagent grade was purchased from Tokyo Kasei Industrial Co., Ltd.

Preparation of the Solid Complex HPC aqueous solution (1%) was mixed with CP aqueous solution (1%), and the mixture was incubated at 37 °C for 10 d. The solid complex that precipitated was washed with purified water and dried in a vacuum for 3 d at room temperature. The solid complex thus obtained was ground well in a mortar to make a fine powder. Confirmation of the solid complex formation was done in the same way as reported in the previous paper.[2)]

Preparation of Compressed Tablet Unless otherwise stated, tablets with a diameter of 1 cm were prepared by compressing 100 mg of a sample powder, under the constant pressure of 20 kg/cm^2, using a Shimadzu hydraulic press. As sample powders, HPC, CP, the solid complex and the physical mixture (HPC : CP = 3 : 2 in weight ratio) were used. The powders retained in a 200 mesh sieve (75 μm) and passing through a 60 mesh sieve (250 μm) were used to prepare the tablet. For the dissolution test, 0.5% BBL was mixed into each powder before the tablet preparation.

Disintegration Test The tablet was immersed in a glass dish (diameter, 12 cm), which was filled with purified water, at room temperature. Morphological changes of each tablet were followed for 24 h.

Dissolution Test Unless otherwise stated, a Toyama Sangyo NTR-VS type dissolution tester (paddle method) was used at 25 rpm paddle speed with 500 ml of the dissolution medium at 37 °C. The 1st and 2nd disintegration fluids in JP XI and purified water were employed as the dissolution test media. Samples (5 ml) were withdrawn at appropriate intervals through a Fine filter F (Ishikawa Seisakusho Co., Ltd.) and immediately replaced with a equal volume of the test medium. Samples were analyzed for BBL spectrophotometrically at 630 nm, using a Hitachi 200-20 spectrophotometer. Results are given as the mean values of three determinations.

Results and Discussion

Figure 1 shows the morphological changes of each tablet following water penetration. In the case of CP tablet, disintegration was slow, and was completed at 24 h after the beginning of measurement. The HPC tablet did not disintegrate, but gradually dissolved, exhibiting swelling and gelation. A rapid disintegration was observed in the tablet prepared with the HPC–CP solid complex at the initial stage of the experiment. On the other hand, neither disintegration nor dissolution was observed throughout the experiment when the tablet was prepared with the physical mixture of HPC and CP in a weight ratio of 3 : 2. In the previous study,[2)] we found that the HPC–CP complex was obtained in weight ratio of 3 : 2 as a precipitate when both polymers were mixed in aqueous solution. Therefore, the solid complex powders were considered to have a hydrophobic nature, so that there might be a weakening of the interparticle binding force in the tablet when water penetrates into the tablet. On the other hand, the interpolymer linking between HPC and CP in the tablet prepared with the physical mixture could be brought about by complex formation following water penetration into the tablet. This might explain why the original shape of the tablet was maintained during the experiment.

Next, we determined the dissolution profiles of BBL from these tablets. As shown in Fig. 2, a rapid dissolution was observed when the tablet was prepared with the solid complex. All the BBL was dissolved within 1 h. Prolonged dissolutions were obtained from both HPC and CP tablets.

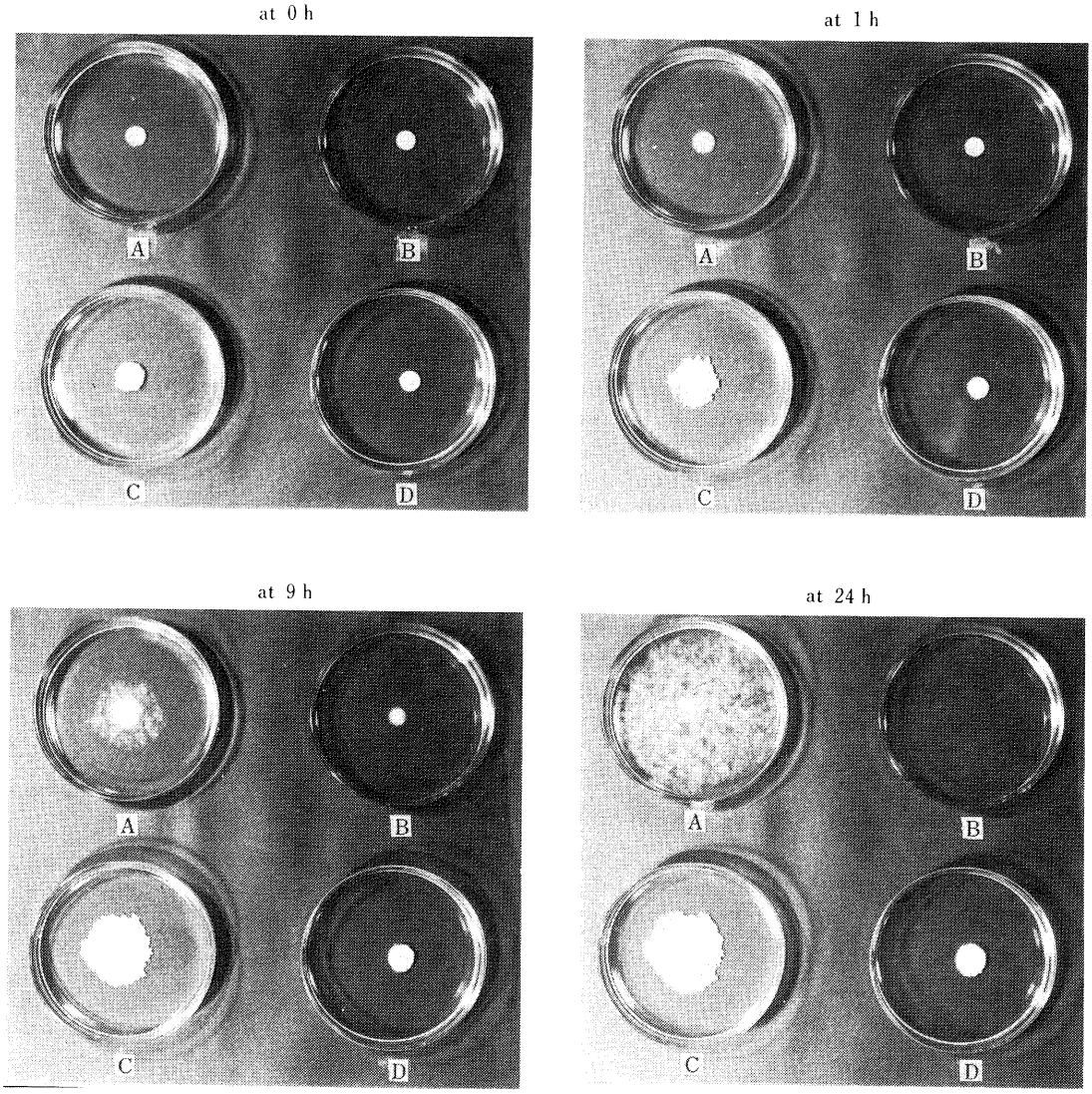

Fig. 1. Progress of Disintegration of Compressed Tablets Prepared with CP (A), HPC (B), HPC–CP Complex (C) and HPC–CP Physical Mixture (D) in Water at Room Temperature

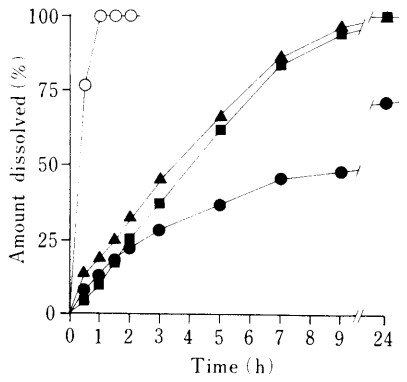

Fig. 2. Dissolution Profiles of BBL from Compressed Tablets Prepared with CP (■), HPC (▲), HPC CP Complex (○) and HPC CP Physical Mixture (●) in Water at 37 C and 25 rpm Paddle Speed

The slowest dissolution was observed when the tablet was prepared with the physical mixture, and approximately 30% of BBL was remained in the solid form in the tablet at 24 h. Therefore, the dissolution of BBL was considered to be controlled by the three-dimensional network structure, which was produced by the complex formation following water penetration into the tablet. From these observations, the use of a physical mixture of HPC and CP seems to be advantageous for controlling drug release from the tablet.

In order to elucidate other factors affecting the dissolution of BBL from the tablet, we investigated the effects of the pH value and stirring rate of the dissolution medium, and compression pressure of the tablet on the dissolution of BBL. The tablet prepared with the physical mixture of HPC and CP in a weight ratio of 3:2 was employed for these studies. The results are summarized in Table I. The dissolution of BBL in the 1st fluid (pH 1.2) was slower than that in the 2nd fluid (pH 6.8). The size of the tablet in the 1st fluid remained almost constant during the dissolution. On the other hand, the tablet in the 2nd fluid was gradually swollen, and slight disintegration occurred in the final dissolution stage. In the previous paper,[2] we found that the solid complex between HPC and CP was formed only in the acidic medium, but not in the media of pH $\geqq$ 4.5. Although the solid complex could be formed in the tablet owing to the acidity of CP independently of the pH value of the dissolution medium in the initial dissolution stage, the acidity in

TABLE I. Factors Affecting the Dissolution of BBL from Tablets Prepared with the Physical Mixture of HPC and CP (3:2)

Amount of BBL dissolved	pH value of dissolution medium		Paddle speed (rpm)			Compressing pressure of tablet (kg/cm^2)		
	1.2	6.8	25	50	100	20	40	60
At 3 h (%)	11.6	20.8	28.2	31.7	32.5	28.2	29.0	26.5
At 5 h (%)	17.1	30.0	37.6	40.0	42.3	37.6	36.1	35.2
At 9 h (%)	25.9	48.5	48.0	52.6	55.7	48.0	48.2	47.0
At 24 h (%)	41.3	91.5	70.8	66.1	71.0	70.8	70.3	64.8

Unless otherwise stated in this table, dissolution tests were performed in water at 37 °C and 25 rpm paddle speed.

the tablet considered to be decreased with the penetration of the 2nd fluid. This may cause decomplexation between HPC and CP in the tablet. Consequently, a faster dissolution rate of BBL was observed in the 2nd fluid than in the 1st fluid. As summarized in Table I, the stirring rate of the dissolution medium and the compression pressure of the tablet had no effect on the dissolution profile of BBL.

Based on the above observations, we can conclude that the dissolution of BBL from the tablet prepared with the physical mixture is mainly controlled by the three-dimensional network structure produced by complex formation between HPC and CP following water penetration into the tablet.

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References and Notes

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