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Effects of Binders on Pharmaceutical Properties of Aspirin Tablets

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The influences of three binders, hydroxypropyl cellulose(HPC), microcrystalline cellulose (MCC) and polyvinylpyrrolidone(PVP), on the transmittance of compression pressure from upper punch to lower punch and the disintegration of aspirin tablets prepared by direct compression were studied. The optimum concentration of three binders for the disintegration of aspirin tablets was about 20w/w% and several physical properties of the powder and tablets were also investigated. The tablet machine was specially made for the measurement of compression pressure of the tablets.

A tablet made by direct compression is suitable to keep the active ingredients stable. compared with the wet process. Therefore, it is desirable that various kinds of directly compressible vehicles are provided for practical purposes.

But, direct compression as a method of tablet manufacture was reserved for several kinds of crystalline chemicals having the physical characteristics required for the formulation of good tablet. These chemicals must possess cohesive and flow properties which make direct compression possible. Also, formulation additives capable of imparting the characteristics required for direct compression are used to make this method more useful and applicable.[1~3]

Microcrystalline cellulose(MCC) has been widely used as a vehicle for tableting,[4~6] and applications of hydroxypropyl cellulose(HPC)[6~8] and polyvinylpyrrolidone(PVP)[6),9] as extremely valuable tableting agents have also been reported. And many works have been reported on directly compressed tablets of acetaminophen[8], theophylline[4] and ascorbic

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acid.[10] Fukuoka et al.[11~12] reported the rate of penetration of liquid into tablets using a two-dimensional model and Krycer et al.[13~14] reported an evaluation of tablet binder employing paracetamol(Graessar salicylates) having extremely cohesive nature as the model system for wet granulation.

The purpose of this investigation was to study the effects of three binding agents, that is, MCC, HPC and PVP, on the hardness and disintegrating properties of aspirin tablets prepared by direct compression. Furthermore, the compression behavior of aspirin powders was exammined with binders in direct compression tableting and scanning electron microscopy was used in an attempt to visualize the binding agents within the tablet matrix.

Experimental

Materials—Aspirin(KP Ⅳ, Hanil Pharm., Korea), hydroypropyl cellulose(Hercules Incorp., U.S.A.), microcrystalline cellulose(Weiming, Thailand), polyvinylpyrrolidone (Tokyo Chemical Industry, Japan; MW. av. 40,000) were used.

Direct Compression Process—A portion of aspirin was mixed with binders in a laboratory-scale V-type mixer for 15min., and the compositions of tablets are listed in Table. Ⅰ. Aspirin tablets were directly compressed on laboratory tablet machine (Fig. 1 ~2) with 8.1mm round flat-faced punches, and compression pressure of 300kg/cm² was maintained for 1min and quickly removed. In addition, aspirin tablets with 20w/w% binders were prepared with compression pressure of 150, 250, 350, 450 and 550kg/cm², respectively.

Measurement of Hardness of Tablets—Erweka hardness tester (Type TDT-S, West Germany) was used.

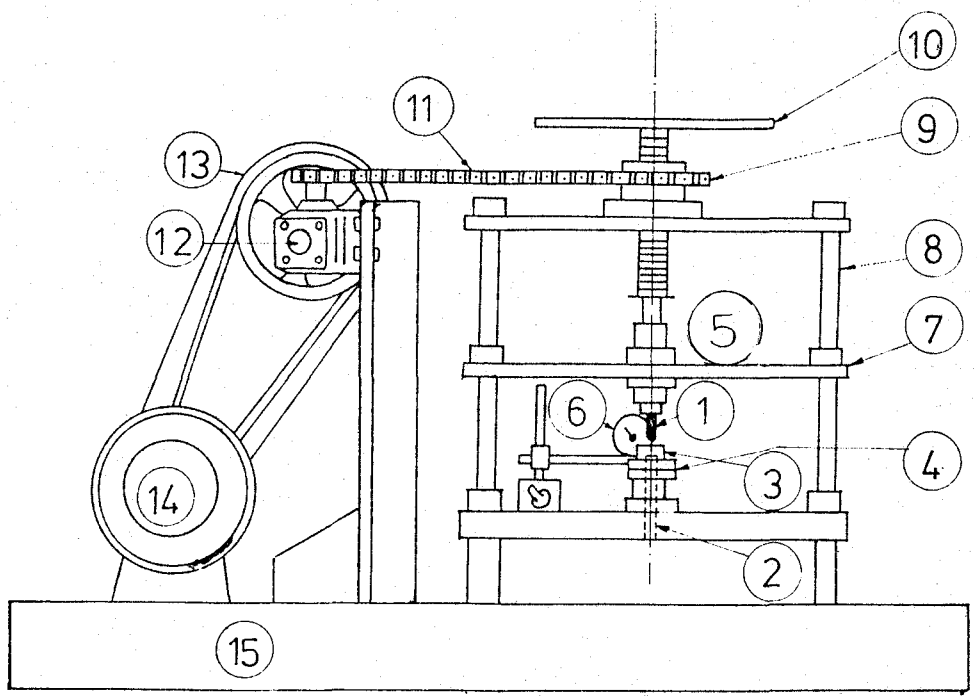
Measurement of Disintegration Time of Tablets—Disintegration time of the tablets was measured according to the method of KP Ⅳ.

Compressibility of Tablets—Compressibilities of powder were measured by load cells (Kyowa Co., Japan). Paraffin, silicon rubber and proving ring were used for standardization of compression pressure of tablet machine.

Characteristics of Surface for the Mixture of Pulverized Aspirin-Binders—Each of the physical mixtures of aspirin-binders was mounted onto sample stubs with double adhseive tape. After vaccum coating with gold, their photographs was taken using

Table I—Composition of Aspirin Tables.

Tablet No.	Materials			
	Aspirin(mg)	HPC(mg)	PVP(mg)	MCC(mg)
1	270	30		
2	240	60		
3	210	90		
4	180	120		
5	150	150		
6	120	180		
7	270		30	
8	240		60	
9	210		90	
10	180		120	
11	150		150	
12	120		180	
13	270			30
14	240			60
15	210			90
16	180			120
17	150			150
18	120			180



1. Upper punch, 2. Lower punch, 3. Die, 4. Die holder, 5. Strain gauge, 6. Dial gauge, 7. Sliding plate, 8. Guidebar, 9. Gear, 10. Handle, 11. Chain, 12. Worm gear, 13. Pulley, 14. Motor, 15. Base table,

Figure 1—Schematic diagram of tablet machine.

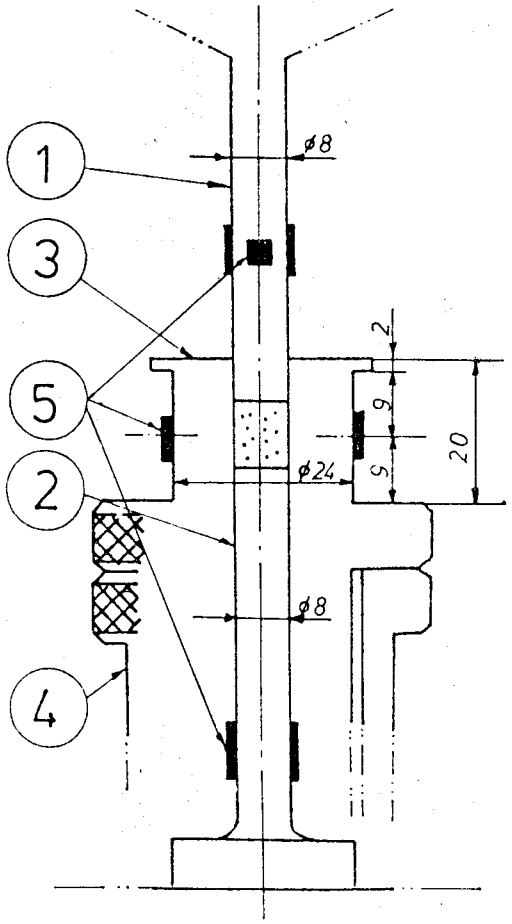


Figure 2—Details of punch & die.

SJM-35CF scanning electron microscope(Jeol, Japan), as shown in Fig. 4, 5 and 6.

Thickness of Tablets and True Density of Binders—Thickness of tablets was obtained by means of the micrometer and the true density of binders was measured using a pycnometer with xylene at 25°C.

Porosity of Tablet—The apparent density of aspirin tablets was calculated from the volume of tablets measured by means of a micrometer and the true density of the powders.

The porosity of tablets was calculated as follows; porosity = 1 − (apparent density/true density)

Results and Discussions

The Transmittance of Compression Pressure—Fig. 3 shows the relationship between compression pressure and time, when aspirin tablets with 20w/w% of binders were directly

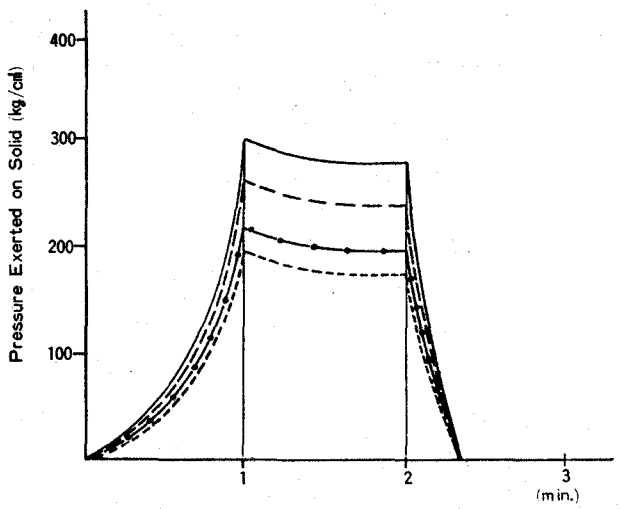
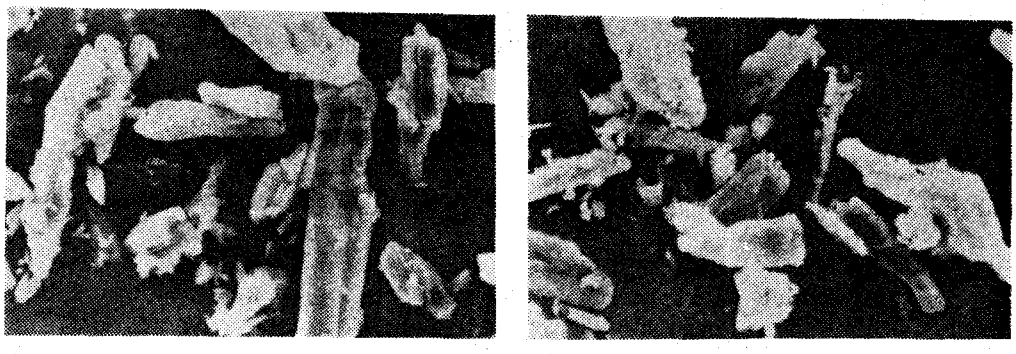


Figure 3—Relationship between compression pressure and time.
Key ; —, upper punch only ; - - -, HPC ; -·-·-, MCC ; ·····, PVP.

compressed. As shown in Fig. 3, HPC is the best of three binders for the transmittance of comression pressure from upper punch to lower punch and MCC and PVP are in the next order. It is expected that three binders have various transmittances, because they have different particle shapes. As shown in scanning electron micrographs of Fig. 4, 5



600 X 600 X

Figure 4—Scanning electron micrographs of aspirin and MCC. The dark and bar-like particles are aspirin and the amorphous particles, MCC.

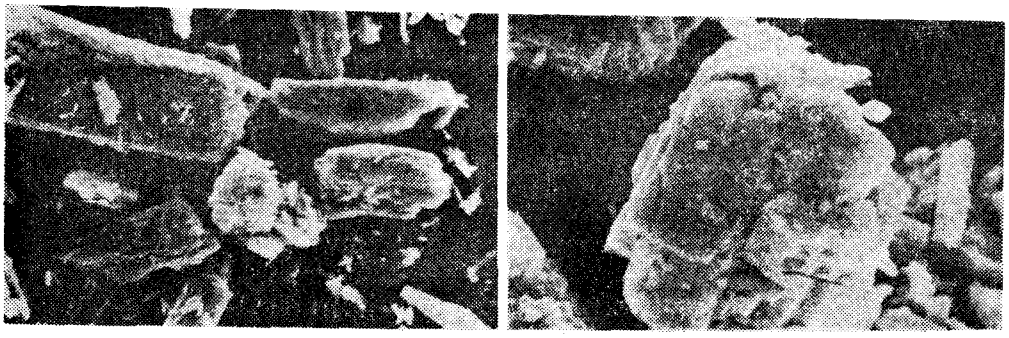


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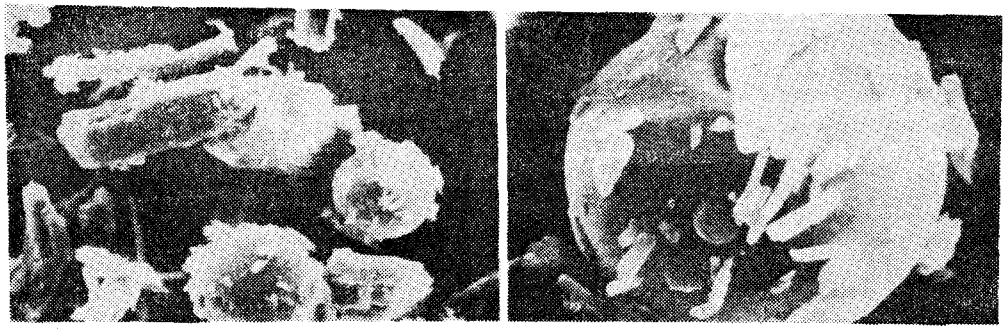
Figure 5—Scanning electron micrographs of aspirin and HPC.
The dark and bar-like aspirin particless are distinguished from HPC.



400 X 1500 X

Figure 6—Scanning electron micrographs of aspirin and PVP.
PVP is spherical and aspirin is bar-like form.

and 6, PVP is spherical and HPC is amorphous. The transmittance of compression pressure is poor if the particles of powders have spherical form. In contrast with this, the transmittance is good if the particles have amorphous form. However, though both of HPC and MCC are amorphous, HPC is better than MCC. But it is uncertain what kind of reasons it was resulted from, and more study is needed.

Relationship betweem Compression Pressure and Thickness of Tablets—As shown in Fig. 7, the thickness of aspirin tablets with 20w/w% of binder is decreased almost linearly with the increase of compression pressure. Moreover, HPC is decreased most greatly and PVP is the least. It is considered to be attributed to the fact that HPC, an amorphous form, has the great transmittance of compression pressure from upper punch to lower punch, different from PVP, a spherical form, having the less transmittance.

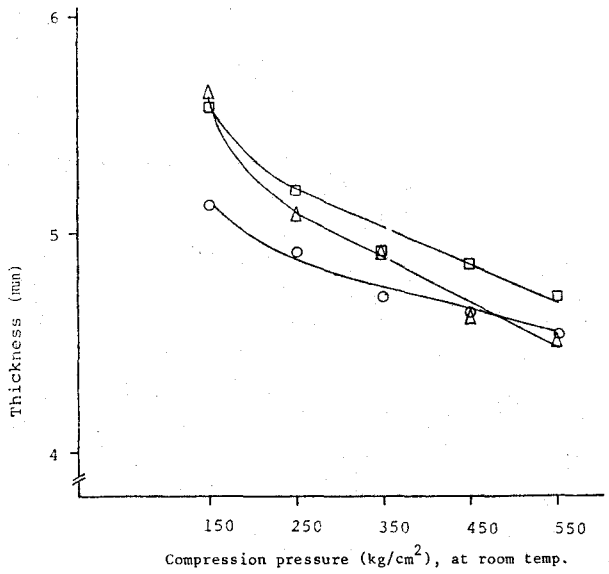


Figure 7—Relationship between compression pressure and thickness of aspirin tablets with 20w/w% of binder.
Key : ○, HPC ; □, PVP ; △, MCC

Relationship between Concentration of Binders and Disintegration Time of Tablets—Fig. 8 shows the disintegration time of aspirin tablets containing various concentrations of binders from 10 to 60w/w%.

The disintegration times of aspirin tablets containing various concentions of three binders were significantly different. Generally, the disintegration time of aspirin tablet

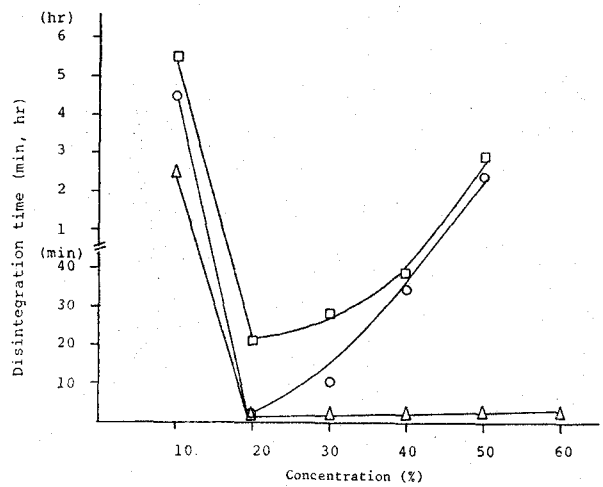


Figure8—Relationship between concentration of binders and disintegration time of tablets compressed at 300kg/cm².
Key : ○, HPC ; □, PVP ; △, MCC

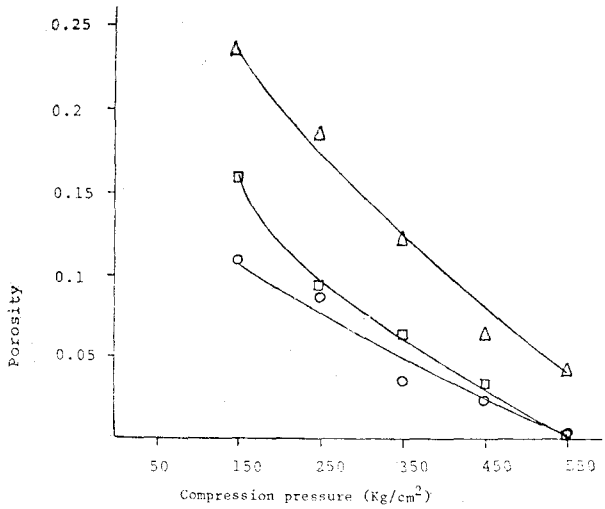


Figure 9—Relationship between compression pressure and porosity of tablets
Key : ○, HPC; □, PVP; △, MCC

containing PVP is longer than that containing MCC or HPC. The disintegration of aspirin tablet containing MCC was very fast, while aspirin tablet containing more than 50w/w% of HPC or PVP was not disintegrated within the experimental period(60min). Moreover, aspirin tablets containing each of three biners had the optimum concentrations to give minimum disintegration times. The optimum concentration of three binders for the disintegration of aspirin tablets was altogether about 20w/w%.

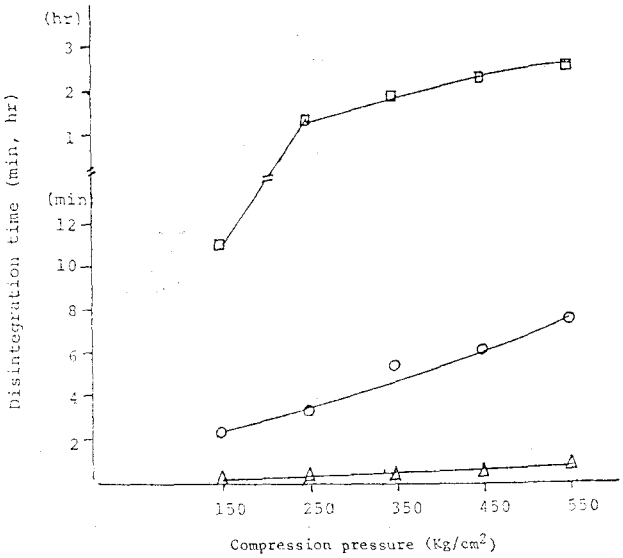


Figure10—Relationshiq between compression pressure and disintegration time of aspirin tablets with 20w/w% of binder.
Key : ○, HPC; □, PVP; △, MCC

Relationship between Compression Pressure and Porosity of Tablets.—The effect of compression pressure on porosity is shown in Fig. 9. Aspirin powders with each of 20w/w% binders were compressed under pressure of the range from 150 to 550kg/cm². It is evident that the porosity is decreased with the increase of compression pressure.

Relationship between Compression Pressure and Disintegration Time of Tablets—The increase of disintegration time with the increase of compression pressure in the mixture of aspirin-PVP was much greater than that in the mixture of aspirin-MCC or aspirin-HPC in the range of compression pressure from 150 to 550kg/cm², as shown in Fig. 10. Especially, aspirin tablets containing PVP that were compressed more than the compression pressure of 150kg/cm² were not disintegrated within 60 min. But the compression pressure did not give remarkable effects on the disintegration time of aspirin tablets containing MCC or HPC.

Relationship between Concentration of Binders and Hardness of Tablets—The hardness of aspirin tablets containing various concentrations of binders is shown in Fig. 11. The hardness of aspirin tablets containing PVP was a little higher than that of containing HPC or MCC at the concentration more than 20w/w% of binders.

Relationship between Concentration of Binders and Porosity of Tablets—Fig. 12 shows the relationship between the concentration of binders and the porosity of aspirin tablets compressed at the constant compression pressure, 300kg/cm². It is known that the porosity was increased with the increased concentration of binders.

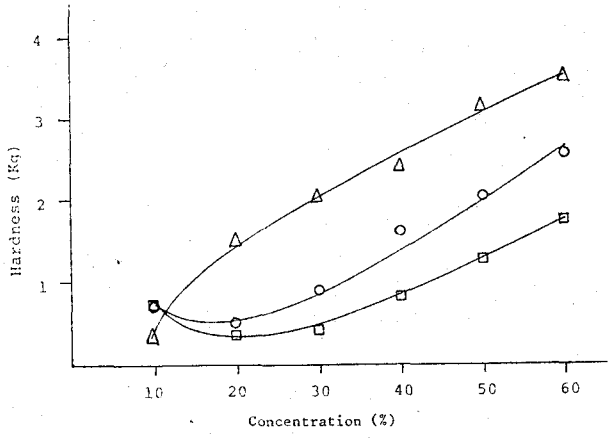


Figure 11—Relationship between concentrations of binders and hardness of aspirin tablets compressed at 300kg/cm².
Key : ○, HPC; □, MCC; △, PVP

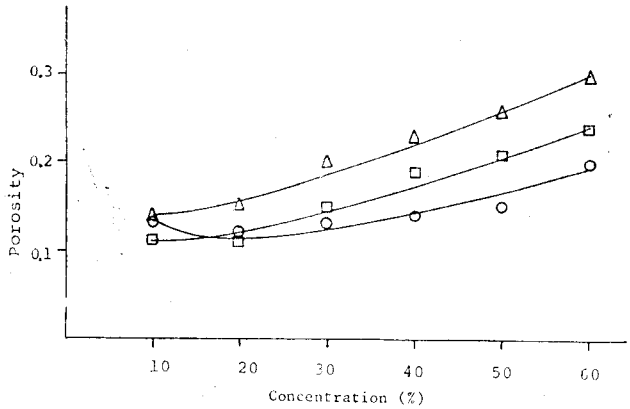


Figure 12—Relationship between concentration of binders and porosity of tablets compressed at 300kg/cm².
Key : ○, HPC; □, PVP; △, MCC

Conclusion

1. For the transmittance of compression pressure from upper punch to lower punch, HPC was the best, then, in turn, MCC and PVP.

2. The optimum concentration of three binders for disintegration of aspirin tablets were altogether about 20w/w%.

3. For hardness of aspirin tablets, PVP was the best. But aspirin tablets containing 20w/w% of PVP is needed to be compressed at the compression pressure less than 200kg /cm² because it was not disintegrated when aspirin tablets containing PVP were prepared under the compression pressure more than 200kg/cm².

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