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COMPRESSION OF MICROCAPSULES II: EFFECT OF EXCIPIENTS AND PRESSURE ON PHYSICAL PROPERTIES

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ABSTRACT

Drug-resin complexes were microencapsulated and compressed into tablets with the aid of various excipients. Compression of the microcapsules at pressures ranging from 35 MPa to 281 MPa produced tablets of acceptable physical properties only with Avicel. When Emdex or Fast Flo Lactose were used an unacceptably high tablet friability was seen. The tablet porosities varied in accordance with their physical properties.

INTRODUCTION

Tabletting of microcapsules offers a convenient method for formulating microencapsulated drug particles into a dosage form (1,2). Acceptable tablets containing microcapsules should exhibit sufficient physical integrity to withstand handling, while maintaining a drug release profile similar to the uncompressed microcapsule. Drug release after compression of microcapsules may be faster or slower depending on the effect of compression on tablet porosity and microcapsule integrity (3-6).

Tablet strength is derived from interparticle bonding during compression. Volume reduction from fragmentation of particles under pressure may be an important parameter affecting the extent

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of interparticle bonding by increasing the surface area available for contact (7,8). To limit the potential for microcapsule breakage during compression mixing the microcapsules with excipients of good compressibility is essential (9). Sayed and Price showed that the tablet performance was affected by the percentage of microcapsules in tablets but not by the microcapsule size (10).

The purpose of this investigation was to compare the performance of 3 excipients in tablet formulations containing microcapsules.

EXPERIMENTAL

Microencapsulation

The phenylpropanolamine-resin complexes were prepared by a batch process and microencapsulated with cellulose acetate butyrate using the emulsion-solvent evaporation technique. The microcapsules were compressed with various excipients. The details of these processes are described elsewhere (11).

Tablet Evaluation

The thickness and hardness of 6 tablets were measured individually. The friability tests (4 minutes at 25 rpm) were performed on samples of 6 tablets and the weight loss was expressed as a percentage of the tablet. The true densities of the tablet components were determined using an air comparison pycnometer.

RESULTS AND DISCUSSION

Porosity calculations

The true density of the tablets was taken to be the sum total of the true densities of its components corrected for the fraction incorporated into the tablet (D_{sum}). The calculated densities of the tablets (D_{calc}) were obtained by dividing the weight, W, of the tablet by its calculated volume (V_{calc}):

$$V_{calc} = \pi r^2 h \qquad (1)$$

$$D_{calc} = W / V_{calc} \qquad (2)$$

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where r is the radius and h is the thickness of the tablet. The tablet relative density (D_{rel}) was the ratio of these densities.

$$D_{rel} = D_{calc} / D_{sum} \quad (3)$$

Substitution and rearrangement yields:

$$D_{rel} = V_{sum} / V_{calc} \quad (4)$$

Assuming that $V_{calc} = V_{sum} + V_{void}$ (5)

then $V_{sum}/V_{calc} = 1 - V_{void}/V_{calc}$ (6)

where V_{void} is the volume occupied by the interparticle spaces in the tablet. Substitution of equation 6 into equation 4 yields:

$$D_{rel} = 1 - V_{void}/V_{calc} \quad (7)$$

or $V_{void}/V_{calc} = 1 - D_{rel}$ (8)

The term V_{void}/V_{calc} is the tablet porosity.

Effect of excipient

As expected, an increase in the compression pressure produced tablets with lower friability and higher hardness. Tablets containing Emdex or Fast Flo Lactose compressed at pressures below 176 MPa did not allow handling. Tablets containing Avicel showed the lowest friability and the highest hardness. Even at high pressures tablets formulated with Emdex or Fast Flo Lactose did not produce tablets of acceptable physical integrity, with friability above 50% (see Table 1). The release of drug from tablets, as indicated by the time required for 75% of the drug to be released ($T_{75\%}$), was only slightly affected by pressure when Avicel was used compared to tablets containing Emdex or Fast Flo Lactose, at equal pressure ranges (see Table 2).

Effect of pressure

The influence of pressure on tablet porosity closely correlated with the impact on physical properties. Compression reduces the tablet porosity probably by forcing the particles into a closer packing arrangement (see Figure 1). The reduction in porosity allows for an increased powder consolidation due to interparticle contact and bonding, resulting in harder tablets (see Figure 2). Apparently, some microcapsule fracturing did

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TABLE 1: Physical properties of tablets containing 50% MCP (mean ± sd).

DILUENT	PRESSURE MPa	FRIABILITY %	HARDNESS kg	POROSITY	$T_{75\%}$ hrs
Avicel	176	0.89±0.02	6.95±0.31	0.193±0.001	5.8±0.35
	211	0.83±0.02	7.28±0.07	0.179±0.002	5.5±0.07
	246	0.82±0.03	7.50±0.18	0.170±0.002	5.5±0.06
	281	0.69±0.07	7.97±0.09	0.165±0.002	5.4±0.05
Emdex	176	97.73±0.88	1.05±0.07	0.231±0.004	5.6±0.11
	211	93.74±4.49	1.15±0.07	0.222±0.002	5.0±0.12
	246	78.61±2.42	1.25±0.07	0.217±0.003	4.7±0.13
	281	64.82±4.75	1.40±0.14	0.208±0.002	4.1±0.15
Lactose	176	100	0.75±0.07	0.248±0.003	5.5±0.03
	211	100	0.90±0.10	0.240±0.003	4.7±0.03
	246	100	1.05±0.07	0.226±0.002	4.0±0.05
	281	100	1.20±0.14	0.216±0.002	3.0±0.02

TABLE 2: Effect of microcapsule percentage on tablet properties (mean ± sd)

DILUENT	PERCENT	FRIABILITY	HARDNESS
Avicel	25	0.00±0.00	14.8±0.28
	50	0.83±0.02	7.3±0.07
	75	100.00±0.00	1.0±0.07
Emdex	15	0.08±0.01	7.8±0.64
	25	1.43±0.42	3.9±0.57
	35	7.65±0.95	2.1±0.07
	50	93.74±4.49	1.2±0.07
Lactose	15	0.76±0.16	4.0±0.57
	25	2.32±1.06	2.8±0.42
	35	56.23±1.32	1.5±0.10
	50	100.00±0.00	1.0±0.07

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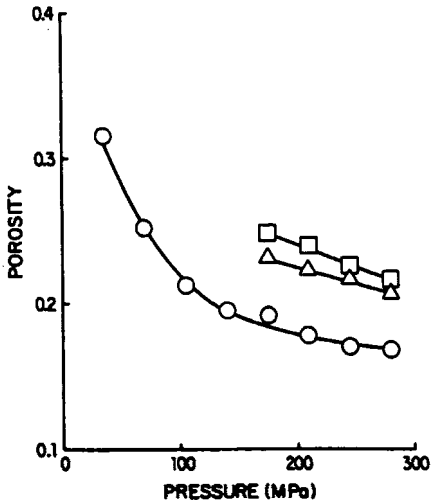

Figure 1: Effect of pressure on the porosity of tablets containing 50 % MCP. (○) Avicel; (△) Emdex; (□) FF Lactose

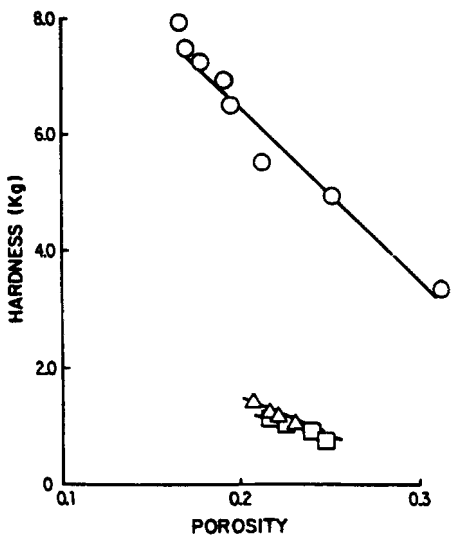

Figure 2: Effect of tablet porosity on tablet hardness. (○) Avicel; (△) Emdex; (□) FF Lactose

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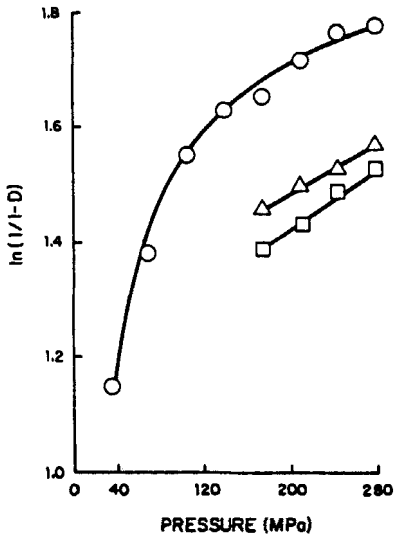

Figure 3: Heckle plots for tablets containing 50% MCP. (○) Avicel; (△) Emdex; (□) FF Lactose

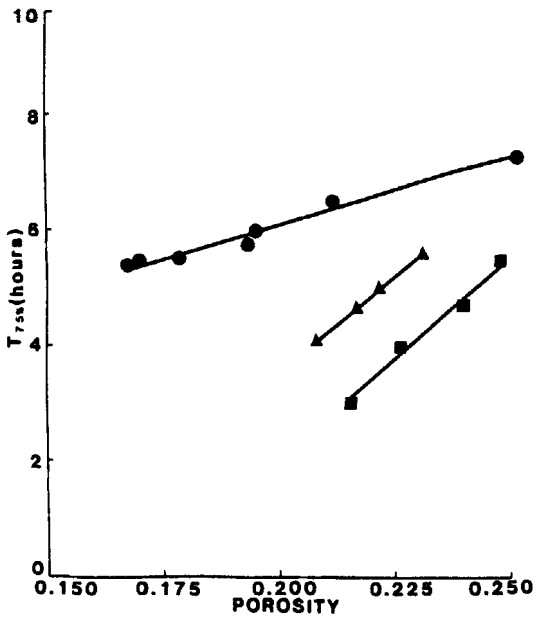

Figure 4: Effect of tablet porosity on the release of drug. (●) Avicel; (▲) Emdex; (■) FF Lactose

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occur during compression, as indicated by the increase in drug release rate at lower porosities (see Figure 4).

Heckle developed a first-order relationship between pressure and porosity (12), which can sometimes be used to ascertain the mechanism of consolidation (13,14). Compression of formulations containing Avicel did not yield linear Heckle plots. Similar results were obtained by other investigators (15-17). Heckle plots for Emdex and Fast Flo Lactose were linear (see figure 3).

Effect of microcapsule percentage

For each excipient there seemed to be a limit to the amount of microcapsules which could be incorporated into the formulation and still produce acceptable tablets. Avicel allowed incorporation of a greater percentage of microcapsules without serious degradation of tablet performance or microcapsule control over drug release. The apparent superiority of Avicel over Emdex or Fast Flo Lactose in protecting microcapsules from possible damage during compression may be attributed to Avicel's excellent compressibility.

CONCLUSIONS

Avicel proved superior to Emdex or Fast Flo Lactose both in its ability to form tablets containing microcapsules of acceptable physical properties at lower pressures and in its capacity to incorporate larger quantities of microcapsules without any critical deterioration in the tablet's physical properties.

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