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COMPRESSION OF MICROCAPSULES I : EFFECT OF EXCIPIENTS AND PRESSURE ON DRUG RELEASE.

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ABSTRACT

Microcapsules containing phenylpropanolamine-resin complexes were compressed with various diluents. Compression of microcapsules produced an increase in the release rate. An average reduction of 0.50 hours was observed when Emdex or Fast Flo Lactose were compared to Avicel at various pressures (35 to 281 MPa). Increasing the amount of microcapsules in the formulation reduced the T50% with all three diluents.

INTRODUCTION

Drug release from microcapsules is controlled primarily by the polymer membrane surrounding the core (1-3). Compression of microcapsules may cause rupturing of the diffusion retarding membrane (4-7). The release of drug from tableted microcapsules can be retarded beyond that of untableted microcapsules by preventing disintegration (8-10). The purpose of this investigation was to study the influence of compression pressure, and type and concentration of excipient on the release of drug from compressed microcapsules.

EXPERIMENTAL

The drug-resin complexes prepared by a batch process were dispersed in 10% cellulose acetate butyrate in acetone (polymer:complex 1:1) and emulsified in a dispersion medium composed of magnesium stearate (1%), and sorbitan sesquioleate (1%) in liquid paraffin. Following evaporation of the acetone, the microcapsules were collected, washed with hexane and dried. The required amounts (5-15 gm) of microcapsules (125-250 um) and direct compression excipients were mixed in a twin-shell blender for 5 minutes. Samples (600 mg) of the formulation were compressed (Carver Press) for 30 seconds at various pressures (35-281 MPa) to form tablets 12.7 mm in diameter. For each variable duplicate batches of tablet formulation were prepared. Drug release studies were conducted at 37^{o}C using simulated intestinal fluid (SIF, pH 7.5) at 100 rpm, with a spectrophotometric assay at 256 nm.

RESULTS AND DISCUSSION

Tablets containing Emdex or Fast Flo Lactose compressed at pressures below 176 MPa were too soft to allow handling. Compression of the microcapsules with the three diluents resulted in faster drug release from the microcapsules (see Table 1). Microcapsules (MCS) compressed with Avicel (A) had the least deterioration in the release profile compared to Emdex (E) or Fast Flo Lactose (F). The comparatively smaller differences in T50% at higher pressures may be indicative of the limited protection offered by the diluents to the microcapsules (see Table 2). As with compression pressure, larger differences in T50% were seen at lower microcapsule percentages (see Table 4). Avicel was able to accept larger quantities of microcapsules compared to Emdex or Fast Flo Lactose without similar increases in drug release rate. The largest increases in T50% upon adding Lubritab (LUB) were seen with Avicel, which correlated with the disintegration time data (see Table 3).

TABLE 1

Effect of Compression on Time Required for 50% Drug Release

(Hours, Mean+SD)

PRESSURE (MPa)	MCS %	LUB %	A	E	F
0	50	1	3.0+0.05	3.0+0.05	3.0+0.05
35			2.4+0.19	-	-
70			2.0+0.04	-	-
105			1.7+0.04	-	-
140			1.6+0.06	-	-
176			1.6+0.05	1.1+0.03	1.2+0.02
211			1.5+0.08	1.0+0.02	1.1+0.02
246			1.6+0.05	0.9+0.03	0.8+0.00
281			1.5+0.05	0.7+0.02	0.7+0.00
211	15	1	-	4.2+0.29	2.2+0.10
	25		3.2+0.10	2.7+0.33	1.4+0.02
	35		-	2.0+0.04	1.3+0.02
	50		1.5+0.08	1.0+0.02	1.1+0.02
	75		1.5+0.01	-	-
211	50	1	1.5+0.08	1.0+0.02	1.1+0.02
		2	3.0+0.01	1.6+0.03	1.3+0.05
		3	3.5+0.01	1.9+0.06	1.5+0.03

TABLE 2

Linear Contrasts of T50% (hours) between Diluents and Compression Pressures (MPa)

COMPARISON	DF	SS	F	X-X*	95% C.I.
A VS E,F	1	4.96	2480	0.50	0.02
E VS F	1	0.00	0.32	-0.02	0.04
PRESSURE					
0 VS Rest	1	51.03	25515	1.88	0.04
176 VS Rest	1	0.61	305	0.21	0.02
211 VS Rest	1	0.36	180	0.18	0.01
246 VS 281	1	0.15	76	0.13	0.01

* difference between means

TABLE3

Effect of Tableting Parameters on Disintegration Times

(Minutes, Mean+SD)

PRESSURE (MPa)	MCS %	LUB %	A	E	F
35	50	1	1.2+0.21	-	-
70			2.8+0.35	-	-
105			2.9+0.14	-	-
140			3.3+0.35	-	-
176			3.8+0.35	0.2+0.02	0.2+0.03
211			3.3+0.35	0.3+0.02	0.2+0.01
246			4.2+0.21	0.4+0.03	0.3+0.02
281			4.4+0.56	0.5+0.06	0.3+0.02
211	15	1	-	4.5+0.41	0.7+0.03
	25		210.0+4.24	1.5+0.24	0.5+0.06
	35		-	1.6+0.05	0.3+0.03
	50		3.3+0.35	0.3+0.01	0.2+0.01
	75		0.6+0.14	-	-
211	50	1	3.3+0.35	0.3+0.01	0.2+0.01
		2	13.5+2.12	0.5+0.04	0.3+0.02
		3	35.0+4.24	0.5+0.06	0.3+0.20

TABLE 4

Linear Comparison of T50% (hours) Between

Microcapsule Percentage Within Diluent

COMPARISON**	DF	SS	F	X-X*	95% C.I.
A25 VS A50,A75	1	10.89	17.85	1.67	1.22
A50 VS A75	1	0.00	0.05	0.03	0.40
E15 VS E25,E35,E50	1	23.74	38.92	2.30	2.44
E25 VS E35,E50	1	5.86	9.60	1.21	1.22
E35 VS E50	1	2.91	4.77	0.98	0.40
F15 VS F25,F35,F50	1	3.89	6.38	0.93	2.44
F25 VS F35,F50	1	0.15	0.25	0.20	1.22
F35 VS F50	1	0.14	0.23	0.21	0.40

* difference between means

CONCLUSION

The drug release rate increased with compression pressure and microcapsule percentage. Formulations containing Avicel as the diluent were less succeptable to pressure effects while capable of accepting larger quantities of microcapsules.

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