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COMPARATIVE TABLETING PROPERTIES OF SIXTEEN MICROCRYSTALLINE CELLULOSES

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ABSTRACT

The tableting characteristics of sixteen NF grade microcrystalline celluloses produced by seven manufacturers were investigated. Nine samples were type 1 celluloses (fine powders) and seven corresponded to type 2 celluloses (coarse powders). Some samples were second batches of the same products. The powders were examined for their moisture content, particle-size distribution, for their true, bulk and tap densities and for their flow properties. The effect of adding a lubricant with a low friction coefficient (0.5% magnesium stearate) on the packing and flow properties was evaluated.

Basic compression studies were made on an instrumented eccentric tableting machine at an axial pressure

of 100 MPa. The work of compression and the elastic recovery of the compacts were determined, as well as many friction parameters. The tabletability of the powders was assessed by measuring the diametral crushing force of the compacts.

In a second set of experiment, we examined the effect on the compactability of the powders of adding 0.5% magnesium stearate.

Weight variations of lubricated tablets were studied on a high speed rotary machine. In these runs, the force required to prepare tablets of a given mechanical strength was monitored. The uniformity of dimensions, the friability and the disintegration time of the tablets were also checked.

Great differences in packing and tableting properties and in sensitivity to the addition of a lubricant were generally observed between products from the various manufacturers. In contrast, lot-to-lot variability was quite acceptable.

INTRODUCTION

Microcrystalline cellulose is certainly regarded as the best excipient for direct tableting. It was introduced in the early sixties (1-5) but until recently only products from one manufacturer were generally available. The particle-size distribution, packing and flow properties of these materials, as well as their tableting and disintegration characteristics are well documented. Now, several other microcrystalline celluloses have appeared on the market but to our knowledge only three investigations report data on new products. Pesonen and Paronen (6) compared the crystallinity, particle size, densities, flow and binding properties of Emcocel®

with those of Avicel® PH-101. Doelker et al. (7) determined the degrees of polymerization (molecular weights) and crystallinities of several microcrystalline and powdered celluloses. In a comprehensive investigation on the compactability of celluloses, the same authors compared four microcrystalline and four powdered celluloses of varying crystallinity. Generally, microcristalline celluloses showed better tableting properties but the mechanical strength of the compacts was not directly related to the crystallinity index, nor to the morphology of the particles (8).

The aim of this study was to examine the packing and the tableting properties of several new microcrystalline celluloses. Based on particle-size distribution, these materials were classified in type 1 and type 2 microcrystalline celluloses by reference to the pioneer products Avicel® PH-101 and Avicel® PH-102, respectively. Ten powders were compared to the two Avicel® grades. In some cases, second batches of the same products were investigated to check the lot-to-lot variability. Packing characteristics included the bulk and tap densities of the powders. Flow properties were considered only for type 2 celluloses. For type 1 celluloses preliminary trials gave highly unreproducible results. These were in agreement with previous observations on Avicel® PH-101 (9-16).

The basic compressional behavior was estimated from the work of compression, the elastic recovery and various friction parameters, as determined with an instrumented tableting machine. The tabletability was assessed through the diametral crushing strength of the compacts. The effect on the mechanical strength of the tablets of adding a hydrophobic lubricant to the materials was evaluated. Weight and dimension uniformity of

lubricated tablets was studied on a high speed rotary machine equiped with a force-feeding fill shoe and a compaction force monitor. Friability and disintegration time of the tablets were also determined.

MATERIALS

The sixteen samples of microcrystalline cellulose chosen were used as received from the suppliers: Avicel® PH-101, batches 1 and 2, and Avicel® PH-102, batches 1 and 2 (F.M.C. Corp.); Emcocel® and Emcocel® 90M (manufactured by Finnish Sugar Ltd, Finland, and marketed by Edward Mendell Co., U.S.A.); Ex-Cel® (manufactured by Cellulose Products of India Co. and supplied by Sitco, U.S.A.); Medicel® 101 and Medicel® 102 (manufactured by Cargile Corp., Taiwan, under a license of Medipulp, W. Germany, and supplied by G. Walther AG, Switzerland); MCC type 101, batches 1 and 2, and MCC type 102, batches 1 and 2 (manufactured by Ming Tai Chem. Co., Taiwan, and supplied by Trans-Medica, W. Germany, or L.C.M. Trading, Italy); Sanaq® 101 L (manufactured by Wei Ming Pharm. Mfg. Co., Taiwan, and supplied by Pharma Trans Sanaq AG, Switzerland); Unimac® MG-100 and Unimac® MG-200 (Unikita Rayon Co., Japan). In some experiments 0.5% magnesium stearate (Siegfried, Switzerland) was added to the powders using a tridimensional Turbula® blender (W. Bachofen, Switzerland) and a mixing time of 5 min.

METHODS

Characterisation of powders

The moisture content was assessed by the Karl Fischer method (Metrohm type 633) in conjunction with the one-component Hydranal® Composite 5 reagent (Riedel-deHaën).

Particle-size distribution was checked in duplicate using air-jet sieving (Alpine 200, W. Germany). The weight geometric mean diameters and geometric standard deviations were obtained from log-normal plots. The arithmetic volume-surface mean diameters were calculated using the appropriate Hatch-Choate equation (17) to facilitate comparison with reported data.

The true density was measured with an air comparison pycnometer (model 930, Beckman Instruments). The bulk density and tap density of the powders without lubricant and with 0.5% magnesium stearate were determined using a Neumann type volumenometer (18) (25-ml graduated glass cylinder filled with 6 g of material). The minimum volume of powder was generally attained after 1000 1-cm tamps. The Hausner ratio (19) was calculated from the quotient of tap to bulk density.

Flow rate was measured for the type 2 celluloses with a vibratory hopper technique similar to that of Graf et al.(20). Here, the 50-Hz vibrator (Vibro-Mischer type EL) was connected to a normalized glass funnel (21). The internal diameter of the efflux tube (8 mm) corresponded to that of the dies used for the tablet weight variation experiment (see below). The flow of 50 g of powder was measured using a strain gauge balance (22) and the flow rate was calculated from the recorder tracing.

Packing and flow property determinations were made at least in triplicate.

Basic compression properties

Basic compression characteristics of the powders were investigated on an instrumented single punch tableting machine (Korsch EK-O, W. Germany), as previously (8,23,24). A quantity of powder corresponding to a 3-mm thick tablet at zero theoretical porosity was manually

filled into the unlubricated die (12 mm). Flat compacts were prepared at a nominal axial pressure of 100 MPa. Compaction was achieved at 30 strokes/min. Work of compression, punch force ratio, residual lower punch force, ratio of radial stress to axial stress, residual die wall pressure, ejection force and elasticity recovery of the compacts were determined as described elsewhere (8). The porosity of the compacts was calculated from their actual weight and dimensions and from the true density of the powders.

The diametral crushing force of these compacts was measured with a universal testing machine (Schenck Trebel, type RM 50, W. Germany) at a strain rate of 3 mm/min. Results are the mean values of 5 runs.

Sensitivity to lubricant

Tablets from the various materials added with 0.5% magnesium stearate were prepared and characterized as above. A strength reduction ratio, i.e. the ratio between the radial crushing force with and without the lubricant addition, was calculated as a sensitivity index.

Tablet weight variation

The study of tablet weight variation was performed on a high speed 27-station double rotary tableting machine (Manesty Unipress, U.K.), equipped with a forced feeding system and a compaction force monitor. Flat bevel-edged 8-mm diameter tablets with a breakline were prepared from the lubricated powders at a rate of 1400 tablets/min. A weight of 160 mg and a crushing force of 60 ± 10 N were targeted and the force necessary to prepare the tablets was estimated through the compaction force monitor.

Samples of 30 tablets were weighed (±0.1 mg) and the coefficients of variation (CV) were calculated. Additionally, tablets were caracterized for their uniformities of diameter, thickness and crushing force using a Heberlein hardness tester (Schleuniger, Switzerland). Friability was evaluated from the weight loss of 20 tablets tumbled 100 revolutions in a TAB Erweka friabilator (W. Germany). Finally, disintegration testing (12 tablets) was performed at 37°C in water using the European Pharmacopeia (USP) apparatus, with and without discs (Sotax DT-3, Switzerland).

RESULTS AND DISCUSSION

Powder characteristics

Values for moisture content (MC), true density (ρ), weight geometric mean diameter (d_{gw}), geometric standard deviation (σ_g) and volume-surface mean diameter (d_{vs}) are listed in Table 1. For the purpose of comparison, we have separated results concerning type 1 (the first nine samples) and type 2 (the last six samples).

Moisture contents are around 5% and no value exceeds the 8% limit of NF XVI. The possible effects of a variation in moisture content on the properties of the powders will be discussed below.

Particle-size distributions of products of similar types are surprisingly close, with the exception of the coarser Unimac® MG-200. It should be noted however that this material and Ex-Cel® did not satisfactorily fit a log-normal distribution (r^2 = 0.891 and 0.919, respectively), with the consequence of poorly significant d_{gw} and thus d_{vs} values. In contrast, coefficients of determination for the other materials were always better that 0.97.

TABLE 1
Characteristics of Unlubricated Powders

Material	MC (%)	ρ (g/cm^3)	d_{gw} (µm)	σ_g	d_{vs} (µm)
Avicel® PH-101, batch 1	4.7	1.532	40	1.74	34
Avicel® PH-101, batch 2	4.6	1.553	46	1.82	39
Emcocel®	5.0	1.543	43	1.94	35
Ex-Cel®	4.5	1.537	40	4.10	15
Medicel® 101	5.1	1.541	49	2.20	36
MCC type 101, batch 1	5.0	1.537	47	2.62	30
MCC type 101, batch 2	3.8	1.555	42	2.95	23
Sanaq® 101 L	4.4	1.542	40	2.29	28
Unimac® MG-100	3.7	1.547	39	1.99	31
Avicel® PH-102, batch 1	4.9	1.564	73	2.25	53
Avicel® PH-102, batch 2	5.1	1.537	82	2.65	51
Emcocel® 90M	4.6	1.557	77	2.41	52
Medicel® 102	5.1	1.542	64	2.48	42
MCC type 102, batch 1	5.1	1.536	75	2.95	42
MCC type 102, batch 2	5.0	1.535	79	2.94	44
Unimac® MG-200	3.8	1.541	105	3.69	45

Inter-batch variations are quite acceptable (see Avicel® PH-101 or PH-102 and MCC type 101 or 102) and of the same order of magnitude as the inter-product variability. This lot-to-lot uniformity explains the good agreement observed with data reported in the literature when referring to the same particle-size determination technique and for the same mean diameter: Avicel® PH-101 (6,13,14,25-29), Avicel® PH-102 (13,23,26,28,29) and Emcocel® (6).

Packing characteristics of the powders

Table 2 shows the bulk densities (ρ_b), tap densities (ρ_t), Hausner ratios (H) and flow rates (v) for the various powders as received and with 0.5% magnesium stearate.

All microcrystalline cellulose samples exhibit low bulk and tap density values, as cited many times in the literature for Avicel® PH-101 (6,9,10,12,13,15,23,27,28, 30-34,36,37), Avicel® PH-102 (10,12,13,15,21,28,30,35) and Emcocel® (6). In general, both parameters are higher for type 2 celluloses, but the increase is more pronounced for values of bulk density than those of tap density, so that lower Hausner ratios result.

Differences in packing properties of products in the same group can probably be ascribed to the differences in particle-size distribution (see σ_g values in Table 1) and particle shape (8), but not in particle size, seeing that Mc Kenna and Mc Cafferty (38) have noted only slight variations in Hausner ratio with changes in particle size.

Inter-batch variations for packing properties, like inter-product variations, are more pronounced than for particle-size distribution and can be explained as above.

TABLE 2

Packing and Flow Properties of Unlubricated and Lubricated Microcrystalline Celluloses

Material	Without lubricant				With 0.5 magnesium stearate			
	ρ_b (g/cm^3)	ρ_t (g/cm^3)	H	v (g/s)	ρ_b (g/cm^3)	ρ_t (g/cm^3)	H	v (g/s)
Avicel® PH-101, batch 1	0.263	0.342	1.30	---	0.267	0.341	1.28	---
Avicel® PH-101, batch 2	0.297	0.370	1.25	---	0.328	0.392	1.20	---
Emcocel®	0.294	0.370	1.26	---	0.327	0.408	1.25	---
Ex-Cel®	0.240	0.351	1.46	---	0.250	0.308	1.23	---
Medicel® 101	0.282	0.409	1.41	---	0.287	0.349	1.22	---
MCC type 101, batch 1	0.312	0.432	1.39	---	0.331	0.392	1.18	---
MCC type 101, batch 2	0.297	0.395	1.33	---	0.303	0.366	1.21	---
Sanaq® 101 L	0.262	0.333	1.27	---	0.276	0.346	1.25	---
Unimac® MG-100	0.324	0.408	1.26	---	0.351	0.432	1.23	---
Avicel® PH-102, batch 1	0.283	0.368	1.30	6.7	0.297	0.351	1.18	9.1
Avicel® PH-102, batch 2	0.305	0.390	1.28	9.0	0.337	0.387	1.15	9.6
Emcocel® 90M	0.295	0.360	1.22	9.4	0.335	0.382	1.14	10.8
Medicel® 102	0.255	0.375	1.47	1.4	0.261	0.314	1.20	7.0
MCC type 102, batch 1	0.331	0.451	1.36	6.8	0.350	0.414	1.18	14.3
MCC type 102, batch 2	0.366	0.423	1.16	15.4	0.361	0.422	1.17	14.8
Unimac® MG-200	0.375	0.458	1.22	10.9	0.423	0.517	1.22	12.0

Adding a low friction coefficient lubricant results in denser packing for both grades of microcrystalline celluloses. This small increase in bulk and tap densities and a decrease in Hausner ratio have been reported by Bolhuis et al. (10) and Lamberson and Raynor (12), but the change is important only for "loose" materials.

Because of their low packing densities, microcrystalline celluloses of both types are non free-flowing powders, but flow properties for type 2 materials could nonetheless be evaluated satisfactorily using a flow test through an orifice. This technique was adopted by many workers (2,6,13,15,21,27,35,39) for Avicel® PH-101 and PH-102 and for Emcocel® (6).

With the vibratory hopper technique used, type 2 microcrystalline celluloses demonstrate a broad range in flow properties. Adding 0.5% magnesium stearate only slightly improves the flowability of the powders as reported for Avicel® (12,39) and reduces inter-batch variations. The increase in flow rate is more pronounced for poorly flowing materials.

Differences in flow properties can be attributed to differences in moisture content (which affect cohesiveness), in particle shape and particle-size distribution, as reflected in the packing properties. Thus, a nearly perfect rank correlation is observed for unlubricated materials between flow rates and Hausner ratios (Spearman's coefficient of 0.982). For lubricated powders H values were too close to be considered.

Basic compression properties

Table 3 shows the mean values for upper punch work (UPW), lower punch work (LPW), punch force ratio (R), friction work (FRW) according to Järvinen and Juslin (40), ratio of FRW to UPW as percentage (FRR), residual

TABLE 3

Compressional Properties of the Sixteen Samples Compacted at 100 MPa and Properties of the Resulting Compacts (Unlubricated Die)

Material	UPW (J)	LWP (J)	R	FRW (J)	FRR (%)	RLPF (N)	η	RDWP (MPa)	EJF (N)	E (%)	ε (%)	F_c (N)
Avicel® PH-101, batch 1	12.83	9.82	0.788	1.52	11.9	119	0.54	4.5	173	5.1	13.4	460
Avicel® PH-101, batch 2	13.54	9.60	0.730	2.06	15.2	263	0.48	5.1	256	6.0	17.6	428
Emcocel®	12.52	10.31	0.836	1.14	9.1	112	0.52	4.5	188	5.3	16.1	417
Ex-Cel®	11.87	8.65	0.732	1.72	14.5	262	0.51	5.9	277	8.0	18.1	266
Medicel® 101	11.59	8.68	0.752	1.54	13.3	217	0.53	5.1	241	8.2	17.4	205
MCC type 101, batch 1	12.43	9.90	0.780	1.38	11.1	223	0.52	5.2	264	7.2	17.8	268
MCC type 101, batch 2	13.01	9.64	0.741	1.80	13.8	305	0.50	5.8	324	7.1	20.4	403
Sanaq® 101 L	12.41	8.43	0.699	2.10	16.9	416	0.54	6.5	399	6.7	18.4	377
Unimac® MG 101	11.91	8.17	0.703	1.96	16.4	360	0.53	6.4	339	4.9	18.2	373
Avicel® PH-102, batch 1	13.94	10.43	0.770	1.77	12.7	156	0.53	4.4	198	5.3	15.6	451
Avicel® PH-102, batch 2	12.67	9.89	0.783	1.47	11.6	149	0.53	4.2	188	5.7	14.6	430
Emcocel® 90M	12.86	8.98	0.714	2.06	16.0	236	0.54	6.0	252	7.2	18.0	403
Medicel® 102	12.26	8.68	0.734	1.85	15.1	260	0.50	5.6	301	9.9	19.9	183
MCC type 102, batch 1	12.65	9.73	0.771	1.53	12.1	156	0.51	5.3	199	6.3	17.7	229
MCC type 102, batch 2	12.98	9.64	0.757	1.74	12.4	249	0.49	5.7	260	6.1	18.3	349
Unimac® MG-200	12.41	8.76	0.735	1.87	15.1	247	0.51	6.0	263	6.4	18.7	315

lower punch force (RLPF), ratio between radial and axial stresses (η), residual die wall pressure (RDWP) and ejection force (EJF). Data on the resulting compacts are also included: the percentage elastic recovery (E) defined as the ratio of the height difference after ejection and under pressure to the height under in the literature for Avicel® products (67,68,71-75). The sensitivity to lubricant has been explained by the densification mechanism of Avicel®, i.e. plastic deformation, which in contrast to brittle fracture does not provide new uncontaminated crystal faces for particle bonding. Here, the two batches of Avicel®, both PH-101 and PH-102 grades, demonstrated quite differing sensitivity to lubricant, but figures remain in the limits normally reported for similar mixing times. Compared with that of Avicel® compacts, strength reduction for other microcrystalline celluloses varies greatly, ranging, in the type 1 series, from less than 2% (Ex-Cel®) to more than 20% (Unimac® MG-100), and, in the type 2 series, from 3% (Medicel® PH-102) to more than 60% (Unimac® MG-200). Type 2 celluloses are generally more sensitive to magnesium stearate than type 1 celluloses, which is rather surprising in one sense when considering the agglomerated structure of type 2 materials which could be supposed to be a protective factor against contamination of the microcrystals by the lubricant. Increased intragranular porosity could have led to increased interparticulate friction and thus to higher plastic deformation with increased contamination (76). Inter-batch variation is more pronounced for the series 1 products. Finally, no correlation could be established between the ability of a material to give strong or soft compacts and its sensitivity to lubricant.

Characteristics of tablets prepared on the rotary machine

Mean values and coefficients of variation of the various characteristics are given in Table 4, together with the approximate forces necessary to prepare the tablets, as measured from the compaction force monitor.

Great differences in the force necessary to compact the various materials and the batches at the desired rection is made for compact voidage (calculation of tensile strength using the cross-sectional area occuped by solid, $1 - \varepsilon^{2/3}$).

A possible effect of the moisture content of the powders on the strength of the compacts cannot be excluded (2,4,49,67-69), although its importance must be limited when we consider the figures of water content given in Table 1. Nor can differences in tabletability be entirely attributed to differences in friction properties, radial stress transmission or compressibility. It must therefore be assumed that the internal structure of the particles is mainly involved, although we have demonstrated that the mechanical strength of the compacts was for example not related to the crystallinity of the starting materials. The role played by the morphology of the particles could also be excluded (8). Structure differences are nevertheless quite conceivable if reference is made to possible variations in the processing conditions during the manufacture of the microcrystalline celluloses that involves hydrolysis of the wood cellulose, intensive shearing of the slurry and spray drying.

Sensitivity to lubricant

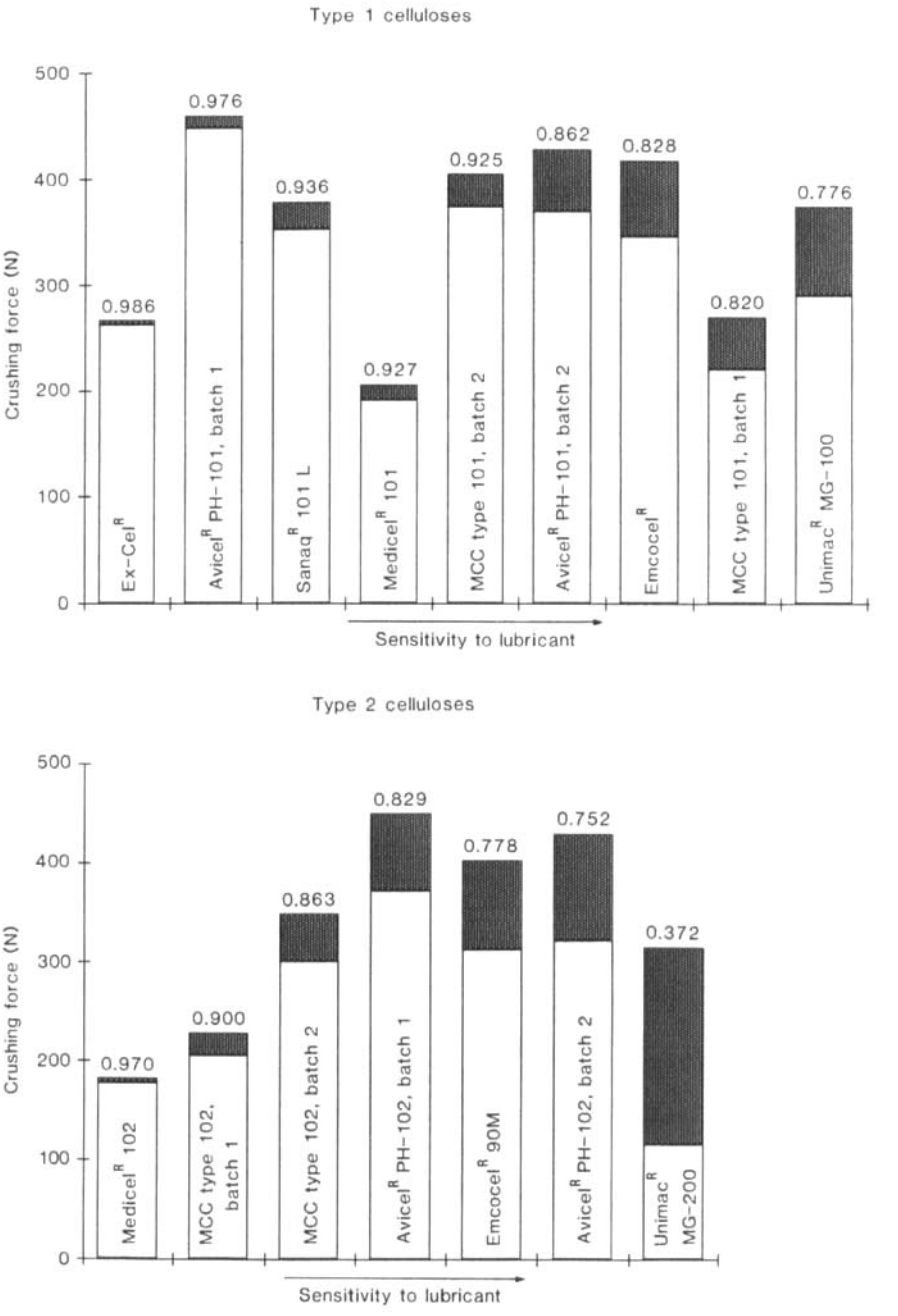
Figure 1 combines values of crushing strength for both lubricated and unlubricated compacts. Celluloses of both types are classified by increasing order of sensitivity

TABLE 4

Force of Compaction, Uniformities of Weight, Dimensions and Crushing Strength, and Friability and Disintegration Time of the Lubricated Tablets Prepared on the Rotary Machine

Material	Compaction force (N)	Weight mean (mg)	Weight CV (%)	Thickness mean (mm)	Thickness CV (%)	Diameter mean (mm)	Diameter CV (%)	Crushing force mean (N)	Crushing force CV (%)	Friability (%)	Disintegration time (min) with discs	Disintegration time (min) without discs
Avicel® PH-101, batch 1	1500	159.2	1.90	3.37	0.32	8.04	0.16	74	9.3	0	1.5	3.5
Avicel® PH-101, batch 2	2125	157.7	0.76	3.42	0.55	8.06	0.09	57	4.8	0.14	1.0	1.5
Emcocel®	2100	158.9	0.96	3.31	0.58	8.05	0.10	72	7.7	0.18	1.5	5
Ex-Cel®	--	141.3	4.49	3.03	0.46	8.06	0.09	47	17.8	0.11	2	7
Medicel® 101	3000	161.0	1.52	2.96	0.30	8.05	0.14	67	8.4	0.11	18	63
MCC type 101, batch 1	3400	160.5	0.87	3.07	0.38	8.07	0.14	64	5.2	0.05	1	8.5
MCC type 101, batch 2	2650	157.5	1.05	3.27	0.47	8.07	0.12	66	4.6	0.01	2	>240
Sanaq® 101 L	2250	160.2	1.31	3.31	0.51	8.06	0.14	63	12.2	0.32	2	20
Unimac® MG-100	2450	158.8	1.20	3.32	0.23	8.06	0.12	56	11.5	0.09	2	10
Avicel® PH-102, batch 1	1850	161.2	0.63	3.38	0.59	8.06	0.14	74	6.2	0.03	1.5	2.5
Avicel® PH-102, batch 2	1875	159.2	0.70	3.26	0.32	8.06	0.09	72	4.4	0.05	2	4.5
Emcocel® 90M	2150	160.8	0.39	3.26	0.33	8.06	0.14	71	4.7	0.09	2	3
Medicel® 102	2800	155.9	2.36	3.07	0.77	8.07	0.11	52	11.6	0.24	11	43
MCC type 102, batch 1	3550	161.1	0.62	2.97	0.58	8.06	0.15	66	4.7	0.12	0.5	5
MCC type 102, batch 2	3150	165.1	0.85	3.22	0.42	8.07	0.11	69	3.7	0.03	1	6.5
Unimac® MG-200	3850	160.6	0.67	2.93	0.28	8.07	0.12	60	6.7	0.10	0.5	1

*Because of the low packing density of this material, the target weight and thus crushing force could not be technically attained.



to lubricant, i.e. decreasing order of strength reduction ratio (70).

When mixed with 0.5% magnesium stearate, all samples give softer compacts than those made of pure materials, even though their porosity was diminished by about 4% on the average, expressed in relative value. This reduction in mechanical strength has been reported many times magnitude depends on the time of measurement. Such high elasticity has previously been reported for Avicel®, MCC type 101 and Unimac® MG-100 compacts using the above-mentioned index (8,44,47,61-64), but also using calculation of the work for elastic deformation (8,10,43,47,48, 50) and indentation testing (8,65,66).

The compressibility of the powders, i.e. their ability to reduce in volume on compression, varies significantly from one product to another and, for type 1 materials, from one batch to another. This intra-product variability for Avicel® PH-101 is in contrast with previous densification data (37). Differences in compressibility are probably related most of all to the structure of the particles, which dictates the extent of plastic flow, and partly to differences in friction properties.

The compactability of all celluloses, i.e. their ability to form coherent tablets as assessed by crushing strength, is high. This ability to constitute strong compacts even at low pressure is not inconsistent with

FIGURE 1

Crushing Strength Values for Unlubricated Compacts (Shaded and Unshaded Areas) and Lubricated Compacts (Unshaded Areas Only) Prepared at 100 MPa (Figures are for Strength Reduction Ratios)

the high work of compaction required to deform the highly hydrogen bonded microcrystal aggregates. Having been brought close together by plastic flow, particles again strongly bond to form highly resistant compacts. The compactability of the samples tested, nevertheless, differs greatly (by a factor of 2.5 between the two extremes).

Within-product variation is higher for MCC type 101 and 102 batches than for the corresponding Avicel® products. Difference in the Brittle Fracture Index of compacts prepared from two Avicel® PH-101 batches have already been observed by Hiestand and Smith (66). Variation in mechanical strength is somewhat reduced if compressure (41), porosity (ε) and radial crushing force (F_c).

The work of compression of microcrystalline celluloses -essentially Avicel® and Heweten® products- has been evaluated by many investigators (42-50). It generally appeared that gross input was high because of the structure of the material resistant to consolidation. Present results confirm this, but values are surprisingly close for all samples. Observations on the friction properties reported for Avicel® products (10,35,43,45, 48,51-54) can be made for other microcrystalline celluloses, although some variations are noted between samples. Friction on compression is quite significant, as reflected by the values of work recorded on the lower punch (LPW), punch force ratio (R) and work of friction (FR). In contrast, friction parameters after loading (RLPF) and during ejection (EJF) are low.

Like Avicel® (45,47,53,55,56) all samples are good transmitters of axial to radial stress and thus are expected to form strong tablets (57), although some

studies (47,58-60) have demonstrated that this is not a sufficient criterion.

Low residual die wall pressures would normally result in unsatisfactory tablets with a tendency to cap or laminate (58). This is obviously not the case for microcrystalline celluloses and former assumptions on the predictability of this parameter are not applicable to viscoelastic materials (45).

Elastic recovery is a simple measure of the elasticity of the material and has been found to be directly proportional to the work for elastic deformation as measured from double compression cycles (8). Elastic recovery of microcrystalline cellulose compacts is high in reference to that of other diluents, although its crushing strength are observed, Avicel® and Emcocel® products giving the lowest values. Nevertheless, as a whole, type 1 and type 2 celluloses give similar values. These observations are in agreement with results obtained from the basic compression study showing that some powders exhibit very poor compactability: Medicel® 101, one batch of MCC type 101, MCC type 102 and Unimac® MG-200. The correlation between the forces required to prepare 8-mm compacts on the rotary machine and the crushing strengths of the 12-mm compacts compressed at the fixed pressure of 100 MPa on the eccentric machine (see Fig. 1, lubricated compacts) was less satisfactory, however, than expected (Spearman's rank correlation coefficients of 0.815 and 0.884 for types 1 and 2 celluloses respectively). Many factors may explain this, such as the range of compaction pressures used, the difference in the dwell time (77-81) and the presence of a pre-compression roll in the rotary machine (74).

Tablets from all products (except Ex-Cel®) have good uniformity of weight. As expected from flow properties,

coefficients of variation values for type 2 celluloses are smaller than those of type 1 materials. This has been reported for Avicel® PH-101 and PH-102 with single punch (10) and multiple punch (12) tableting machines. The only exception is the better uniformity found for Medicel® 101 than for Medicel® 102, as consistent with their respective flow rates. It should be mentioned however that no strict rank correlation can be observed between weight variations and flow rates (determined only for type 2 materials). This poor correlation has been reported by Ho et al. (33) for other directly compressible vehicles, but these authors found a satisfactory relationship between weight variation and cohesiveness or flow factor as determined from shear cell studies.

The good weight uniformities generally observed for the celluloses tested are partly due to the excellent performance of the forced feeding system of the rotary machine used. Reported coefficients of variation generally relate to tablets prepared with eccentric machines and are therefore higher, if reference is made to the tablet size (6,10,28,32,33,44,67,71). Magnesium stearate is reputed to have a slight effect on weight variation of Avicel® tablets (10,12), but no experiments without lubricant were conducted in this work because of the high tableting speed used. Finally, our results confirm the slightly better weight uniformity of Avicel® PH-101 tablets over that of Emcocel® noticed by Pesonen and Paronen (6).

Differences in tablet thickness (and thus porosity) from one product to another have already been discussed; these were due to differences in compressibility (plastic deformation) of the powders and elasticity of the compacts. Here coefficients of variation also differ because of weight variability but no direct relationship between

the two parameters can be found. Figures are of the same magnitude as those of Chilamkurti (28).

Actual diameter values depend on the elastic recovery of the materials, but dispersions are low and no individual values exceed the ±5% BP limit. Crushing strengths vary quite differently from one product or batch to another, and again no correlation is establishable with weight coefficients of variation. However, the greatest CV values are again obtained with Ex-Cel® and the two types of Medicel®.

Like the pioneer Avicel® products (6,12,28,30,67, 82-84) and Emcocel® (6), all celluloses tested show low friability indices (the 1% limit generally accepted was not exceeded). At the compaction forces used (maximum ca. 75 MPa) no capping tendency was detectable although the compacts contained 0.5% magnesium stearate. At 1% level Ritter and Sucker (84) observed for Avicel® PH-102 a capping tendency above about 110 MPa which increased with increasing pressure, though friability remained very low. These authors concluded that radial tensile strength and bending strength quantify adequately the capping tendency. Finally, it should be pointed out that no relationship can be found in microcrystalline celluloses between tablet friability indices and crushing forces, as frequently demonstrated for other excipients.

Disintegration properties of pure and lubricated Avicel® compacts have been discussed quite extensively in the literature (2,4,5,10,12,28,30,40,44,68,69,83,85, 86). It is generally stated that disintegration time is very short up to a certain compaction pressure, beyond which it strongly increases (2,5,28,69).

The effect of adding magnesium stearate on the disintegration of Avicel® compacts has been studied by many

investigators (10,12,68). Disintegration appeared more rapid when 0.25 to 1% magnesium stearate was incorpored. It was concluded that with these hydrophilic vehicles, bonding strength and porosity (compaction pressure) are the main factors affecting disintegration (68). Here, we compare compacts lubricated with 0.5% magnesium stearate compressed at a low pressure. When using discs as officially requested, disintegration is very rapid for the majority of materials. Only one product, Medicel® 101, failed to pass the 15 min limit of the European Pharmacopeia. When using the more discriminating test without discs (87), an acceptable prolongation of disintegration is observed, except for Medicel® 102 and MCC type 101, batch 2. For the latter product, some tablets, surprisingly, did not disintegrate completely in 4 hrs.

CONCLUSIONS

To summarize al the data a comparative evaluation of the celluloses tested, based on the main factors for tableting, is presented in Table 5. Properties of less importance or parameters which do not differ significantly among products, are not considered. The criteria used are the compressibility of the powders under vibrating or tapping, as assessed by the Hausner ratio which is known to correlate with the flow properties (91), compactability, as given by the mechanical strength of the compacts at a fixed pressure, sensitivity to the addition of a lubricant such as magnesium stearate, as determined from the strength reduction, the regularity of weight of the tablets, as deduced from the coefficient of weight variation of the tablets prepared on the rotary machine and the desintegration time of these tablets.

Best evaluation corresponds to a H value lower than 1.25 (equivalent to a compressibility of 20%), a crushing

TABLE 5

Comparative Evaluation of the Tableting Properties of the Celluloses
(+++ : excellent, ++ : adequate, + : poor, - : inadequate)

Material	Compressibility on tapping	Compactability (hardness /pressure ratio)	Sensitivity to a lubricant	Regularity of weight[1]	Disintegration[1] with discs	Disintegration[1] without discs
Avicel® PH-101	++	+++	+++	++	+++	+++
Emcocel®	++	+++	++	+++	+++	+++
Ex-Cel®	--	++	+++	--	+++	+++
Medicel® 101	+	+	+++	++	+	+
MCC type 101	+	++	++	+++	+++	--
Sanaq 101 L	++	++	+++	++	+++	++
Unimac® MG-100	++	++	+	++	+++	+++
Avicel® PH-102	++	+++	++	+++	+++	+++
Emcocel® 90M	+++	+++	+	+++	+++	+++
Medicel® 102	-	+	+++	+	++	++
MCC type 102	++	++	++	+++	+++	+++
Unimac® MG-200	+++	++	-	+++	+++	+++

[1]Tablets lubricated with 0.5% magnesium stearate and prepared on the rotary machine to a target crushing strength of 60 N.

force of more than 400 N when compacted at 100 MPa, a strength reduction ratio of more than 0.90 (equivalent to a strength reduction of 10%) upon addition of 0.5% magnesium stearate, a weight variation of less than 1% with the high speed tableting machine used and disintegration times of these lubricated tablets of ca. 60 N crushing strength of less than 5 min with discs and less than 15 min without discs.

A Hausner ratio over 1.35 (26% compressibility), a crushing force of less than 250 N, a strength reduction ratio in presence of the lubricant lower than 0.80 (strength reduction of 20%), a coefficient of weight variation over 2% and respective disintegration times of more than 15 and 45 min are considered as "poor". Intermediate values are classified as "adequate". In a few cases, some data were well outside these limits and

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