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The properties of tablets manufactured on an automatically-controlled rotary machine

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Four direct-compression bases: Celutab in the hydrous and the anhydrous form, Emcompress Special, and spray-dried lactose, have been compared with a traditional lactose granulation with respect to initial physical properties of the powder, tabletting performance and the characteristics of the tablets produced. The tablets were made on an instrumented rotary machine with feedback weight control operating to minimize time-dependent change within a batch, compression force being continuously monitored. Tensile strength by diametral crushing, porosity, disintegration time and surface indentation hardness were assessed and correlated with changes in compaction force, machine speed and tablet thickness. All materials gave well-formed tablets with no evidence of capping between 90 and 350 MN m^{-2}, and weight variation was small except for Emcompress Special at the highest machine speed, when die filling became erratic.

The intention underlying the use of direct compression tablet bases is that powdered active ingredients can be mixed with the base in a dry solids blender, and the resultant blend can be fed to a tabletting machine. Good tablets should result, and the compression characteristics should remain satisfactory until at least 20% of other powder has been added to the base. The stage of wet granulation is eliminated. The properties of such bases are thus of some importance.

Spray-dried lactose and conventionally prepared lactose were compared by Gunsel & Lachman (1963) who suggested that only the former was suitable for compression as a simple admixture. Batuyios (1966) studied anhydrous lactose and concluded that it was suitable for use in high-speed rotary machines. Duvall, Koshy & Dashiell (1965) compared dextrose with spray-dried lactose and found that dextrose could be partially or wholly substituted for the lactose in some formulations. Henderson & Bruno (1970) investigated the use of lactose beadlets and dextrose (Celutab), and concluded that these two materials are generally superior to others as fillers. Starches have been found suitable for use as direct-compression bases (Manudhane, Contractor & others, 1969, Kwan & Milosovich, 1965). Microcrystalline cellulose was studied by Fox, Richman & others (1963) who found that, when it was present as at least 70% of the formulation, no other additive was needed.

All the foregoing investigators, apart from Henderson & Bruno, examined the tabletting characteristics only qualitatively, by making tablets under conditions where the compaction force particularly was not accurately known. Shotton, Deer & Ganderton (1963) instrumented a rotary machine using strain gauges, transmitting the signal by radio telemetry to avoid the use of slip rings. This was essentially a research tool, as several compaction stations were occupied by the radio transmitter. Accurate

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measurements using instrumented rotary machines capable of industrial use have been made by Knoechel, Sperry & others (1967) and by Goodhart, Mayorga & others (1968), but these authors do not specify, except in very general terms such as "antacid formulation" what material was compressed. Reference may also be made to the instrumentation of a rotary machine in a similar manner by Wray, Vincent & others (1966) together with the work of Henderson & Bruno (1970) who used this machine.

In the present work, a rotary tabletting machine, instrumented and automatically controlled as described by Ridgway, Deer & others (1972) has been used to produce tablets from four direct compression bases (Emcompress Special, Celutab hydrous, Celutab anhydrous, spray-dried lactose) and also from a conventional lactose granulation. The machine was operated so as to produce tablets from each material at three thicknesses at each of three machine speeds and four compaction pressures. Tablets from the resulting batches were assessed for tensile strength by diametral crushing, porosity, disintegration time and surface indentation hardness. Thus various properties normally measured as tablet quality controls have been examined as a function of manufacturing variables for a range of available and frequently-used tablet base materials.

MATERIALS AND METHODS

Materials

The materials were: Celutab, hydrous (Kingsley & Keith (Chemicals) Ltd., Croydon); Emcompress Special (same supplier); spray-dried lactose (Whey Products Ltd., Crewe); conventional lactose granulation (Thomas Kerfoot Ltd., Ashton-under-Lyne).

Celutab is composed of maltose-dextrose porous spheres; the anhydrous form was prepared from the hydrous by heating in an air oven for 16 h at 60°. Emcompress—a form of dicalcium phosphate dihydrate—and Celutab were lubricated by the addition of 1·5% by weight of magnesium stearate, the proportion recommended by the manufacturers. No disintegrant was added. The lactose granulation had the composition: lactose 50%, sucrose 33%, maize starch 16%, magnesium stearate 1%. To give comparability with the other materials, 1·5% of magnesium stearate was added to the spray-dried lactose.

Methods

To determine the particle size distribution by weight, 50 g of each material were sieved for 10 min through the appropriate B.S. sieves (between 16 and 350 mesh). True particle densities were determined by specific gravity bottle at 20° using dekalin as the displacement fluid. Tap densities were determined before and after the addition of lubricant by tamping 100 g of each powder in a 250 ml measuring cylinder for 500 taps on a small machine operated by a rotating cam.

Each material was used to make batches of tablets on a Betapress (Manesty Machines Ltd., Speke), which had been instrumented as described by Ridgway & others (1972). The machine had 16 stations and was fitted with 12 mm diameter flat-faced punches. Each material was used to make tablets of three thicknesses: 3, 4 and 5 mm, at three machine speeds: 700, 1100, and 1500 tablets/min, at four compaction force levels: 10, 20, 30 and 40 kN. These latter forces correspond to pressures of 88, 177, 266 and 354 MN m^{-2}. A total of 180 batches of tablets was prepared, about 100-200 tablets being collected during operation at each set of conditions.

At least 24 h elapsed between making and testing any tablet. Ten tablets from each

batch were then weighed individually and their thicknesses were determined. The porosity could then be calculated since

$$\% \text{ porosity} = 100\ (1 - \text{tablet density/true density}).$$

The diametral crushing strengths of the weighed tablets were measured using either the apparatus described by Shotton & Ganderton (1960) or an Instron physical testing instrument. The latter was essential for some batches where the tablets had breaking loads in excess of 25 kg. A number of tests were run to ensure comparability of the results from the two machines. Tensile strengths (Fell & Newton, 1970) were calculated for all tablets, although only the Instron machine gave ideal tensile fracture. The Instron readings were divided by 1·216 to give comparability with the Shotton & Ganderton method. Tensile strengths determined on the Instron were higher, and more reproducible. The results have been expressed in terms of the Shotton & Ganderton method because a greater proportion of the measurements were made in this latter manner, and because the overall precision of this method is not so high.

Five tablets from each batch were tested individually for disintegration according to the B.P., using deionized water at 37°, but in five separate baskets, so that individual disintegration times could be measured, rather than the maximum of five values.

Surface microindentation hardness of the tablets was determined by the method of Ridgway, Aulton & Rosser (1970) using a pneumatic microindenter (I.C.I. Ltd.). Measurements were made of the Brinell hardness at the centres of the faces and at points near the periphery. Determinations were restricted to tablets made at 1100 tablets/min with a thickness of 4 mm. Five tablets were measured from each batch.

RESULTS AND DISCUSSION

The densities of the five materials are listed in Table 1. In all cases, the tap density was increased slightly by the addition of the lubricant. The particle size distributions are shown in Fig. 1. All are unimodal and very approximately log normal.

Table 1. *The densities of the materials used.*

	True density g cm^{-3}	Tap density, g cm^{-3} before lubrication	Tap density, g cm^{-3} after lubrication
Celutab hydrous	1·49	0·72	0·78
Celutab anhydrous	1·51	0·68	0·72
Spray-dried lactose	1·50	0·87	0·88
Emcompress Special	2·17	0·99	1·01
Lactose granulation	1·51	—	0·78

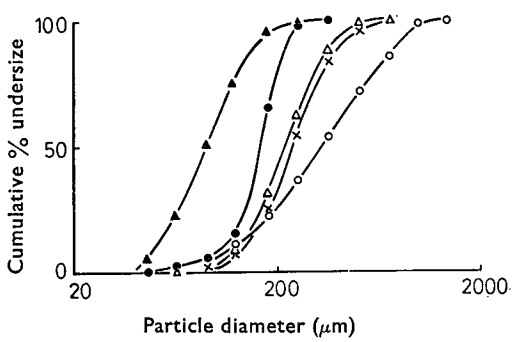

FIG. 1. Particle size distributions of the five materials used to make tablets. Spray-dried lactose ▲, Emcompress Special ●, Celutab anhydrous △, Celutab hydrous ×, lactose granulation ○.

All the materials flowed well, and compressed without any sign of capping or difficulty in ejection. At the highest machine speed, Emcompress gave some difficulty because the fill of the die became irregular, so that at the maximum force level, serious overloading was occurring.

The results obtained in the compaction tests are given in Table 2, which lists coefficient of variation in weight, porosity, breaking load, tensile strength and disintegration time. These quantities are given as a function of tablet thickness and weight, machine speed and compaction pressure. Table 2 contains the results for Celutab hydrous.*

Table 2. *The properties of the tablets made from Celutab hydrous*

Thickness mm	Compact. press. MN m^{-2}	Machine speed Tabs min^{-1}	Weight g	C. v. of wt %	Porosity %	Breaking load kg	Tensile strength MN m^{-2}	Disint. time min
5·00	109·3	700	0·733	0·12	14·70	20·87	2·154	13·6
5·11	103·8	1100	0·741	0·59	15·60	19·49	1·968	13·0
4·99	110·4	1500	0·726	0·50	15·40	18·96	1·960	12·5
5·02	180·0	1500	0·778	1·16	9·80	33·85	3·481	14·8
5·01	183·6	1100	0·779	0·30	9·49	33·96	3·499	16·3
4·98	186·1	700	0·777	0·69	9·28	36·17	3·745	16·0
4·92	261·5	700	0·789	0·39	6·58	41·94	4·403	16·3
4·92	256·1	1100	0·788	0·70	6·73	40·82	4·284	16·4
5·00	256·1	1500	0·799	0·73	6·92	41·41	4·277	16·4
5·19	324·9	1500	0·843	0·80	5·41	46·32	4·606	18·6
5·02	335·8	1100	0·814	0·61	5·66	42·89	4·410	18·9
5·02	332·2	700	0·819	0·45	5·16	45·86	4·711	19·1
4·02	328·6	700	0·652	0·47	5·65	36·22	4·650	15·0
3·99	328·6	1100	0·647	0·29	5·61	35·58	4·602	14·8
3·91	330·4	1500	0·636	0·89	5·26	36·09	4·763	15·3
4·05	256·1	1500	0·646	1·01	7·06	34·87	4·448	14·2
4·03	256·1	1100	0·646	0·18	6·66	34·34	4·403	14·8
4·01	261·5	700	0·640	0·85	7·09	34·39	4·424	14·1
3·96	185·4	700	0·614	0·30	9·81	27·22	3·548	13·2
3·95	180·0	1100	0·618	0·22	8·92	27·93	3·647	14·1
4·07	180·0	1500	0·630	0·90	9·80	29·16	3·700	13·3
3·99	107·5	1500	0·575	0·87	16·13	15·16	1·955	10·8
3·98	111·1	1100	0·574	0·62	15·98	13·68	1·775	11·7
3·97	107·5	700	0·578	0·79	15·11	21·52	2·111	12·3
2·95	111·1	700	0·430	0·69	15·13	11·61	2·033	9·1
3·07	114·7	1100	0·449	0·40	14·85	11·89	2·001	10·5
3·05	107·5	1500	0·440	0·65	16·10	10·82	1·829	9·1
2·94	180·0	1500	0·451	0·79	10·85	18·50	3·246	10·2
3·08	183·6	1100	0·477	0·35	9·72	20·99	3·519	10·8
3·02	183·6	700	0·466	0·56	10·04	19·67	3·364	11·4
3·01	258·6	700	0·478	0·33	7·68	24·38	4·174	11·0
2·94	259·7	1100	0·470	0·61	7·09	24·69	4·331	10·1
3·01	259·7	1500	0·479	1·17	7·57	24·39	4·185	10·9
2·92	335·8	1500	0·468	1·67	6·63	25·87	4·572	11·7
3·06	324·9	1100	0·497	1·09	5·58	28·04	4·724	11·6
3·00	339·4	700	0·483	0·65	6·40	26·64	4·578	11·3

Weight variation was small, in the region of 0·4% coefficient of variation, for all materials, with the exception of Emcompress as mentioned above. This means that all tablets were well within the B.P. limits; no tablets deviated by even 2% of their mean weight. In general, the variance increased with increasing machine speed, but there did not seem to be a clear-cut relation between variance in weight and tablet thickness. At best, there appeared to be a loose relation between increasing variance and decreasing thickness. The limit on the variance is the quality of the granulation or the ease of flow of the powder; added to the variance from this cause is that due to inequality of punch lengths, but this latter was small, the tooling being new and the punch lengths constant to within 0·025 mm.

Surface hardness and elasticity were independent of compaction force for all five materials, once a sufficient force had been applied to make a good tablet: this was

* Copies of similar tables giving the results of measurements made on Celutab anhydrous, spray-dried lactose, Emcompress Special and lactose granules, may be obtained from the senior author (K.R.).

usually the case at the 180 MN m^{-2} pressure level, and often at 90 MN m^{-2}. This is shown graphically in Fig. 2 and Table 3. However, the hardness was greater at the centres of the tablets than at the peripheries. This is probably a normal occurrence

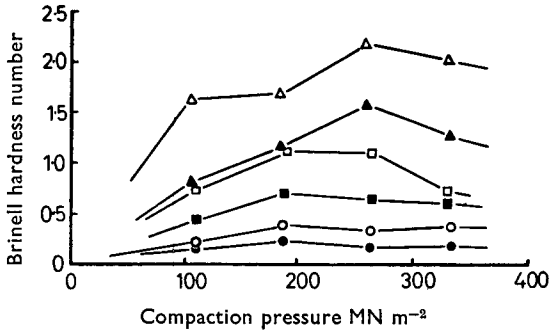

FIG. 2. Surface microindentation hardness as a function of compaction pressure. Open points: hardness at the centre of the tablet face; closed points: at the periphery; circles: lactose granules; triangles: Emcompress Special; squares: Celutab anhydrous.

Table 3. *Central and peripheral Brinell hardness values for tablets of the five materials, all made at* 1100 *tablets per minute at* 4 *mm nominal thickness.*

Material	Compaction pressure MN m^{-2}	Brinell hardness no. centre	Brinell hardness no. periphery
Celutab hydrous	111·1	0·88	0·49
	180·0	1·29	0·65
	256·1	0·76	0·48
	328·6	0·66	0·38
Spray-dried lactose	108·5	0·59	0·25
	183·6	0·41	0·34
	260·4	0·54	0·36
	322·0	0·73	0·35
Emcompress Special	103·8	1·61	0·81
	180·0	1·69	1·15
	254·3	2·17	1·57
	326·0	2·00	1·25
Celutab anhydrous	107·5	0·79	0·45
	183·6	1·16	0·72
	259·7	1·10	0·67
	324·9	0·75	0·61
Lactose granulation	108·5	0·20	0·18
	183·6	0·39	0·24
	257·5	0·35	0·18
	328·6	0·38	0·19

with flat faced punches. When the die is filled initially, the voidage will be greater at the die wall than at the centre of the powder mass. With a uniform vertical compression, the pressure at the centre, where there is more powder, will reach a higher value than at the periphery. Using concave punch faces should give a greater degree of uniformity through the body of the tablet: this is currently being investigated.

The mean time taken for disintegration depended primarily upon tablet thickness and compaction pressure. Some of the data are shown graphically in Fig. 3. Celutab anhydrous tablets dissolved more quickly than did the comparable hydrous ones, presumably because the anhydrous material had a greater affinity for water. Both

types dissolved rather than disintegrated, giving a fairly clear solution, and in both cases the dissolution rate would appear to be dependent on the external surface area. Dissolution proceeded uniformly until the undissolved core was small enough to pass through the wire mesh of the basket. Tablets made from spray-dried lactose behaved

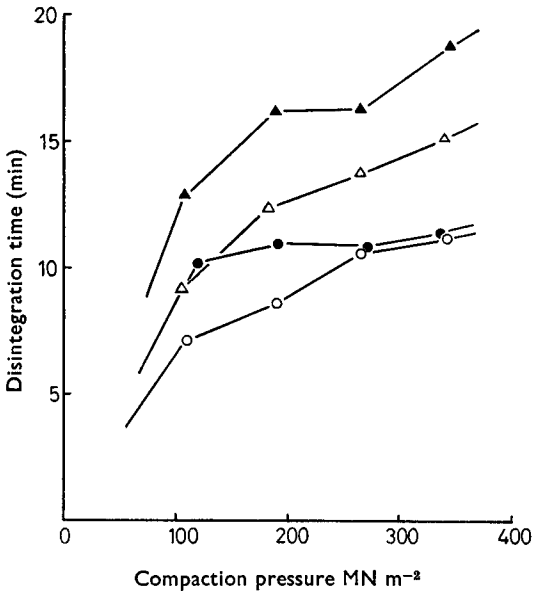

FIG. 3. Disintegration time as a function of compaction pressure for Celutab. Machine speed 1100 tablets/min. Closed points represent the hydrous form, open points the anhydrous. Circles are for 3 mm thickness, triangles for 5 mm thickness of the tablet.

differently, and took longer to disintegrate. They dissolved until they were about 30–40% of their original size, when they broke into several fragments, only a few of which were too large to pass through the basket mesh; these larger fragments were quickly further reduced in size by dissolution and passed the mesh. The tablets made from the conventional lactose granulation took about the same time to pass the B.P. test as the Celutab anhydrous tablets, but formed a cloudy suspension.

Tablets made from Emcompress did not disintegrate at all under B.P. test conditions: after 2 h at 37° the outlines of the tablet were still sharp.

The tensile strength decreases in the order Celutab hydrous, Celutab anhydrous, Emcompress, spray-dried lactose, lactose granulation. Machine speed had little effect on tensile strength, although it is possible that differences due to better stress relaxation by plastic flow at lower speeds, all other factors remaining constant, might be shown if the tablets were tested immediately upon leaving the machine.

Plots of tensile strength against compaction pressure for spray-dried lactose and lactose granulation are shown in Fig. 4. They were linear, confirming the results of Fell & Newton (1970). This linearity cannot extend indefinitely, of course, but it certainly covers the entire range of compaction pressure normally used. The spray-dried tablets were slightly weaker than the lactose granulation tablets. The sucrose in the latter would tend to increase the strength, and the starch to reduce it, the sucrose effect being preponderant. For all the materials tested, the tensile strength was independent of tablet thickness, and depended only upon the compaction pressure.

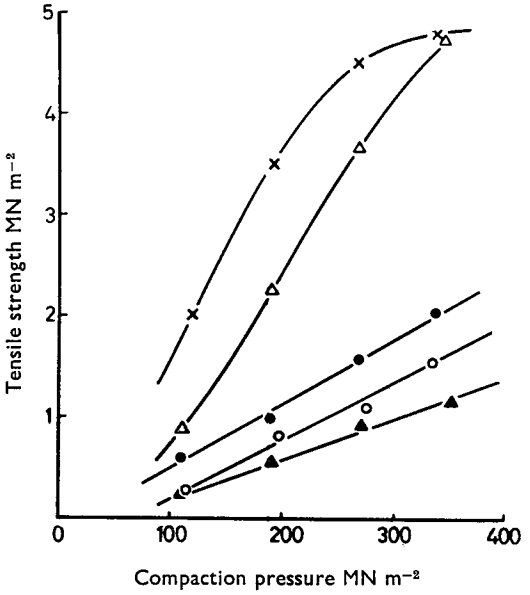

FIG. 4. Tensile strength, obtained by diametral crushing, as a function of compaction pressure. The lines are plotted for 3 mm thickness tablets at 1100 tablets/min machine speed. Lines for other thicknesses of each material coincide with the 3 mm lines. Point convention as for Fig. 1.

This confirms the usefulness of the tensile strength as a tablet parameter (Newton, Rowley & others, 1971), since it is independent of tablet dimensions and is a measure of the strength of the as-compacted material.

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