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Notes

Assessment of powder cohesiveness in spheronization studies

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Abstract

The effect of water on the cohesiveness of lactose-Avicel and lactose-Emcocel powder formulations was studied. Rod penetration depth and power consumption methods were used to demonstrate the change in the cohesiveness pattern of the moistened powder mass. The results showed that the amount of water necessary for successful spheronization could be ascertained. The two brands of microcrystalline celluloses (MCC) showed differences in their cohesive properties under wet massing and thus, in spheronization, adjustments must be made when one brand is substituted with another.

Keywords: Microcrystalline cellulose; Cohesiveness; Moistening liquid; Rod penetration depth; Power consumption

The amount of moistening liquid (Wan et al., 1993) and type of MCC (O'Connor et al., 1984; O'Connor and Schwartz, 1989) can have a marked effect on the spheronization process. The liquid content of the powder mass confers a degree of cohesiveness. Thus, measurement of the changes in cohesiveness of the powder mass undergoing wet massing can be useful in assessing the optimal amount of moisture required.

Lactose (Pharmatose 200M, DMV, The Netherlands) of mean size 41.64 μm, microcrystalline cellulose (MCC; Avicel PH 101, Asahi Chemicals, Japan and Emcocel, Edward Mendell, USA) and distilled water were used for spheronization.

Extrudates obtained from moistened powder mass passing through a 1.0 mm sieve were spheronized (Caleva, Model 120, UK) at 500 and 1000 rpm for 10 min, respectively. Spheroids were oven-dried at 60°C for 6 h before sieving (Endecotts Test Sieves, UK). The penetration depth (Gallenkamp, UK) of a cylindrical aluminium rod with conical tip (weight 39.032 g, cone angle 15.6°) into a moistened powder mixture packed in a cup (diameter 5.30 cm, height 5.75 cm) was determined. The power consumption required for mixing 300 g of powder with water added at a rate of 10 ml/min in a planetary mixer (Kenwood, A701A, UK) was measured with a power meter (Tabor, 4501B, Israel) and recorded using an X-T chart recorder (Hitachi, 056-1002, Japan). Hydration study was carried out by hydrating MCC in water for 4 h followed by centrifugation at 1640 rpm for 10 min, decantation and oven-drying at 120°C for 2 h. Poured and tapped (Stampfvolumeter, STAV 2003, Germany) densities were also determined.

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Table 1 shows that a critical amount of water was required for spheroid formation and was higher for formulations with a greater proportion of MCC. In a powder mass moistened with a limited amount of water, below the critical amount, most was probably absorbed into the interior of the closely matted fibres of MCC (Spiros et al., 1992), leaving little for liquid bridge formation. The resultant aggregates being weak would not withstand the high centrifugal and frictional forces of spheronization. When more water was used, the surfaces of spheroids became saturated. This allowed a certain degree of surface plasticity enabling partial deformation of the spheroids on collision with each other. Coupled with the tackiness of very wet surfaces, coalescence of the spheroids occurs, and large spheroids are formed. Spheroid growth rate with water addition was faster for lactose-Emcocel formulations and more significant with increasing proportion of MCC.

For the rod penetration studies (Fig. 1), the equation for moist powder system (Pilpel, 1971) is:

$$h(t) = \frac{3\pi d_1 d_2}{2(d_1 + d_2)} \sqrt{F_1 F_2} \times \left[1 + \frac{3\pi K}{Y} \sqrt{F_1 F_2}\right] \text{dyn}$$

where $h(t)$ is the adhesive/cohesive strength, d_1 and d_2 denote the radii of particles 1 and 2, F_1 and F_2 are the free surface energies for particles 1 and 2, K is a function of area of contact, shape and thickness of particle, and Y represents the yield pressure of the deformed layer. When little water was added, most of it was absorbed by MCC. As more water was introduced, the sur-

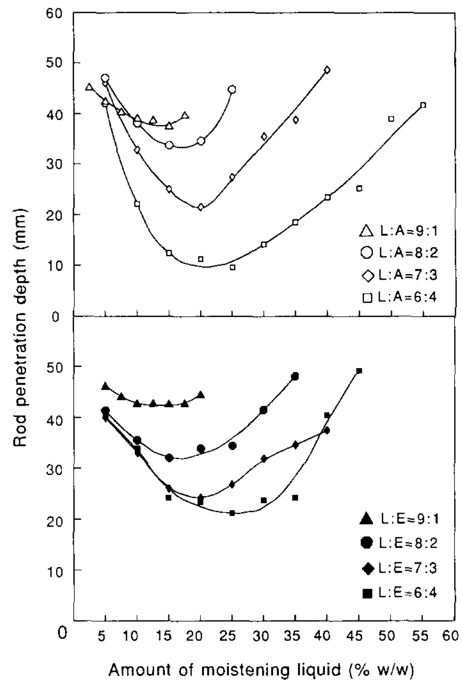

Fig. 1. Effect of the amount of moistening liquid on the depth of rod penetration into wetted lactose (L)-Avicel (A) and lactose (L)-Emcocel (E) mixtures.

Table 1
Effect of the amount of moistening liquid on the median spheroid size of varying proportion of lactose (L)-Avicel (A) and lactose (L)-Emcocel (E) mixtures

Amount of moistening liquid (% w/w)	Median spheroid size (mm) [a]							
	L/A = 9:1	L/A = 8:2	L/A = 7:3	L/A = 6:4	L/E = 9:1	L/E = 8:2	L/E = 7:3	L/E = 6:4
25	0.690	–	–	–	0.620	–	–	–
30	2.170	0.795	–	–	1.180	0.560	–	–
35	> 3.350	0.950	0.450	–	> 3.350	2.340	0.570	–
40	–	2.470	0.670	0.520	–	> 3.350	0.750	0.410
45	–	> 3.350	1.340	0.595	–	–	1990	0.780
50	–	–	> 3.350	0.915	–	–	> 3.350	1.220
55	–	–	–	1.440	–	–	–	> 3.350
60	–	–	–	2.460	–	–	–	–
65	–	–	–	> 3.350	–	–	–	–

[a] Median size could not be determined due to very few large spheroids being formed or when spheroid was not formed.

faces of lactose particles dissolved and the asperities present were reduced. This increased the contact area between particles, resulting in an increased K and decreased the deformation pressure (Y). The overall result was a greater cohesiveness of the powder mass, given by the initial progressive decrease in rod penetration depth.

On further addition of water, a minimum was reached, corresponding to maximum cohesiveness of the moistened powder, probably with a maximum number of liquid bridges. At this point, lactose-Avicel formulations allowed a smaller as well as a greater change in rod penetration depth compared with the corresponding measurements in lactose-Emcocel formulations. Addition of more water decreases the cohesive strength due to the lubricating effect of moisture on the particle surface. The minimum amount of water required for spheronization was greater than that required for minimum rod penetration depth. The amount of moisture beyond that required for liquid bridge formation was necessary for lubricating particle movement and allowing agglomeration.

Changes in the power consumption during wet massing are a result of changes in the cohesive forces of the moistened powder mass (Fig. 2). During the initial wetting, marked by increasing power consumption, loose agglomerates were formed. Liquid was taken up mainly into the intraparticulate pores. Further increase in the moistening liquid increased the cohesiveness of the powder as reflected by a rise in power consumption. The minimum amount of water for spheronization was about half the volume required for peak power consumption. When the amount of water was equivalent to that required for peak power consumption, extrudates failed to form spheroids. Instead, the powder mass formed a sticky band on the spheronizer wall. Power consumption values decreased rapidly as the powder mass developed into a slurry. At this stage, the droplet state predominated. Water acted as lubricant for the mixer impeller.

The power consumption and rod penetration results showed that the lactose-Avicel powder mixture undergoing wet massing was more cohesive than lactose-Emcocel powder. Using sandwich rheology, the cohesive force associated with moistened Avicel was reported to be comparatively higher than that of the similarly moistened Emcocel (Heng and Staniforth, 1988). The mean particle sizes, determined by laser light scattering (Malvern, 2600 with PS4, UK) of Avicel and Emcocel are 67.5 and 71.1 μm, respectively. Emcocel is larger by 5.3%. The mean percent hydration values for Avicel and Emcocel are 238.4 and 252.9%, respectively. Thus, Emcocel is 6.1% larger and this can be attributed to the greater surface roughness of the Emcocel particles, reflected by the higher Hausner ratio (1.53) compared to that of Avicel (1.49). This indicates greater cohesion and poorer flow properties of Emcocel. There is a small difference in cohesiveness between the two MCCs; the impact of this when mixed with lactose, a poorer flowing powder and in greater proportion, is likely to be minimal.

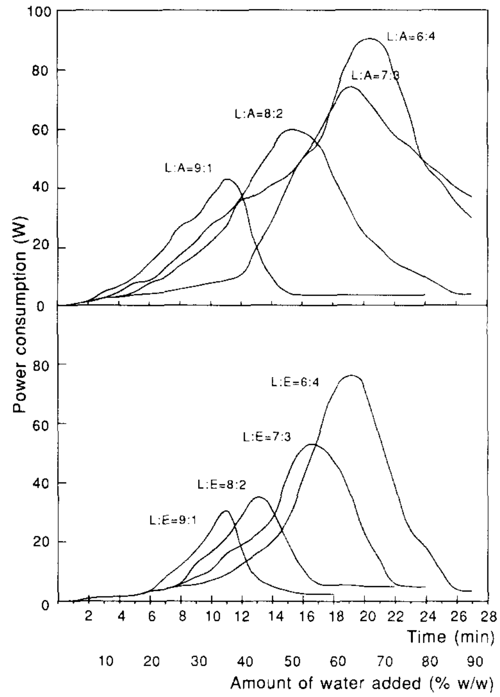

Fig. 2. Effect of the amount of moistening liquid on the power consumption of lactose (L)-Avicel (A) and lactose (L)-Emcocel (E) mixtures.

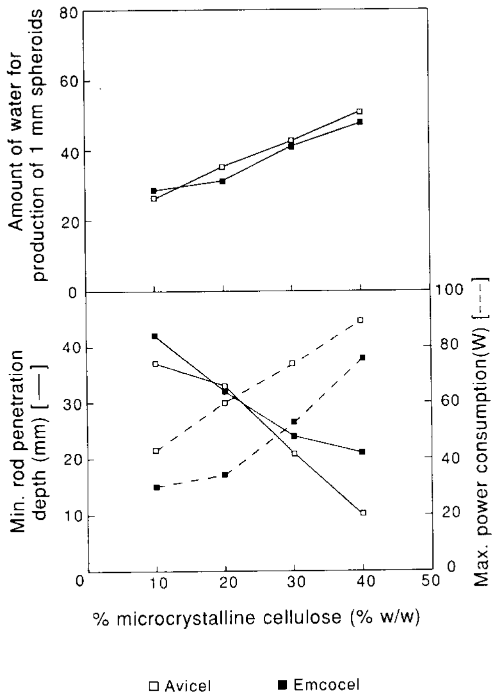

Fig. 3. Effect of the proportion of MCC in a formulation on the amount of water required for the production of 1 mm spheroids, minimum rod penetration depth and maximum power consumption of a wetted powder formulation.

With proportional increase in MCC, the cohesiveness of the powder mass is increased linearly (Fig. 3). The higher water retentive property of Emcocel may contribute to the lower cohesiveness of the moistened lactose-Emcocel powder mass. Firstly, as the insoluble Emcocel has a higher capacity for water retention, less water is available in the powder mass for dissolution of lactose powder. Probably, lactose dissolved in the granulating liquid can contribute to increased cohesiveness. Secondly, a greater amount of MCC increases the cohesiveness of the moistened powder mass, thus the MCC with greater affinity for water should have greater capacity to lubricate itself under the application of shear forces. This would result in lower cohesive forces.

Although the two MCCs show distinct quantitative differences in their cohesiveness profiles with different amounts of granulating liquid, the size of the spheroid produced did not differ as significantly. A linear relationship was obtained between the amount of liquid required to produce 1 mm spheroids and the amount of MCC incorporated. The amount of moistening liquid required was marginally higher for lactose-Avicel systems with Avicel content of 20% w/w or more. Probably, with the same moisture content, the use of Emcocel would result in marginally larger spheroids as the mean particle size of Emcocel is larger than Avicel. At 10% w/w MCC, the water requirement for lactose-Emcocel formulation to produce 1 mm spheroids is higher. Size difference between the two brands of MCC plays a lesser role when MCC content is low. The greater cohesiveness of lactose-Avicel mixture can have its influence, though small, in producing larger spheroids.

The formulation of lactose-Avicel has greater tolerance to varying amounts of moisture, due to the greater cohesiveness of the moistened mass to the processing chamber, preventing mass coalescence. The higher water retentive property of Emcocel can accelerate the coalescence process by making available the excess water under stress to plasticize the process of mass fusion.

In conclusion, rod penetration and power consumption measurements are useful to estimate the amount of the moistening liquid required for successful spheronization. Avicel and Emcocel, can be successfully employed as spheronization aids in similar proportions. However, small adjustments may be necessary when substitution of MCC is made due to differences in their cohesive properties under wet massing.

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