J. Pharm. Pharmacol. 1988, 40: 360–362
Communicated October 20, 1987

The effect of moisture on the cohesive properties of microcrystalline celluloses

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Abstract—A comparative evaluation of two microcrystalline celluloses, Avicel PH101 and Emcocel, revealed some differences in their cohesive properties at different moisture contents. A new method of sandwich rheometry was used to evaluate the cohesive properties of different powder masses. The force required to cause shear failure of a rough-surfaced blade in a powder bed was recorded. Avicel PH101 was found to be more cohesive than Emcocel at moisture contents less than 30 wt%, whereas at higher moisture contents the cohesive behaviour was comparable.

Microcrystalline cellulose (MCC) is commonly used as a principle excipient for tablet production either by direct compaction or following wet granulation. MCC powder is a relatively ductile material, undergoing significant plastic deformation during compaction, although significant loss of plasticity has been found in compacts prepared following wet granulation (Staniforth et al 1987). In addition, flow problems have been described for one commercial form of MCC, Avicel (Rudnic et al 1980). Another commercial form of MCC, Emcocel, has been reported to exhibit similar physical properties to Avicel PH101 in respect of specific surface area, moisture content, particle density, flow & binding properties. The main differences reported were that Avicel PH101 was less crystalline with a narrower size distribution than Emcocel although some differences following wet granulation were also reported by Staniforth et al (1987).

The aim of the present study was to investigate the effect of moisture content on the cohesive properties of Avicel and Emcocel, using a sandwich rheometer method.

Materials and methods

Two commercial forms of Microcrystalline Cellulose NF were used: Emcocel (manufactured by Finnish Sugar Company, Helsinki, Finland, for Edward Mendell & Co Inc, Carmel, NY, USA) and Avicel, type PH101 (FMC Corp Philadelphia, USA).

Moisture content. The moisture content of approximately 2 g of material accurately weighed, was determined following drying in a vacuum oven at 120°C for 2 h. The dried samples were allowed to cool at room temperature under vacuum and were reweighed. Resorption of moisture was determined by leaving dried MCC samples under ambient temperature and humidity. The moisture content was redetermined at intervals up to a maximum of six days using the mean of four determinations.

Cohesive properties. The cohesive properties of MCC samples were investigated using a specially constructed sandwich rheometer (Fig. 1). The shear box was constructed from Perspex and had a centrally located movable Perspex blade. One of the broad sides of the box was removable for purposes of filling. Positioning of the blade at the centre of the shear box was aided by fixed locating guides at the base of the box and a detachable half-guide at the top.

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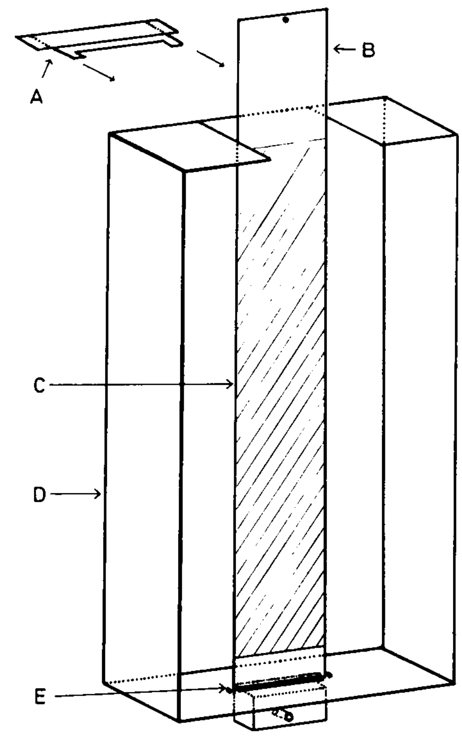

FIG. 1. Shear box with lid removed. Key: A detachable half-guide, B blade, C emery paper, D shear box without lid, E base guides.

Both sides of the shearing blade were covered with emery paper (Klingspor PS11 Autopaper P180c) to ensure that the powder failed at particle-particle contacts during shearing. The box was filled with powder by placing it on its broad side and half filling with MCC which was then levelled, using a broad T-shaped Perspex scraper plate designed to achieve constant fill height, before insertion of the central shear blade using the guides; more material was added to fill the shear box and the lid was then fitted and clamped. The assembled sandwich rheometer was then positioned upright and weighed. Constant packing for each sample was achieved by tapping the shear box and adding more powder through the removable upper half guide until the desired constant mass was achieved. The sandwich rheometer was then located on a tensile tester (type T22K, JJ Lloyd Instr., Southampton, UK) with the shear box anchored to the lower stationary crosshead using a fixed guide & locating pin and with the shear blade similarly attached to a 500N load cell on the upper movable crosshead. During testing the upper crosshead was driven upwards at a constant speed of 10 mm min^{-1}. The shear stress at failure was determined as the quotient of the initial force required to withdraw the embedded shear blade and the total surface area of emery paper in contact with MCC.

Table 1. The moisture content and moisture resorption of Emcocel and Avicel.

	Moisture content (%) (±s.d.)[a]	Moisture uptake[b] (% ±s.d.)[a]			
		10 h	30 h	4 days	6 days
Emcocel	3·62±0·02	1·73±0·10	2·54±0·02	3·02±0·01	3·17±0·02
Avicel	3·42±0·02	1·95±0·15	2·69±0·07	3·11±0·05	3·31±0·06

[a] Standard deviation.
[b] Moisture uptake by oven-dried material under ambient conditions.

Addition of water. Water was added to samples of MCC in a planetary mixer (Hobart Ltd, London, UK) and the wet mass was mixed for approx. 10 min.

Results and discussion

The moisture contents for Emcocel and Avicel were found to be similar (Table 1). In the moisture resorption studies, the uptake rate for Avicel appeared to be slightly faster than for Emcocel which may be a reflection of slight differences in properties such as particle size distribution or crystallinity between the two MCCs.

The specific cohesive property of the material bed measured in these experiments was that determined by the force required to cause the embedded blade to be sheared from the bed.

A typical recorder output is shown in Fig. 2: at point (a), failure of the powder bed occurs. The shoulder region (b) may represent a region of bed expansion caused by particle displacement following shear failure. The slope of the curve at (c) can be equated to particle-particle dynamic shear stress and the residual force (d) is the force exerted by the unloaded blade following withdrawal.

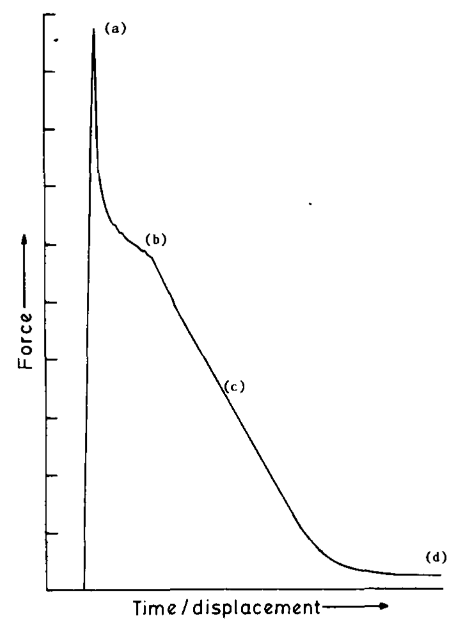

FIG. 2. A typical recording of the force required to shear the powder bed. Letters in parentheses represent the various stages of the powder bed shearing cycle (see text).

Characterization of dry powder beds using a penetrating plate (Hidaka & Miwa 1981) and a penetrating bar (Yuasa & Yamashiro 1985) have been attempted. For the penetrating plate method, a small plate was forced into a powder bed by raising the bed using a motor and jack, and then the force exerted on the plate was recorded. Two main types of curves were obtained: (i) smooth and (ii) step-like curves which were reported to be closely related to the cohesive angular property of the powder bed. In the penetrating bar method, a bar was forced into the powder bed by dropping weights and the depth penetrated by the bar determined. Both of these methods cause bed consolidation rather than expansion and shear as occurred in the comparative evaluation of Emcocel and Avicel powder beds by the withdrawal of an embedded blade. Differences in the cohesive properties of the two microcrystalline celluloses were found (Fig. 3) with Emcocel requiring the lower initial force to produce shear failure of powder. For both microcrystalline celluloses, the shear stress at failure increased with water content within the powder bed to a maximum at around 20 to 30%. At moisture contents greater than approx. 30%, shear stress at failure again decreased. Although the shear stress at failure for Avicel with a *lower* water content was higher than Emcocel, the shear stress at failure of the two microcrystalline celluloses with *high* water contents was similar.

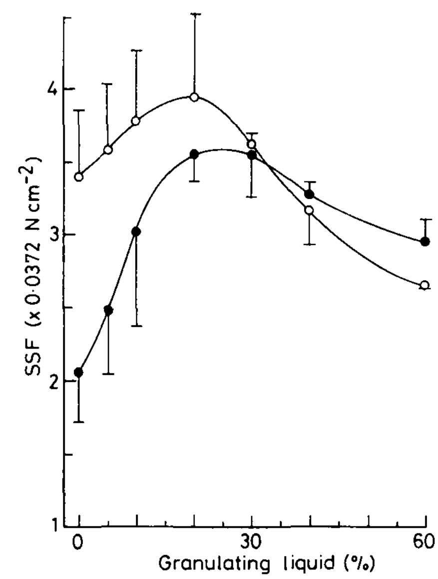

FIG. 3. Effect of the amount of granulating liquid on the shear stress at failure (SSF) for Emcocel (●) and Avicel (○).

In the process of wet granulation, addition of granulating liquid to the powder mass increases its cohesiveness and reduces flowability. Small quantities of a liquid added to a powder mass can form bridges between the powder particles and increase the resistance to flow as the liquid bridges resist the disruption necessary to enable the powder mass to flow. This may account for the increase shown in the shear stress at failure with an increasing water content in the wetted microcrystalline cellulose powders (Fig. 3). The shape and surface properties of the particles within the powder mass can alter the flowability of the mass. Differences in the particle properties between Emcocel and

Avicel have been reported by Pesonen & Paronen (1986). Emcocel was reported to have a wider size distribution than Avicel but its numerical mean diameter of 11·7 μm was similar to the 12·5 μm obtained for Avicel. However, the volumetric mean diameter was reported to be much larger, 22·2 μm for Emcocel against 13·4 μm for Avicel. It is likely that the volumetrically large Emcocel particles have reduced interparticulate points of contact and thus the powder bed may show a lower degree of cohesiveness for this reason.

As the amount of granulating liquid is increased beyond 20%, the shear stress at failure decreased for both Emcocel and Avicel (Fig. 3). This behaviour of the powder bed corresponds to the well-established behaviour of the powder mass undergoing wet granulation. When the water content in the powder mass is sufficiently high to engulf much of the particle surface, the advantageous lubricating effect of the liquid is exhibited thereby promoting flow of the particulate material with significantly reduced frictional forces.

Analysis of the cohesiveness of a powder bed using the sandwich rheometer method appears to be a simple method for characterizing a powder bed and has the ability to determine both the static and dynamic behaviour of the powder bed, providing the variables are standardized.

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J. Pharm. Pharmacol. 1988, 40: 362–364
Communicated August 24, 1987

Presynaptic changes promoted by alloxan diabetes in the cat isolated heart

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Abstract—Adrenergic presynaptic functions were evaluated in the cat isolated perfused heart preparation. The sympathetic nerve endings were labelled with [^{3}H]noradrenaline ([^{3}H]NA) and the effect of electric neural stimulation was determined in the presence of drugs which inhibit neuronal or extraneuronal uptake, or which antagonize α-adrenoceptors. [^{3}H]NA overflow was measured in control and diabetic cats and was significantly increased by electric neural stimulation on both conditions. Perfusion with 0·1 μM phentolamine increased transmitter overflow in control hearts but failed to do so on organs obtained from alloxan-treated cats. The data provide evidence that in alloxan diabetic cats there is an abnormality of the adrenergic synapse.

Experimental diabetes has been shown to induce changes in adrenoreceptor mechanisms (Costa e Forti & Fonteles 1979; Brody & Dixon 1964). In human adipose tissue Arner & Ostman (1976) have demonstrated that treated diabetic patients presented evidence for increased α- as well as β-adrenoreceptor sensitivity. Cseuz et al (1973), using rabbit aorta, found an increase in sensitivity, though with a lack of specificity for the adrenoreceptor blockers, since α-adrenotropic effects could also be blocked by propranolol. Owen & Carrier (1980) observed supersensitivity too, and found that the vascular alterations observed in rat aortas from diabetic animals were related to the duration of diabetes and to the extracellular calcium concentration.

Szentivanyi & Pek (1973) demonstrated an increase in α-adrenergic response in conjunctival vessels of diabetic patients and Christlieb et al (1976) observed an increase in systemic blood pressure elicited by noradrenaline (NA). The same kind of observations were documented by Foy & Lucas (1976) from rat blood pressure data. On the other hand, Fonteles & Matheny (1979) observed a reduced sensitivity to NA in the iris dilator muscle preparations of diabetic animals. Williams et al (1983) observed in streptozocin diabetic rats, a decrease in density of α- and β-adrenoceptors in the myocardium.

The above observations, coupled with those of Kunos et al (1973) and Ahlquist (1977), which demonstrated that the metabolic rate could quantitatively regulate the adrenoceptors, led us to investigate α-presynaptic adrenoceptors in diabetic cats.

Methods

Cats, 1·5 to 3·0 kg were anaesthetized with sodium pentobarbitone (30 mg kg^{-1} i.p.) and heparinized with 2500 u kg^{-1} through the femoral vein. The animal was intubated during surgery under artificial ventilation by means of a Harvard respiratory pump, model 680. The heart was isolated, the sympathetic nerves to the organ intact, and the cardioaccelerator nerve carefully dissected according to the technique of Hukovic &

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