International Journal of Pharmaceutics, 64 (1990) 55–60
Elsevier

IJP 02158

Young's modulus of powders used as pharmaceutical excipients

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(Received 1 March 1990)
(Accepted 4 April 1990)

Key words: Young's modulus; Four-point beam bending; Powder; Microcrystalline cellulose; Sugar; Starch; Inorganic filler; Ductility; Brittleness

Summary

The Young's modulus (E) of 15 representative tableting excipient powders has been measured for compressed rectangular beam specimens over a range of porosities using a four-point beam bending technique. Calculated values of Young's modulus at zero porosity (E_0) provide a means of categorising the mechanical characteristics in terms of elasticity and rigidity (stiffness) and brittleness on a quantitative scale. The order of increasing stiffness for the studied materials was starch < microcrystalline celluloses < sugars < inorganic fillers (calcium carbonate, calcium phosphate), with values of E_0 ranging from 3.71 to 88.28 GPa. Differences in E_0 for alternative sources of similar materials are discussed in terms of manufacturing pretreatment and crystallographic structure.

Introduction

A quantitative understanding of the mechanical properties of pharmaceutical powders is a prerequisite when attempting to predict compaction behaviour. Young's modulus (E), which describes the elasticity or stiffness of a material, is a critical mechanical property in powder compaction.

Whilst several methods of measuring Young's modulus (Roberts and Rowe, 1987a) are available for solids (such as tensile, compression and indentation techniques), these procedures pose practical and theoretical constraints when applied to powder or compressed powder specimens. For pharmaceutical powders and compacts, elasticity has generally been assessed either by the use of elastic or total compact recovery (e.g. Armstrong and Haines-Nutt, 1972; Marshall, et al., 1986) or by an indirect in-die method (Kerridge and Newton, 1986). Recent work has adapted a four-point beam bending technique to monitor Young's modulus for compressed powder samples in rectangular beam form over a range of porosities (Church and Kennerley, 1983; Mashadi and Newton, 1987; Bassam et al., 1988).

Four-point beam bending has been shown to be a preferred test for Young's modulus measurement, since there is a uniform bending moment over the central section of the beam. In addition, there is no significant contribution from shear stresses, which are important considerations and limitations of, for example, three-point bending techniques (Timoshenko, 1968). An important ad-

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vantage of bending tests over tensile tests is that the problem of efficient gripping of specimens to avoid failure at points of attachments is avoided.

Analysis of experimentally measured moduli over a range of porosities according to published empirical and theoretical relationships allows the material constant E_0, Young's modulus at zero porosity, to be derived (Mashadi and Newton, 1987; Bassam et al., 1988). In the present article, E_0 has been examined and evaluated for a range of pharmaceutical tableting excipients, including a series of microcrystalline cellulose powders from different sources, to probe a quantitative classification of their mechanical characteristics. Such information is valuable when attempting to understand and to predict the compaction behaviour of pharmaceutical powders (Roberts and Rowe, 1987a).

Materials and Methods

The powders studied were seven grades of microcrystalline cellulose powder from three sources — Avicel PH101, PH102, PH105 (FMC); Emcocel, Emcocel 90M (Mendell); Unimac MG100, MG200 (Unitika); five sugars — Dipac (Amstar); mannitol (C.C.A. Biochem.); spray-dried lactose (Meggle); anhydrous β-lactose (Humko Sheffield); α-lactose monohydrate (Dairy Crest), and maize starch (Laing National), calcium carbonate (Sturge), and calcium phosphate (Albright and Wilson). All powders were used as received.

Preparation of beam specimens

Beams of rectangular cross section 100 × 10 × h mm, where h is the thickness, were prepared by direct uniaxial compression using a rectangular hardened steel punch and die unit. Powder samples of known weight were compressed using a hydraulic press (Denison 50 Ton Testing Machine) at loads up to 500 kN. Beams of different final porosities were obtained by compressing at various loads, and attempts were made to prepare flaw-free beams with as low a porosity as possible. Beam dimensions and weight were recorded to determine porosity using true density figures from air comparison pycnometry (Beckman Model 930).

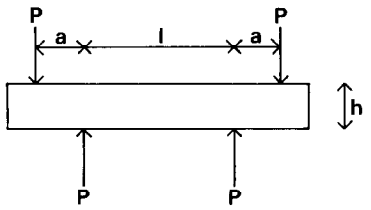

Fig. 1. Arrangement for four-point beam bending. P, applied load; b, beam thickness; h, beam height; l, distance between inner loading points; a, distance between the inner and outer loading point.

Beams were stored at 40 ± 5% relative humidity (RH) and 20 °C for not less than 1 week prior to test, unless otherwise stated.

Four-point beam bending

A CT40 Mechanical Strength Tester (Engineering Systems) was adapted for four-point beam testing, and load applied (P) and beam deflection (δ) were monitored by means of a calibrated (40 kg) load cell and linear voltage displacement transducer. Loads were applied at 0.5 mm/min. Tensile stress (σ) and strain, ϵ, were determined from knowledge of P, and the dimensions of the beam (Timoshenko, 1968) (see Fig. 1)

$$\sigma = 3Pa/h^2b \quad (1)$$

$$\epsilon = \delta h/2\left(l^2/8 + al/2 + a^2/3\right) \quad (2)$$

where δ is the vertical deflection of the midpoint relative to the outer contact points. A typical stress/strain curve is shown in Fig. 2, and Young's modulus (E) for the specimen is obtained from the gradient of this graph.

Results and Discussion

As expected, a decrease in Young's modulus with increasing porosity was observed for all materials (see Fig. 3) with a more rapid decrease at lower porosities. Preliminary experiments also confirmed that Young's modulus was independent of beam thickness within the range used and loading rate below 15.0 mm/min. Whilst beam orientation was found to have a small effect, this was

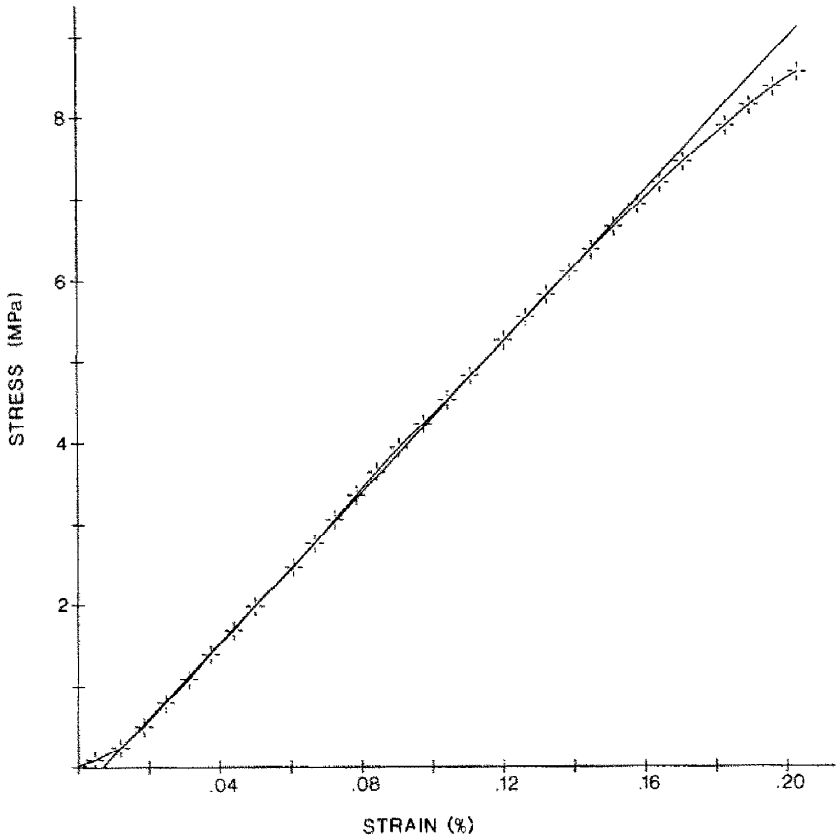

Fig. 2. A representative stress-strain plot of microcrystalline cellulose (Avicel PH105; porosity of beam = 0.08).

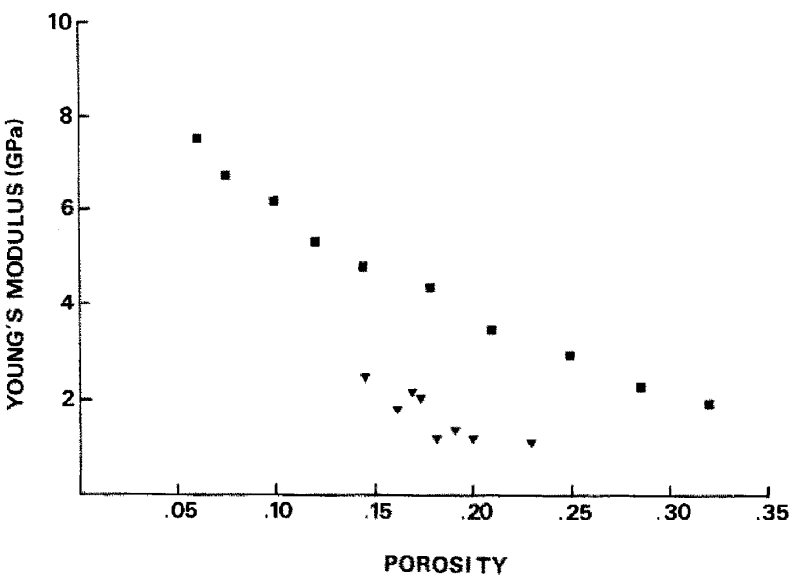

Fig. 3. Effect of porosity on Young's modulus. (■) Avicel PH105, (▼) mannitol.

eliminated by using equivalent orientation throughout the study.

Numerous equations have been published which describe the relationship between Young's modulus and porosity (P_1) (Dean and Lafez, 1983). Certain equations are based on theoretical considerations (e.g. Wang, 1984; Kendall et al., 1987), whilst others are empirical curve-fitting functions (e.g. Spriggs, 1961; Spinner et al., 1963).

A computer program was constructed and used to test the quality of fit to the range of published equations, based on a minimisation of mean square deviation, for the 15 powders studied (Bassam et al., 1990). The best overall relationship was that proposed by Spinner et al. (1963):

$$E = E_0(1 - BP_1 + CP_1^2) \quad (3)$$

where B and C are constants.

Table 1 lists derived values of Young's modulus at zero porosity together with figures for B, C and root mean square deviation (rms). Low rms values are indicative of the experimental data being well fitted by Eqn 3. It should be borne in mind that the values obtained for E_0 from this equation are marginally different from those determined in the case of the more commonly used Spriggs equation (Spriggs, 1961) applied previously to calculate moduli of microcrystalline cellulose samples (Bassam et al., 1988).

The E_0 value for Avicel PH101 is in agreement with that derived from the data of Church and Kennerley (1983) and that reported by Mashadi and Newton (1987). It is interesting to note from Table 1, however, that E_0 varies with both particle size and source. For two of the three sources of microcrystalline cellulose, an increase in E_0 is observed for decreasing particle size. Whilst unexpected, particle size variations may account for differing mechanical properties of tablets prepared from the various sized materials.

Source differences can be attributed to different prehistory in particle production, and subtle differences in the crystallographic structure of Un-

TABLE 1

Young's modulus at zero porosity (E_0), constants from Eqn 3, and estimate of deviation from fit (rms) for powders studied

	Approximate mean particle size (μm)	E_0 (GPa)	B	C	rms
Microcrystalline celluloses					
Avicel PH102	90	8.67	1.79	8.00	0.25
Avicel PH101	50	9.19	5.41	10.14	0.19
Avicel PH105	20	9.43	3.96	4.71	0.15
Emcocel 90M	90	8.87	4.33	5.69	0.25
Emcocel	56	7.13	3.40	2.82	0.19
Unimac MG200	103	7.34	1.36	5.86	0.16
Unimac MG100	38	8.03	3.90	4.37	0.14
Sugars					
Dipac	258	13.42	6.63	12.66	0.44
Mannitol	88	12.15	8.12	18.31	0.17
Lactose (spray-dried)	125	11.36	6.34	10.77	0.15
Lactose (anhydrous, β-)	149	17.91	6.11	10.83	0.55
Lactose (monohydrate, α-)	63	3.21	3.25	0.00	0.10
Polysaccharides					
Starch	16	3.71	4.63	5.67	0.07
Inorganics					
Calcium carbonate	8	88.28	4.46	5.10	0.14
Calcium phosphate	10	47.79	2.98	2.24	0.25

TABLE 2

Young's modulus at zero porosity (E_0) estimated using Eqn 3 for Avicel PH 101 samples stored at 40% and 76% relative humidity at 20°C

Storage condition (% RH)	E_0 (GPa)
40	9.19
76	6.55

imac samples compared with Avicel and Emcocel samples (Parker, 1989). Both these factors may contribute to the observed difference in equilibrium moisture contents under ambient and test storage conditions, with Unimac samples, for example, attaining a lower moisture content than Avicel materials. Since increased moisture content in microcrystalline cellulose decreases E_0 (see Table 2), the differences in E_0 between sources listed in Table 1 would be increased if materials were compared at equivalent moisture contents.

The range of E_0 values obtained for the microcrystalline cellulose (7.13–9.43 GPa) corresponds to low values similar to those of other polymers such as polyvinylchloride (Roberts and Rowe, 1987a). On an elasticity scale ranging from hard, rigid materials ($E_0 > 70$) to soft elastic materials ($E_0 = 1$–10 GPa), these materials can be regarded as ductile, which is consistent with their wide usage and claimed multifunctional role as diluent and dry binder in pharmaceutical tablet formulations.

Apart from α-lactose monohydrate, the sugar samples, whilst essentially ductile, have higher derived E_0 values than the celluloses, indicating a degree of brittle character. This observation is consistent with the findings of workers describing the compaction properties of lactose samples using instrumented machines and pressure/volume data analysis (e.g. Fell and Newton, 1971; York, 1979; Vromans et al., 1986).

For the three lactose samples, E_0 appears to be dependent on the chemical structure as well as the preparation and pretreatment route, which influence structural properties such as crystallinity. For the spray-dried form, which contains an amorphous, non-crystalline polymer-like component, a reduction in E_0 to 11.36 GPa from 17.91 GPa for the anhydrous-β-lactose is obtained. The low figure for α-lactose monohydrate (3.71 GPa) is somewhat surprising but may be explained by localised microscopic cracks in specimens which were extremely difficult to prepare at low porosities. Such cracks were not unexpected, since the particle size of the α-lactose monohydrate was well in excess of that corresponding to its brittle/ductile transition (i.e. the particle size below which the material flows but above which it fractures; Roberts and Rowe, 1987b).

The inorganic materials calcium carbonate and calcium phosphate have E_0 values of 88.28 and 47.79 GPa, respectively, indicating increased brittle/stiffness characteristics, particularly calcium carbonate. This classification is again consistent with previous reports regarding the compaction of these calcium salts (Rue and Rees, 1978; York, 1978).

The analysis of Young's modulus at zero porosity for the range of pharmaceutical excipients thus provides a means of quantitating and categorising their elastic behaviour. Numerical values are consistent with the limited data available in the literature (Roberts and Rowe, 1987a). As a result, a range order of increasing rigidity of the materials can be listed: starch < microcrystalline cellulose < sugars < inorganic fillers (calcium carbonate, calcium phosphate). Such information provides a quantitative measurement and reflects the elastic property of the materials. When linked with the measurement of other important mechanical properties which contribute to the controlling of the compaction process, such as the yield stress (Roberts and Rowe, 1987a) and the fracture mechanics parameter (K_{IC}), the critical stress intensity factor (Mashadi and Newton, 1987), the mechanisms of tablet formation will be more fundamentally understood and a predictive capability for powder compaction behaviour achieved. This will be the subject of future reports.

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