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Definition of indices for the mechanical design of wet powders: application to the study of a natural polymer, microcrystalline cellulose

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Abstract

The formulation of a mixture for obtaining pellets by extrusion/spheronisation is based on experience and trials and not on a complete scientific understanding of the process. It has not been possible to exploit the progress made in rheology for characterizing the wet mixtures designed for use with this process. This is no doubt because of the difficulty of studying them by using existing rheometry apparatus in the traditional manner for substances possessing specific properties. For the essential conditions for conducting a conventional rheological study, i.e. the presence of a laminar flow with assumed perfect die wall adhesion, represents a difficult challenge to take up when working with heterogeneous materials whose density changes under the impact of pressure. This article is based on the use of an apparatus, the compresso-rheometer, which enables the extrusion process to be simulated on a reduced scale. It presents an original, precise study protocol resulting in mechanical characterisation through the use of two indices (visco-elasticity and plasticity) for microcrystalline cellulose/water mixtures. These new indices were established for the purpose of forecasting the behaviour of raw materials mixed with a liquid when subjected to a shaping process, and also for indirectly addressing the problems of formulation and dissolution. © 1997 Elsevier Science B.V.

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1. Introduction

Pellets (French Pharmacopoeia, 1990) are mostly obtained by extrusion/spheronisation (Vervaet et al., 1995) using wet powders. Under the effect of extrusion stresses, these wet masses take the form of small rods that are subsequently spheronised. Drying gives the pellets thus obtained, a permanent form by endowing them with a sufficient degree of resistance to allow them to be used. Specifications depend on the particular use envisaged, i.e. pharmaceutical industry, agribusiness, etc. The characteristics of these pellets depend on technological determinants such as the mechanical stresses of extrusion (pressure) and of spheronisation (centrifugal force). However, it is the deformation, flow and cohesion properties that govern the possibility of obtaining pellets. These properties are related on the one hand to the intrinsic physico-chemical properties of the powders themselves (Eaves and Jones, 1973; Benbow et al., 1987), and on the other to the composition and quantity of the wetting liquid (Bataille et al., 1990; Heng and Staniforth, 1988; Elbers et al., 1992).

In pursuance of different extrusion/spheronisation studies that have been conducted (Barrau et al., 1992; Sonaglio et al., 1995), highlighting the interest in obtaining a commanding knowledge of wet mixtures before their technological transformation, we designed and developed an apparatus, the compresso-rheometer (Baylac et al., 1995; Delalonde et al., 1996) enabling the mechanical study of these substances. In short, the measuring-cell of this apparatus is made of an instrumented piston which enters a barrel with a corresponding diameter. There are two possible modes of functioning according to the equipment selected at the base of the barrel, flow test when the base is fitted with a plate with a small diameter orifice (die) or compressibility/relaxation test when the barrel is shut with an unperforated plate. This article aims to present new relevant indices based on a study protocol enabling wet masses to be characterised with the aid of measurements of microcrystalline cellulose/water mixtures carried out with the compresso-rheometer.

Table 1
Loss on drying, particle volume and density of Avicel PH101 ($n = 5$)

Loss on drying (%) w/w	Particle volume (cm^3) of 10 g sample	Particle density (g/cm^3)
4.45 S.D. 0.2	6.55 S.D. 0.08	1.527

2. Materials and methods

2.1. Materials

Microcrystalline cellulose (Avicel PH101-F.M.C.-lot6112) commonly used for the formulation of pellets was chosen for the study. The wetting liquid was purified water. The quantities used in the study expressed as a percentage of added liquid (44.44; 50.00; 54.54; 58.33; 61.54% w/w) were defined in order to delineate symmetrically the optimum wetting defined at 54.54% w/w for Avicel PH101 (O'Connor, 1983) for obtaining pellets of standardised particle size.

2.2. Methods

2.2.1. Study of the raw material

The loss on drying of Avicel is determined according to the protocol of European Pharmacopoeia (1990) on a 1 g sample. The particle volume is measured on 10 g of microcrystalline cellulose by pycnometry (Beckman air comparison pycnometer). This makes it possible to calculate the theoretical volume occupied by 35 g of wet mixture (standardised sample) after exclusion of empty spaces, for each level of water content.

Table 2
Theoretical volume of zero porosity wet powders

Water added (%) w/w	Theoretical volume (cm^3) of 35 g sample
44.44	28.29
50.00	28.96
54.54	29.51
58.33	29.97
61.54	30.36

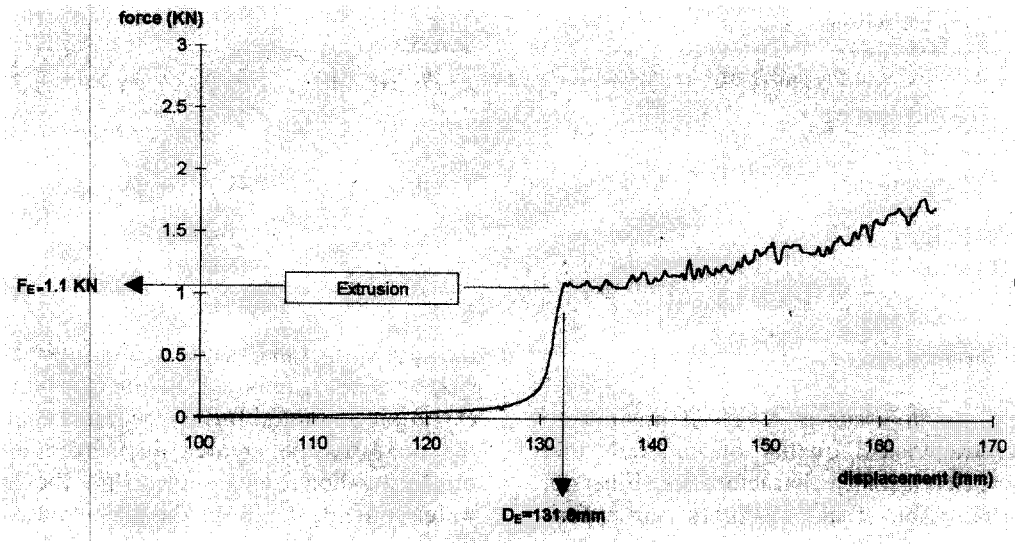

Fig. 1. Flow curve of wet Avicel at 54.54% w/w.

2.2.2. Study of wet powders

A planetary mixer (Kenwood 2 l) operating at 50 rpm for 10 min is used for the different wettings. The wet mixture is then immediately placed in the barrel of the compresso-rheometer (Baylac et al., 1995; Delalonde et al., 1996).

Tests are carried out in two stages: the first stage comprises flow tests using the open measuring-cell. A sample of 35 g of each wet mixture is extruded through a die 2 mm in diameter, 5 mm in length with a piston descent speed of 0.5 mm/s. The force exerted on the piston by the material is recorded relative to its displacement in the barrel. The beginning of the extrusion is observed visually and the displacement noted (D_E). The curves obtained make it possible, under our particular operating conditions and for each wetting, to determine a critical point whose co-ordinates are the displacement D_E (abscissa) and the force required for the flow F_E (ordinate). Flow tests constitute a first step which allows to know the displacement that brings the material into a state of compaction identical to that obtained at the moment that flow occurs. In the second stage, a new 35 g sample of the same mixture is placed in the barrel of the compresso-rheometer with the measuring-cell closed at the base. The piston is then brought to, and maintained at the value of the displacement that enabled the flow (D_E). From that moment, the relaxation curves are recorded. For each of them, two values are noted: maximal force (F_m) and residual force (F_r).

The maximal force may assume different values (always below F_E) for the same D_E. Consequently, there are different couples (F_m, F_r) for each wetting. The residual force is noted 2 min 30 s after maximal force is recorded. It shows the stabilising of the stress relaxation phenomenon.

3. Results and discussion

The results of the loss on drying, of the particle volume and the density of Avicel PH101 are given in Table 1. Since the Avicel is insoluble in water (F.M.C., 1985; European Pharmacopoeia, 1984), the theoretical volume occupied by 35 g of each wet mixture of zero porosity is calculated by adding the volume of water to the particle volume. The results in Table 2 show that the value of the zero porosity volume is higher when there is increased wetting. This is easily explained, given that the density of the Avicel is greater than that of the water (Table 1, $1.527 > 1$).

Table 3
Caracteristical flow curves values

Water added (%) w/w	Force at the flow start (KN)	Plotted displacement at the flow start (cm)	Barrel volume at the flow start (cm^3)
44.44	2.20	13.39	28.38
50.00	1.40	13.30	28.88
54.54	1.10	13.18	29.49
58.33	0.60	13.09	29.90
61.54	0.30	13.00	30.40

3.1. Flow curves

Studying the flow curves makes it possible to assess the rheological quality of materials and especially their plasticity characteristics (Elbers et al., 1992; Harrison et al., 1985). In our experiments, flow curves relating to microcrystalline cellulose at varying degrees of moisturisation show that our materials are only able to flow beyond a precise stress threshold. The flow threshold corresponds to the critical point of the co-ordinates (D_E, F_E) mentioned above. However, the value of the force F_E measured at this level for the different wettings cannot represent the plastic flow threshold (yield value) in absolute value, for account must be taken of the force required to be developed at the beginning of the experiment to bring the material to a state of compaction allowing it to flow. As we have already established (Delalonde et al., 1996), these curves show an approximate equivalent profile for the various moisture contents studied but different amplitudes. Fig. 1 shows the profile for a 54.54% w/w wetting.

The characteristic values of these curves (Table 3) are indispensable in carrying out relaxation test. The value of the displacement corresponding to the start of the extrusion makes it possible to calculate the volume of the barrel at this exact instant for the different mixtures. A comparison of this volume with the theoretical volume of the sample after exclusion of empty spaces (Table 2) reveals very close values and allows us to confirm that the flow of wet powders occurs at zero porosity, regardless of the water content of the sample. This findings agree with the results obtained by Shepphard and Clare (1972) who observed that in the case of metallic powders the interparticle free spaces were eliminated before the start of the extrusion. It should further be noted that the drier the mixture, the greater the force required for producing flow. This shows that the higher the water content, the lower the plastic flow threshold (Shah et al., 1995; Baert et al., 1991).

3.2. Relaxation curves

Relaxation tests are thus conducted after having brought the material to a state of compaction that ensures zero porosity. It is essential, in fact, to take account of the porosity factor together with the water content (Pietch et al., 1969) in studying these mixtures. Fig. 2 shows an example of flow and relaxation curves obtained with a 54.54% w/w mixture. These tests reveal the relaxation properties of wet powders in the state they are in (in term of compaction) at the time of extrusion. The maximal and residual forces are noted for each wetting.

A plot of the different residual forces (F_r) against the maximal forces (F_m) shows that the residual forces change linearly with the maximal forces for wetting from 44.44 to 58.33% w/w (Fig. 3). It is not possible to establish any linear correlation for the 61.54% wetting. This is because of the low residual force values recorded, which are in the nature of the sensitivity of the response. The straight lines equations calculated for 44.44–58.33% w/w wettings are presented in Fig. 3. They enable us to obtain two characteristic values for each line. One corresponds to the slope (b), the other to the intercept (a). The equations of the different lines have the form: $F_r = b \cdot F_m + a$. Values of slope and intercept for wetting from 44.44

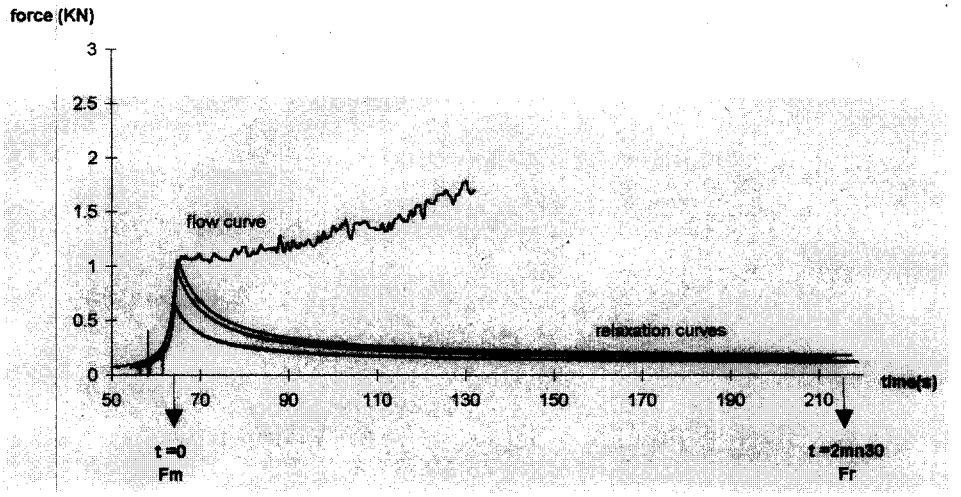

Fig. 2. Flow and relaxation curves of wet Avicel at 54.54% w/w.

to 58.33% w/w are presented in Table 4. The slopes recorded for the different moisture contents are of noticeably identical values (slope not significantly different to the risk 0.05 (analysis of covariance, $F_{calc(D.D.L.3,\ 26)} = 0.69$), the small variations recorded among the wettings being unable to be considered as significant in relation to the sensitivity of the response. The intercepts, on the other hand, are significantly different to the 0.05 risk (analysis of covariance, $F_{calc(D.D.L.3,\ 29)} = 690.08$). The intercept assumes a very low value in the case of wettings above 54.54% w/w. The b and a values as we have just defined them can be interpreted from the mechanical aspect. We shall call them the visco-elasticity index and the plasticity index respectively.

3.3. Interpretation of the slope or visco-elasticity index

In the case of a solid, in the linear elasticity zone, deformations are completely reversible, which implies the recording of a residual force equivalent to the force exerted initially. The slope of the line linking the applied force to the residual force is then equal to 1. It follows that the slope (b) then assumes a value of 1 in the theoretical case of an ideal elastic solid. In practice, wet powders of a highly elastic propertie will logically be less cohesive since internal tension will tend to dissociate the particles after liberation from the stress. Conversely, a material for which the recorded minimal force is then equal to 0, has dissipated all the mechanical energy initially supplied in the form of viscous friction (which implies a flow). Such materials display no internal elasticity. The slope $b = 0$. According to case, b will vary between two limits: 0–1. The Avicel for the different moisture contents studied displays an intermediate behaviour and its average value of 0.13 places it in the range of materials which flow and whose elastic response is poor. This is in conformity with the extrusion process involving a flow of wet powders through perforated screens. As in soil mechanics, the macroscopic deformations of wet masses can be largely attributed to the relative displacements of particles in relation to other particles (Leroueł et al., 1985). This can explain the fixed value of the slope for all studied wetting. For this value would be attributed to the solid skeleton of Avicel and the response would in fact be the resultant of the intrinsic physical properties of the solid particles (morphology, particle size, etc.).

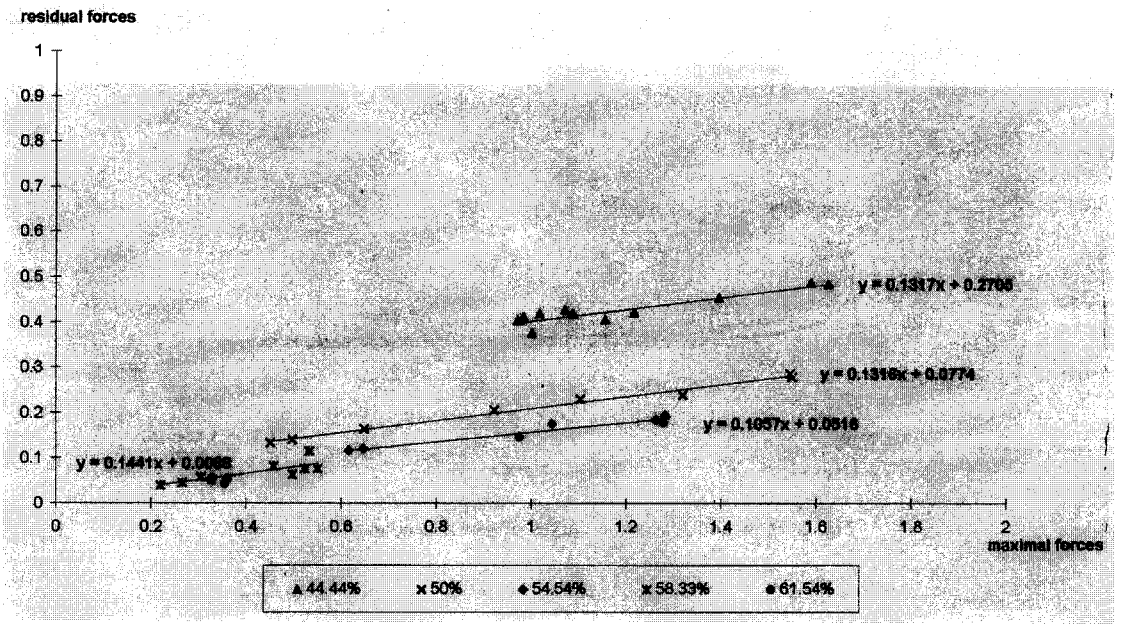

Fig. 3. A plot of residual forces against the maximal forces for Avicel at different moisture contents.

3.4. Interpretation of the intercept or plasticity index

The extrusion operation implies a flow since a product has to flow to be shaped, but this condition is not sufficient, for the product must be able to maintain the form it has just been given. To this end, it must possess a yied value corresponding to a minimal force, below which it does not flow and maintains the form imposed. The yield value may be put into relation with the intercept as defined above. The intercept value for the different wettings agrees with the observations made during flow measurements, for it is necessary to apply a force that increases as the degree of wetting decreases in order to induce a flow (Table 3). The value of the intercept very close to zero for wetting above 54.54% w/w would indicate predominance of the water in relation to particle solid and would explain the low value recorded for a in the case of excess wetting. From the physical aspect, this could result in the passage of the moistened solid to a state of slurry for which the solid particles are dispersed in a liquid. The value of a is to be correlated with the amount of liquid saturating the interstitial space and tends towards zero when the properties of the aqueous phase become dominant. This result brings out the importance of a maximal quantity of wetting liquid and makes it possible to establish a relationship between experimental observations such as obtaining a soft, viscid extrusion for wetting above 58% (Miyake et al., 1973) and the value of the intercept.

Table 4
Calculated values of slope b and intercept a

Water added (%) w/w	Slope b	Intercept a
44.44	0.1317	0.2705
50.00	0.1316	0.0774
54.54	0.1057	0.0516
58.33	0.1441	0.0088

The value of the extrusion/spheronisation process can be enhanced by understanding and mastering the mechanical properties that materials destined to be shaped must display. To this end, we have designed and developed an instrument of

measure, the compresso-rheometer, essential for quantifying these properties. This article confirms the interest of this apparatus in putting forward an original protocol for the study of wet powders, especially those containing polymers such as cellulose derivatives. The two indices obtained are sufficiently significant to serve as indispensable guides in the context of studies of preformulation and notably in the determination of the granulating end-point (optimal quantity of fluid for a given formulation). The establishment of a classification according to these indices for different formulations (binary, ternary mixtures, etc.) should result in a command of granulation process in general and of pelletisation in particular.

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