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A comparison between the extrusion forces and sphere quality of a gravity feed extruder and a ram extruder

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Summary

The forces involved during extrusion of mixtures of various proportions of excipients of different solubility, microcrystalline cellulose and water were compared on an instrumented ram extruder and an instrumented gravity feed extruder. The difference between the two extruders is that a gravity feed extruder is a discontinuous system while the ram extruder is a continuous system. The extrusion forces recorded with the ram extruder were always greater than those with the gravity feed extruder. The quality of the spheres produced by the two different extruders was compared. For an equivalent quality a lower water content was required for formulations processed by the ram extruder.

Introduction

The extrudate for the process of extrusion spheronisation can be produced by several types of extruder (Fielden and Newton, 1992a). The resultant spheres, produced via extrusion of the same basic mixture by a ram and a gravity feed extruder, have been shown to be different for microcrystalline cellulose/lactose/water mixtures (Fielden and Newton, 1992b). While the forces involved in formation of the extrudate by the ram extruder can be measured, it was not until an instrumented gravity feed extruder was reported by Baert et al. (1991) that a comparison between these types of extruders became possible. The present paper describes such a comparison.

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Materials and Methods

Materials

Microcrystalline cellulose MCC (Avicel PH 101–FMC, Wallingstown, Little Island, Cork, Ireland) was used as a pellet-forming agent and a α-lactose monohydrate (Pharmatose 200 M), β-lactose (DCL 21) and dicalcium phosphate dihydrate (DCPD) representing a medium soluble, a highly soluble and an insoluble drug, respectively. Lactose was supplied by De Melkindustrie Veghel, Veghel, The Netherlands, and dicalcium phosphate dihydrate by C.N. Schmidt, B.V., Amsterdam, The Netherlands. In all the experiments demineralised water was used as the granulating fluid.

Methods

Composition of the mixture used for the determination of the extrusion forces

Microcrystalline cellulose was granulated with water for 2 min in a planetary mixer (Kenwood Chef, Hamsphire, U.K.) at 60 rpm using a K-shaped mixing arm.

Mixtures of lactose or DCPD and MCC were dry blended for 10 min in the above planetary mixer at 60 rpm using the same arm. The mixtures were granulated with water for 2 min at 60 rpm. The compositions of the mixtures were (lactose or DCPD/MCC/water) (w/w): 0 : 50 : 50, 5 : 47.5 : 47.5, 10 : 45 : 45, 15 : 42.5 : 42.5 20 : 40 : 40. Additionally, the following mixtures were used for the two lactoses 25 : 37.5 : 37.5, 30 : 35 : 35, 40 : 30 : 30 besides the 50 : 25 : 25 and 60 : 20 : 20 mixtures which were prepared with β-lactose.

Composition of the mixtures used for the spheronisation experiments

Different mixtures consisting of DCPD and MCC were dry mixed for 10 min in the same planetary mixer (Kenwood Chef) at 60 rpm using the same K-shaped mixing arm and subsequently were granulated with demineralised water for 2 min at 60 rpm.

Water movement tests

Mixtures were extruded using a ram extruder (Harrison et al., 1984) with a single hole die having a length to radius ratio of 4 and a ram speed of 400 mm/min. Fractions of extrudate were collected at 3-s intervals. These were then dried in an oven (Pickstone Equipment Ltd, Thetford, Norfolk, U.K.) at 102°C for 4 h. The water content of the various fractions was determined as a percentage of the wet weight.

Extrusion procedure

Gravity feed extruder Mixtures were extruded with an instrumented gravity feed extruder (Extruder 40, GB Caleva Ltd, Dorset, U.K.) as described by Baert et al. (1991). The rotational speed of the axes was 30 rpm. Mixtures were considered not to be extrudable if the extrusion forces were higher than 2500 N.

Ram extruder Mixtures were extruded using a ram extruder as described by Harrison et al. (1984). A barrel of 2.54 cm diameter and 20 cm length and a multi-hole (31 holes) die with a length to radius ratio of 4 were used. The ram speed was fixed at 400 mm/min. After 0.42 min, extrusion was stopped in order to ensure that only steady-state extrusion conditions occurred. Mixtures were considered not to be extrudable if the extrusion forces were high than 20 000 N.

Spheronisation

Spheronisation after ram extrusion 200 g of the extrudate were spheronised on a radial friction 228 mm diameter plate in a spheroniser (Caleva Ltd) for 10 min at 1000 rpm. The spheres were dried in an oven for 24 h at 60°C.

Spheronisation after gravity feed extrusion 200 g of the extrudate were spheronised on a friction plate with cross-hatch geometry in a spheroniser (Spheroniser Model 15, Caleva Ltd, Dorset, U.K.) for 10 min at 750 rpm. The spheres were dried in

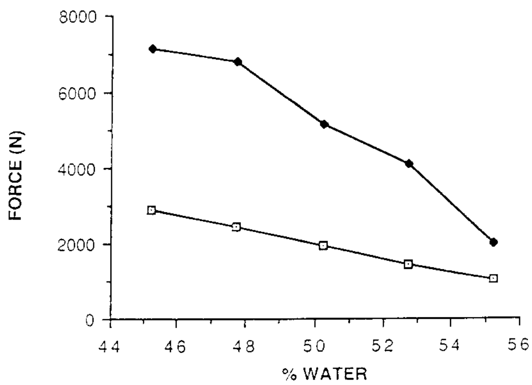


Fig. 1. Influence of the amount of water on the forces (N) recorded during extrusion of a mixture of Avicel PH 101/water with a ram extruder (♦——♦) and a gravity feed extruder (□——□). Each point is the mean of six values. The C.V. is always lower than 3%.

a fluidized bed (Aeromatic AG, Basel, Switzerland) for 20 min at 50°C.

Evaluation of spheres

Spheres were evaluated according to the criteria described by Baert et al. (1992). They were considered of acceptable quality if more than 90% showed a particle size between 710 and 1400 μm, the friability was lower than 0.2% and the calculated E value (roundness index) was between 1 and 1.20.

Results and Discussion

In this study two different types of instrumented extruders were compared: a gravity feed extruder with two contra-rotating gear wheels as described by Baert et al. (1991) and a ram extruder as reported by Harrison et al. (1984). In previous work, Baert et al. (1991) showed that the amount of fluid phase had a dramatic influence on the extrusion forces recorded. The fluid phase consists of the granulating liquid or when water-soluble components are present, a solution. Thus, for DCPD systems, the fluid phase would be water, whereas for the lactose systems, the fluid phase would consist of a solution of lactose, the concentration varying with the type of lactose and the quantity within the formulation as well as the granulation process. In the case of higher fluid phase contents, lower extrusion forces were recorded. The correlation between extrusion forces recorded on a gravity feed extruder and the quality of spheres was also described (Baert et al., 1992). The purpose of this work was to investigate the possibility of extrapolating the results obtained in sphere quality using a ram extruder to produce extrudate in comparison with those of a gravity feed extruder. A ram extruder functions as a continuous system while extrusion by a gravity feed extruder should be considered as a discontinuous process.

The results in Fig. 1 show the forces recorded during the extrusion of binary MCC/water mixtures on both types of extruders. A decrease in extrusion force with increase in the amount of granulating water was observed. The values of the forces recorded and the slope of the curve differed. For an MCC/water (50:50) mixture, extrusion forces of 1770 and 4952 N were recorded for a gravity feed extruder and a ram extruder, respectively. The quantity of water present has a far greater effect on the extrusion force for preparations used in the ram extruder than that of the gravity feed extruder. The relation between

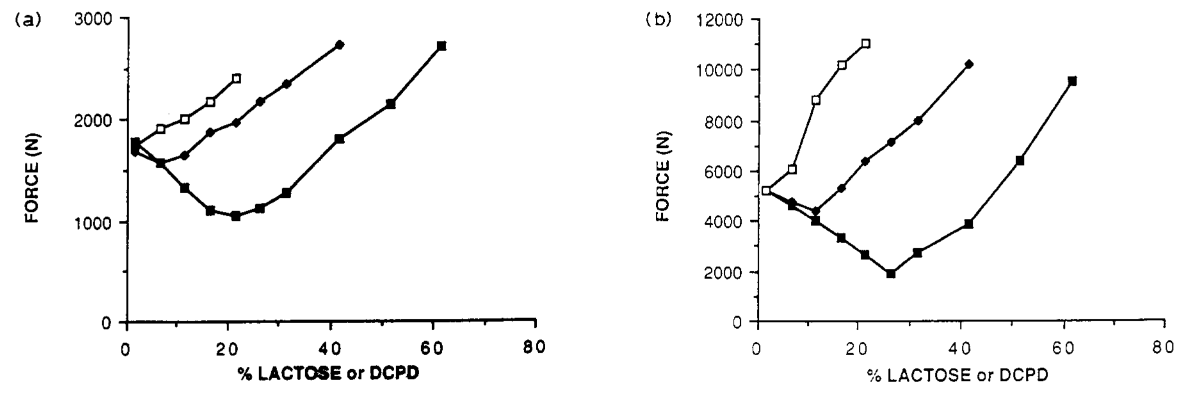


Fig. 2. (a) Influence of the amount of lactose and dicalcium phosphate dihydrate (% of the total weight) on the forces (N) recorded during extrusion of lactoses or dicalcium phosphate dihydrate/Avicel PH 101/water mixtures using a gravity feed extruder. Each point is the mean of six values. The C.V. is always lower than 3%. (b) Influence of the amount of lactose or dicalcium phosphate dihydrate (% of the total weight) on the extrusion forces (N) for mixtures of lactose or dicalcium phosphate dihydrate/Avicel PH 101/water using a ram extruder. Each point is the mean of six values. The C.V. is always lower than 3%. α-Lactose monohydrate 200 mesh (♦——♦); anhydrous β-lactose (■——■); dicalcium phosphate dihydrate (□——□).

extrusion forces recorded during processing of ternary mixtures and the total percentage of lactose of DCPD is demonstrated in Fig. 2. The ratio of MCC to water remained constant in all the experiments. As in the case of the binary mixtures, the profiles obtained for the two extruders were different as regards the slope of the forces recorded. The forces generated by ram extrusion were always greater. A shift was observed in the point of minimal extrusion forces from 5 to 10% in the case of α-lactose and from 20 to 25% for β-lactose. This shift can be explained by reference to the movement of water that occurs during extrusion in the ram extruder (see Fig. 3). Since extrusion is stopped after 0.42 min, the water content of the extrudate is higher than that of the initial mixture, resulting in a greater amount of lactose that is soluble in the mixture.

Continuous extrusion by the ram results in greater variations in water content of the mixture extruded, particularly for the DCPD systems. This movement of water initially causes an increase in water content, resulting in a decrease of the extrusion forces. As water is lost, the mixture becomes drier, and hence an increase in extrusion force is required. A difference in water movement was observed as a function of the excipient used. β-Lactose tended to hold water best, while DCPD retained the water fraction very poorly (Fig. 3). Being a discontinuous process, these variations in water movement are less likely to occur with the gravity feed extruder. The latter system also exerts a lower extrusion force.

The regions of good sphere quality resulting from the two different extrusion processes and an analogous spheronisation process are illustrated in Fig. 4. It should be borne in mind that the same spheronisers were not used for processing after ram extrusion and gravity feed extrusion but that a comparable distance was covered by the spheres in both spheronisers. In the case of the ram extruder, the zone of good sphere quality moved towards an area of lower water content. This can be explained on the basis of the water movement concept. Water movement in the extrusion process is caused by pressure on the mixture during extrusion. Using the gravity feed ex-

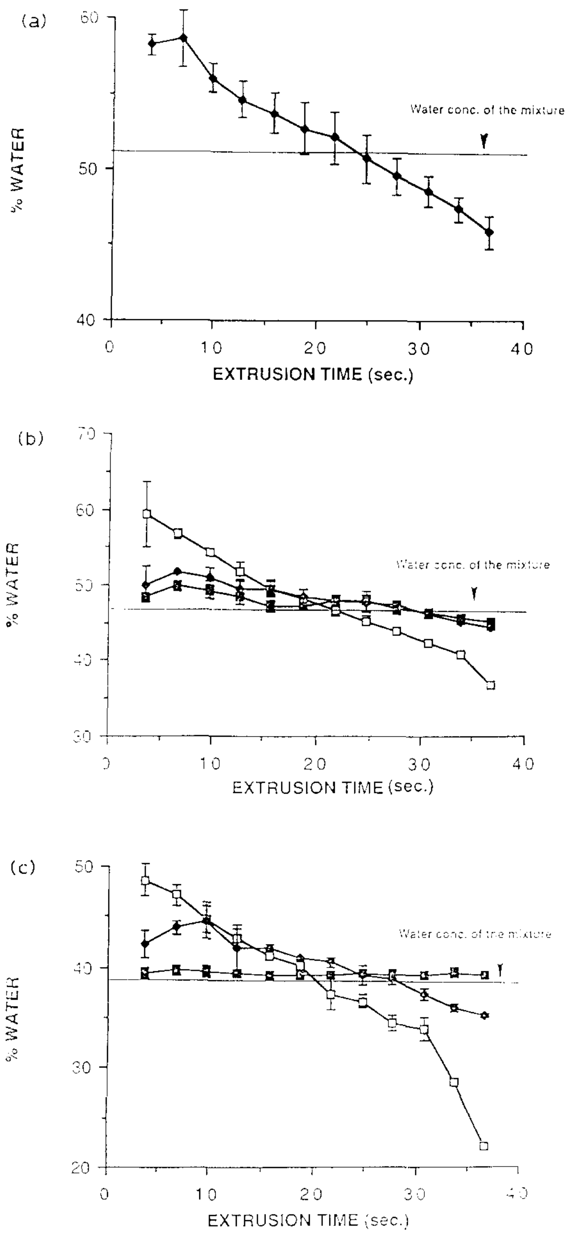
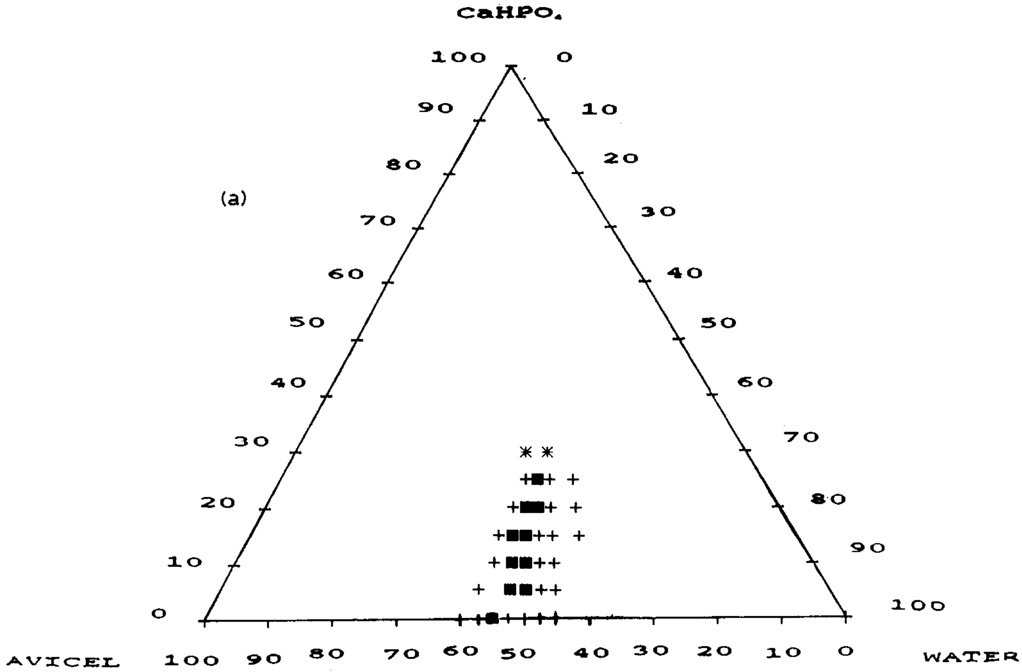


Fig. 3. (a) Variation of water content of extrudate vs extrusion time using a ram extruder for a mixture composed of 50:50 water/MCC (♦——♦). (b) Variation of water content of extrudate vs extrusion time using a ram extruder for mixtures composed of 45:45:10 water/MCC/DCPD (□——□), water/MCC/α-lactose (♦——♦) and water/MCC/β-lactose (■——■). (c) Variation of water content of extrudate vs extrusion time using a ram extruder for mixtures composed of 37.5:37.5:25 water/MCC/DCPD (□——□), water/MCC/α-lactose (♦——♦) and water/MCC/β-lactose (■——■).



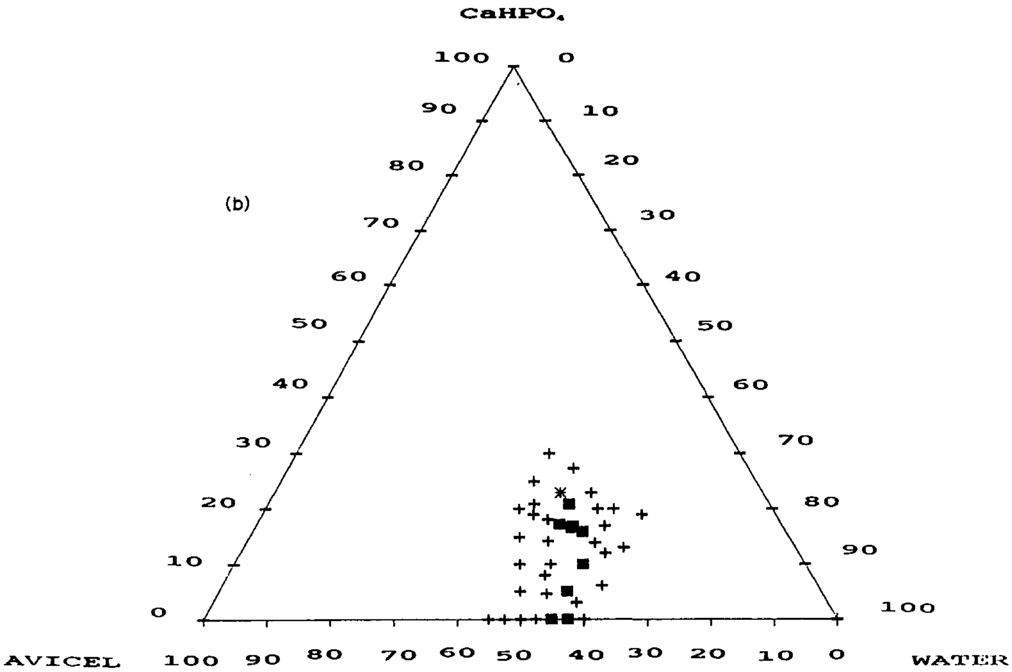


Fig. 4. (a) Phase diagram indicating the quality of spheres made of ternary mixtures consisting of microcrystalline cellulose, dicalcium phosphate dihydrate and water. Extrusion was performed with a ram extruder. (b) Phase diagram indicating the quality of spheres made of ternary mixtures consisting of microcrystalline cellulose, dicalcium phosphate dihydrate and water. Extrusion was performed with a gravity feed extruder. Good quality pellets (■); poor quality pellets (+); no pellet production possible (*).

truder, the pressure is discontinuous and the movement of water slight. With the continuous action of the ram extruder, water movement is more extensive and results in a non-uniform extrudate.

Conclusions

The use of a ram extruder to investigate the ability of formulations to produce spherical granules from gravity feed extruders has been confirmed as a satisfactory approach if one takes into consideration that water movement occurs. This movement of water can be the explanation for the fact that a lower water content will be required when a formulation is transposed from the ram to the gravity feed extruder.

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