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Instrumentation of a Gravity Feed Extruder and the Influence of the Composition of Binary and Ternary Mixtures on the Extrusion Forces

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Abstract—A gravity feed extruder was adapted to monitor the extrusion forces, the temperature during processing and the rotational speed of the extruding cylinders. The extruder was used to evaluate the influence of particle size of insoluble material and of product solubility on the extrusion forces. Microcrystalline cellulose, dicalcium phosphate dihydrate and different lactoses were used as model compounds. Difference in lactose and microcrystalline cellulose particle size did not influence extrusion forces. The amount of water in the mixtures to be processed and the initial difference in solubility for some of the lactose types investigated influenced the extrusion forces dramatically. Extrusion forces recorded during processing of a mixture previously granulated in a high shear granulator were higher than when processed in a planetary mixture. Loss of water during high shear granulation is probably the main cause of this phenomenon.

Extrusion is a process widely used for the preparation of pellets. Pellets are used both as conventional dosage forms and as controlled release delivery systems (Malinowski & Smith 1975; O'Connor et al 1984; Gamlen 1985; Ghebre-Sellassie et al 1985; Rowe 1985). The greatest advantage of pellets as a controlled drug delivery system is that the total drug dose is divided in small fractions avoiding problems of dose "dumping". Several authors have reported (Conine & Hadley 1970; Woodruff & Nuessle 1972; Malinowski & Smith 1975; O'Connor et al 1984; O'Connor & Schwartz 1985; Gamlen 1985, 1986; Ghebre-Sellassie et al 1985; Elbers et al 1990; Hasznos et al 1990). Rowe (1985) classified the extruders according to the type of transport mechanism of the mass towards the die and differentiated between screw extruders (axial or radial) and gravity feed extruders. Few data are available on the forces generated during extrusion. Harrison et al (1985) described force/displacement curves for different mixtures of microcrystalline cellulose/lactose/water mixtures using a ram extruder. Elbers et al (1990) measured the power consumption of a Fuji Paudal Twin Extruder (EXD 60) during extrusion of different mixtures of sodium carboxymethylcellulose and theophylline. In this paper the instrumentation of a gravity feed extruder is described. The instrumented extruder was used to evaluate the influence of the particle size of microcrystalline cellulose and lactose and the influence of material solubility on the extrusion forces. Dicalcium phosphate dihydrate and different lactoses were used as model compounds for good and poorly soluble materials.

Materials and Methods

Instrumentation of the extruder

Apparatus description. An extruder (Extruder 40, GB Caleva Ltd, Butts Pond Industrial Estate, Sturminster Newton, Dorset, UK) was equipped with instruments to measure the extrusion force, the rotational speed of the axes and the temperature during extrusion.

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Extrusion force measurement system. The instrumented extruder is shown schematically in Fig. 1. The detailed plans of the added parts are shown in Figs 2, 3. The force generated during extrusion has a vertical and a horizontal component. The two force components are measured with two load cells (19 Fig. 1) (Huntleigh, model 601, class D2, capacity 50 kgf, Penko, Veenendaal, The Netherlands) connected to a Wheatstone bridge.

The force is transmitted from the shaft (01) to the load cell (19) by means of a bearing block (10) fixed to the base plate (12) with spring plates (11) in order to exclude friction. The bearing block is fixed to the shaft (01) with a ball bearing (29) in order to allow rotational movement and guidance of the shaft. The forces measured at the load cells are converted to extrusion forces at the extrusion gear wheels (34) using the following formula:

$$F_m \cdot L_m = F_e \cdot L_e$$

where F_m is the force measured at the load cell, L_m the distance between the load cell and the elastic coupling, F_e the force generated during extrusion, and L_e the distance between the gear wheel and the elastic coupling.

System for measurement of rotational speed of extruding axes To measure the rotational speed of the axes, an encoder (09) was used. Measurement is carried out via a digital pulse train (TTL) (60 pulses per rotation). The pulses were generated by the encoder. In order to obtain reliable measurements at low speeds (30–100 rev min^{-1}) a digital-to-analogue converter was used. Calibration showed that 1·00 V corresponded to 10 rotations min^{-1}.

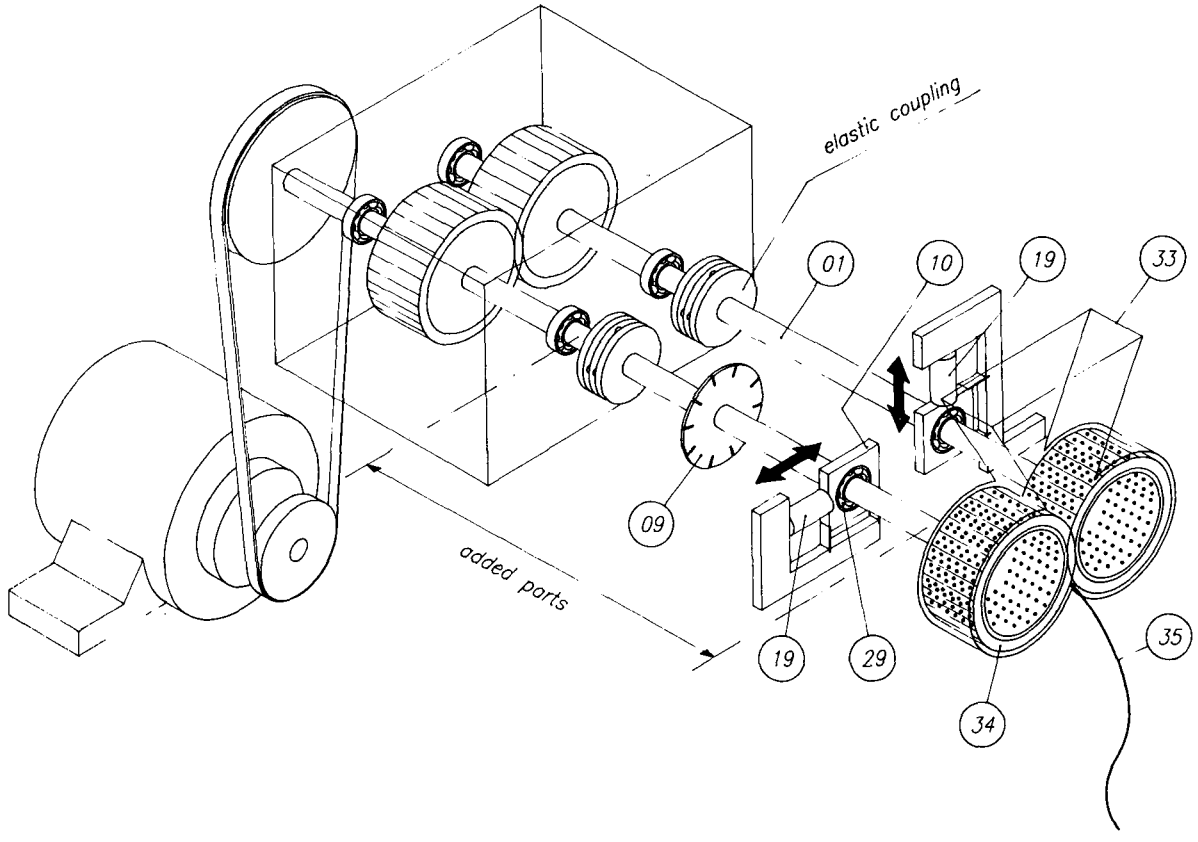

FIG. 1. Schematic representation of instrumented extruder. Legend: shaft (01), encoder (09), bearing block (10), load cell (19), ball bearing (29), existing funnel (feeder) (33), gear-wheel (34), thread connecting strain gauge, with the recorder (35).

Temperature determination during processing

To determine the heat produced during extrusion, a strain gauge (ETG-50 B/E Micro-measurements Division, Raleigh, NC, USA) was placed on the housing around the two gear wheels (Fig. 1). This strain gauge is connected to a Wheatstone bridge. The recorded values were converted to degrees Celsius with an appropriate calibration curve.

Calibration

The load cells were calibrated by loading the axes with an increasing weight up to 3000 N. A linear correlation was obtained between output readings and the weight for the vertical load cell ($y = 0{\cdot}019769$ ($\pm 0{\cdot}000307$ s.d.) $x + 0{\cdot}0337$ ($\pm 0{\cdot}0326$ s.d.), $r^2 = 0{\cdot}9999$) and the horizontal load cell ($y = 0{\cdot}020486$ ($\pm 0{\cdot}000591$ s.d.) $x + 0{\cdot}0223$ ($\pm 0{\cdot}0204$ s.d.), $r^2 = 0{\cdot}9999$). A linear correlation was also obtained between voltage readings and the rotational speed ($y = x + 0$, $r^2 = 1{\cdot}0000$). The temperature probe was calibrated in an electric oven for a temperature range between 25 and 90°C. A linear correlation was obtained between voltage readings and temperature ($y = 0{\cdot}02849$ ($\pm 0{\cdot}00187$ s.d.) $x - 0{\cdot}35138$ ($\pm 0{\cdot}15561$ s.d.), $r^2 = 0{\cdot}9990$).

Validation of the system for measuring the extrusion forces

To validate the system, ten separate batches of the same composition were extruded at a rotational speed of 30 rev min^{-1}. After extrusion of each batch, the machine was taken apart and cleaned. The mixture used for the validation procedure consisted of 2·5 kg Avicel PH 101 (FMC, Philadelphia, USA) granulated with 2·5 L demineralized water during 2 min in a Hobart mixer (Type A 200, 10 L, The Hobart Mfg. Co, London, UK) at a rotational speed of 60 rev min^{-1}. The temperature during extrusion was kept between 30 and 35°C. The mean of the force readings during a 5 min extrusion time was calculated and taken as the reference value. The mean value varied between 1621·6 and 1788·6 N (mean of the means = 1717·2 N $\pm$ 66·1).

Materials

Two different types of microcrystalline cellulose were used: Avicel PH 101 with an average particle size of 50 μm and Avicel PH 102 with an average particle size of 100 μm (FMC, Philadelphia, USA).

Demineralized water was used as granulating fluid. Six different types of lactose were used: α-lactose monohydrate 80 Mesh (177 μm) (Pharmatose 80 M) (80 M), α-lactose monohydrate 200 Mesh (74 μm) (Pharmatose 200 M) (200 M), α-lactose monohydrate 325 Mesh (44 μm) (325 M), spray-dried lactose (DCL 11), anhydrous β-lactose (DCL 21) and anhydrous α-lactose (DCL 30). All lactose samples were supplied by De Melkindustrie Veghel, Veghel, The Netherlands.

Dicalcium phosphate dihydrate ($CaHPO_4$) was supplied by C. N. Schmidt B.V. (Amsterdam, The Netherlands).

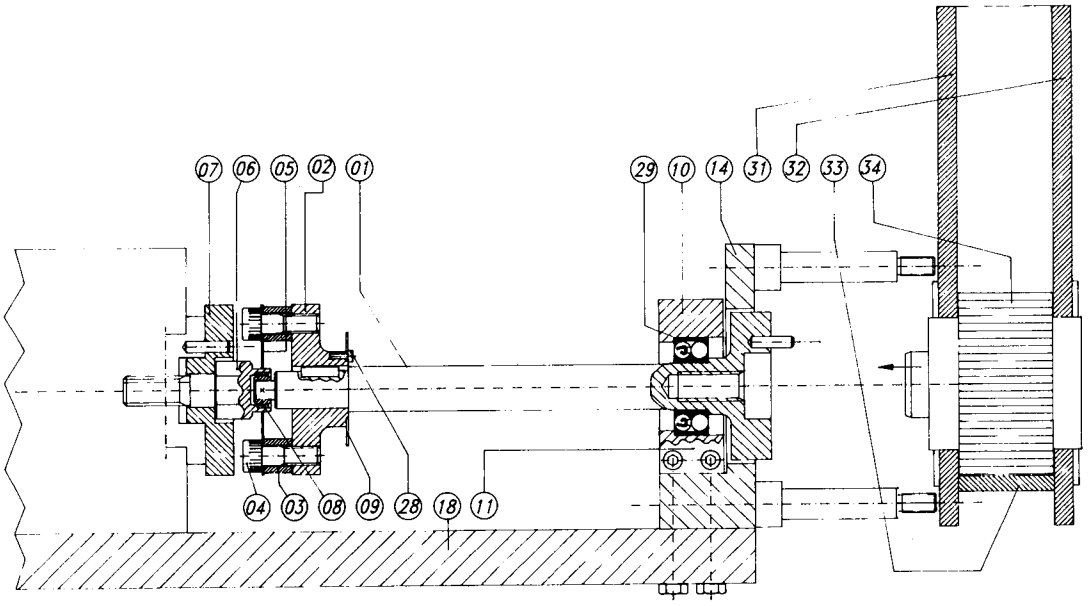

FIG. 2. Side view of the force measuring system. Legend: shaft (01), flange (02), spacer (03), socket head screw (04), spring plate (05), centring bolt (06), flange (07), ball joint (08), encoder (09), bearing block (10), spring plate (11), support square (14), base frame (18), screw (28), ball bearing (29), existing back plate (31), existing front plate (32), existing funnel (33), gear wheel (34).

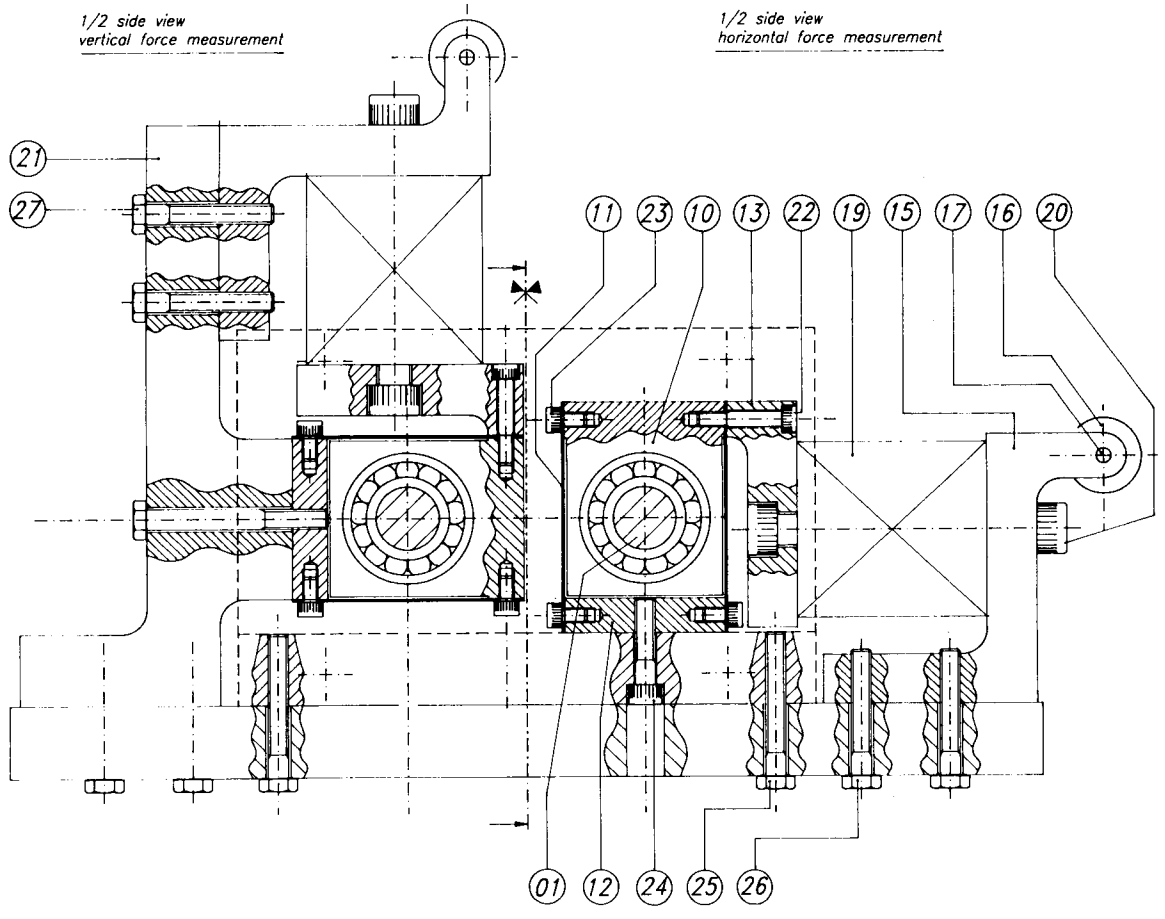

FIG. 3. Front view of the force measuring system. Legend: shaft (01), bearing block (10), spring plate (1), base plate (12), connecting piece (13), support (15), wheel (16), pin (17), load cell (19), socket head screw (22), socket head screw (23), socket head screw (24), bolt (25), bolt (26), bolt (27).

Composition of the mixtures and granulation procedure

Binary mixtures. Different mixtures of water/microcrystalline cellulose (Avicel PH 101 or PH 102) were granulated and extruded. The composition of the different water/microcrystalline cellulose mixtures (1 kg) ranged from 45/55 to 60/40 (w/w).

The microcrystalline cellulose was granulated with water for 2 min in a planetary mixer (Kenwood Chef, Hants, UK) at 60 rev min^{-1} using a K-shaped mixing arm.

Ternary mixtures. Granulation using a planetary mixer. Lactose or dicalcium phosphate dihydrate and microcrystalline cellulose were dry mixed for 10 min in a planetary mixer at 60 rev min^{-1} using a K-shaped mixing arm. Next, the mixture was granulated with water for 2 min at 60 rev min^{-1}. The composition of the different lactose/microcrystalline cellulose (Avicel PH 101)/water mixtures was 0/50/50, 5/47·5/47·5, 10/45/45, 15/42·5/42·5, 20/40/40, 25/37·5/37·5, 30/35/35, 40/30/30, 50/25/25 and 60/20/20 (w/w/w). All six lactose types were processed. The composition of the dicalcium phosphate dihydrate/microcrystalline cellulose (Avicel PH 101)/water mixtures was 0/50/50, 5/47·5/47·5, 10/45/45, 15/42·5/42·5 and 20/40/40 (w/w/w).

Granulation using a high shear mixer. Lactose and microcrystalline cellulose were dry mixed for 10 min in a planetary mixer at 60 rev min^{-1} using a K-shaped mixing arm. Next, the mixture was granulated with water for 4 min using a high shear granulator (Mixer Granulator type GRAL 10, Collette, Wommelgem, Belgium). The mixing arm was rotating at 430 rev min^{-1} and the chopper at 1500 rev min^{-1}. The composition of the different lactose (α-lactose-monohydrate 200 M and anhydrous β-lactose)/microcrystalline cellulose (Avicel PH 101)/water mixtures was 0/50/50, 5/47·5/47·5, 10/45/45, 15/42·5/42·5, 20/40/40, 25/37·5/37·5, 30/35/35 and 40/30/30. With anhydrous β-lactose two supplementary mixtures were processed: 50/25/25 and 60/20/20 (w/w/w).

For one mixture (anhydrous β-lactose/microcrystalline cellulose (Avicel PH 101)/water: 20/40/40; w/w/w) the influence of granulation time was tested. The granulation time varied from 1 to 2, 4, 8, 16 and 32 min respectively for each of the six mixtures. The amount of water in the granulated mass was measured after granulation using a Mettler Infrared Drying Unit LP 16-M (Mettler Instruments, Greifensee, Switzerland) set at a temperature of 110°C with a drying time of 60 min.

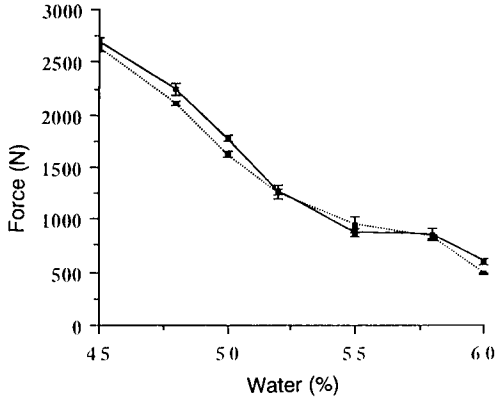

FIG. 4. Influence of the amount of water on the extrusion forces (N) for a mixture of Avicel PH 101/water (——) and a mixture Avicel PH 102/water (····· ● ·····). Each point is the mean of six values (± s.d.).

Extrusion procedure

After granulation the mixtures were extruded in the instrumented extruder. During all the experiments no vertical forces were observed. The temperature measured near the two gears was held between 30 and 35°C. The rotational speed of the axes was 30 rev min^{-1}. For each batch the recorded forces during 5 min processing time were averaged. Each mixture was extruded six times and the mean and s.d. were calculated.

Results and Discussion

Fig. 4 shows the forces recorded during the extrusion of binary microcrystalline cellulose/water mixtures. The extrusion forces decreased dramatically with an increasing amount of water. An extrusion force of 2640 N was detected for a mixture of 45/55 water/microcrystalline cellulose while for a 60/40 water/microcrystalline cellulose mixture the force required was reduced to 487 N which means a reduction of about 80%. No influence of the average particle size of microcrystalline cellulose on the extrusion forces was observed. The forces recorded during extrusion of lactose/microcrystalline cellulose/water mixtures and the dicalcium phosphate dihydrate/microcrystalline cellulose/water mixtures showed a different profile. Fig. 5 shows the relation between extrusion forces and total percentage of lactose or total percentage of dicalcium phosphate dihydrate for mixtures with six different types of lactose and one type of dicalcium phosphate dihydrate. The ratio microcrystalline cellulose/water remained constant (50/50; w/w) in all the

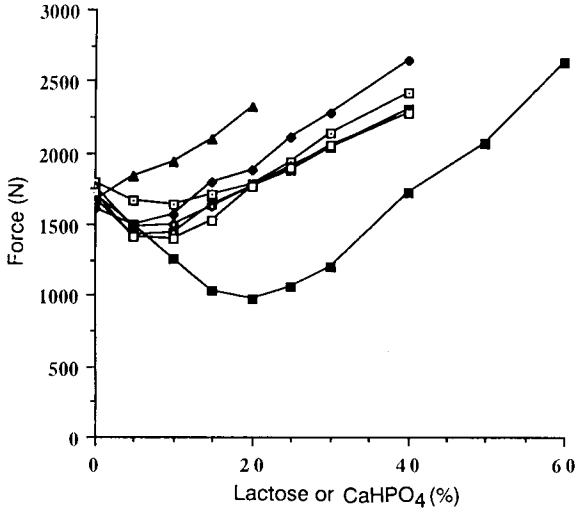

FIG. 5. Influence of the amount of lactose or dicalcium phosphate dihydrate (% of the total weight) on the extrusion forces (N) for mixtures of lactose or dicalcium phosphate dihydrate/Avicel PH 101/water after granulation with a planetary mixer. Each point is the mean of six values. The s.d. is lower than 3% for each point. Six different types of lactose were used; α-lactose monohydrate 80 Mesh (□), α-lactose monohydrate 200 Mesh (◆), α-lactose monohydrate 325 Mesh (■), spray dried lactose (DCL 11) (◇), anhydrous β-lactose (DCL 21) (■), anhydrous α-lactose (DCL 30) (□). One type of dicalcium phosphate dihydrate was used (▲).

experiments. For all types of lactose the same profile between extrusion forces and total percentage of lactose in the mixture was observed.

With an increasing amount of lactose a minimum in the extrusion force was observed at a level of 5–10% lactose, except for β-anhydrous lactose where the minimum shifted towards 20% lactose. With an increasing amount of dicalcium phosphate dihydrate, no minimum in the extrusion force was observed. Three different particle sizes of α-lactose monohydrate were investigated showing no influence of the particle size of the α-lactose monohydrate on the extrusion forces. Differences in the initial aqueous solubility between some lactoses and the very low solubility of dicalcium phosphate dihydrate could explain the phenomena observed. The initial solubility of α-lactose monohydrate in water at 25°C was 86 g L^{-1} and of anhydrous β-lactose 500 g L^{-1} (Kussendrager 1985). This phenomenon might explain why increasing the amount of lactose up to 5–10% for the α-lactoses initially decreased the extrusion forces due to a decrease of the total solid content of the mixture. Beyond the point of maximum initial solubility of lactose in the granulation medium, the extrusion forces progressively increased. As the initial solubility of β-lactose is about six times higher in comparison with the α-lactoses, the point of lowest extrusion force as a function of β-lactose content shifted towards 20% total lactose. Dicalcium phosphate dihydrate is nearly insoluble in water which resulted in an increase of the extrusion forces as a function of higher dicalcium phosphate concentration. For a small concentration of lactose in the mixture, all the lactose dissolved in the water available, resulting in an increase of the fluid phase volume. An increase in fluid phase volume decreased the extrusion forces as was shown in Fig. 4. To support the hypothesis that the amount of fluid phase played a key role in the extrusion forces recorded, the total amount of solid phase was calculated for the mixtures consisting of Avicel PH 101-β-lactose anhydrous and water and plotted against the total amount of anhydrous β-lactose expressed as a percentage of the composition of the mixture. An analogue profile as for the extrusion forces was obtained (Fig. 6). Except for the mixtures with β-lactose, the blends containing 50 and 60% α-lactoses could not be extruded because the required forces were too high (> 2650 N). High shear granulation seemed not to have any influence on the force profiles described previously, although the extrusion forces were higher for a same blend composition. A possible explanation for this phenomenon is the loss of water during processing in a high shear granulator. A mixture of anhydrous β-lactose/microcrystalline cellulose/water (20/40/40; w/w/w) was granulated for different times and the amount of water in the mixture ranged from 40·5 to 33·2% for granulation times of 1 and 32 min, respectively. An increased loss of water correlated well with the increase of the extrusion force (954 and 2172 N for granulation times of 1 and 32 min, respectively).

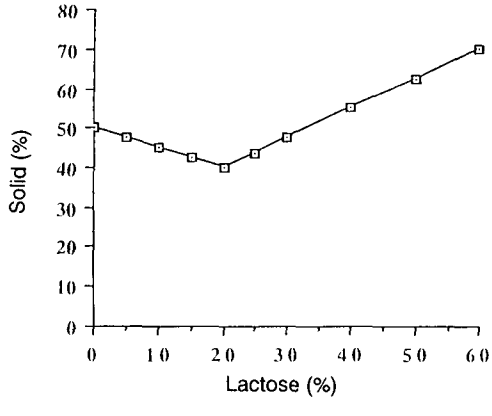

FIG. 6. Relation between the total amount of solid phase (Avicel PH 101 and non-dissolved β-lactose) and the total amount of β-lactose (% of the total weight).

The instrumented gravity feed extruder allowed the determination of the influence on the extrusion behaviour of the composition of ternary mixtures containing a soluble and insoluble ingredient. Solubility and dissolution rate of raw materials and loss of water during manufacturing played an important role on the extrusion forces recorded. The fluid phase volume was an important parameter for mass lubrication.

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