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Influence of impeller design, method of screen perforation and perforation geometry on the quality of pellets made by extrusion-spheronisation

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Abstract

Modifications to the impeller design of a radial basket extruder resulted in a higher efficiency of the process. β-Lactose and dicalcium phosphate were used as model compounds for a high and a low water-soluble drug, respectively. Due to the impeller modifications the concentration of β-lactose and dicalcium phosphate could be increased from 58 to 67% (w/w) and from 18 to 43% (w/w), respectively. The yield of the extrusion/spheronisation process was independent of the extrusion speed using the modified high efficiency impeller. The perforation method of the extrusion screen and the perforation geometry influenced pellet quality as the maximal β-lactose concentration increased from 67% (w/w) for the punched screen to 72 and 78% (w/w) for the drilled and profile screens, respectively. These differences were due to irregular die filling for the punched and the drilled screen at higher β-lactose concentrations. The same influences were seen when β-lactose was substituted for dicalcium phosphate dihydrate although at higher DCP concentrations the profile extrusion screen blocked due to particle bridging inside the screen.

Keywords: Extrusion; Spheronisation; Basket extruder; Pellet quality

1. Introduction

The influence of different processing parameters during extrusion (type of extruder, extrusion speed, extrusion temperature, extrusion screen) has already been well documented. Among those parameters the extrusion screen has proven to have a dramatic influence on the extrudate, and hence on the resulting pellets. The use of a screen with perforations of a different diameter affects the particle size distribution of a formulation (Malinowski and Smith, 1975; Chariot et al., 1987; Hileman et al., 1993). Increasing the thickness of the extrusion screen not only rises the temperature during the extrusion process but also changes the surface structure of the extrudate

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(Harrison et al., 1985; Hellén et al., 1992; Vervaet et al., 1994), the shape (Pinto et al., 1992; Hellén et al., 1993) and the particle size distribution (Dietrich and Brausse, 1988; Pinto et al., 1992; Hellén et al., 1993) of the resulting pellets. Goodhart et al. (1973) reported on a change of the bulk density of pellets when extruding with an extrusion screen with a higher total area of the screen perforations. Baert et al. (1993) described the difference in extrudate quality between extruders equipped with screens of a different 'length-to-radius' (L/R) ratio. Extruding with a screen of a higher L/R ratio produced a smoother extrudate, due to the higher densification inside the screen perforation. This observation was correlated by Vervaet et al. (1994) with the formation of a more robust system when an extrusion screen of a higher L/R ratio was used.

The objective of this work was to study the influence of modifications made to the impeller design and to determine the effect of the perforation technique of the extrusion screen and the perforation geometry on formulations processed on a radial basket extruder.

2. Materials and methods

2.1. Materials

Anhydrous β-lactose (solubility in water (25°C): 500 g/l) (DCL 21, DMV, Veghel, The Netherlands) and dicalcium phosphate dihydrate (DCP) (solubility in water (25°C): 100 mg/l) (C.N. Schmidt B.V., Amsterdam, The Netherlands) were selected as model compounds for drugs with a high and a low water solubility, respectively. Microcrystalline cellulose (Avicel® PH101) (FMC, Wallingstown, Little Island, Cork, Ireland) was chosen as the filler. Demineralised water was used as the granulation fluid in all experiments.

A Nica E-140 extruder (Aeromatic-Fielder Ltd., Eastleigh, Hants, UK) was used to extrude all formulations. Three types of screens were used; punched, drilled and profile, respectively. All were of the same nominal dimensions (1.0 mm thickness and 1.0 mm perforation diameter) but the perforations were formed by different methods. The profile screen had slightly conical drilled holes.

2.2. Composition of the mixtures

Different formulations containing Avicel® PH101, water and β-lactose or DCP (w/w/w) were prepared in order to outline the zones within the phase diagrams where pellets of an acceptable quality were obtained.

2.3. Preparation of the pellets

2.3.1. Granulation

Avicel® PH101 was blended for 10 min with β-lactose or DCP in a planetary mixer (Kenwood Chef, Hants, UK) at 60 rev./min using a K-shaped arm. Next the water was added and mixing was continued for 2 min. In all cases a 1-kg batch was prepared.

2.3.2. Extrusion

The granulated mass was extruded in a radial basket extruder (Nica E-140 extruder, Aeromatic-Fielder Ltd., Eastleigh, Hants, UK) at a rotational speed of the feeder head and the impeller of 40 and 30 rev./min, respectively.

2.3.3. Spheronisation

Two-hundred grammes of the extrudate were processed in a spheroniser (Spheroniser Model 15, Caleva Ltd., Sturminster Newton, Notts, UK) for 10 min at 750 rev./min. Finally the spheres were dried in a fluidized bed at an inlet temperature of 50°C (Aeromatic-Fielder AG, Bubendorf, Switzerland).

To test the influence of the extrusion speed some mixtures were extruded through the drilled screen at a rotational speed of the impeller of 60 and 90 rev./min, respectively. The rotational speed of the feeder head was kept constant at 40 rev./min in all cases. The following mixtures containing β-lactose/Avicel® PH101/water (w/w/w) were tested: 100:500:400, 100:525:375, 300:388:312, 300:400:300, 300:412:288.

2.4. Physical testing of the pellets

The particle size distribution of 100 g of pellets was determined on a sieve shaker (Retsch type VE1000, Haan, Germany) by vibrating at a constant amplitude of 2 mm. After 5 min the amount (%) retained on each sieve was calculated. A nest of sieves of 2000, 1400, 1000, 710, 500 and 250 μm was used.

The roundness (expressed as the E-value) was determined by averaging the ratios of the largest to smallest diameter of 60 individual pellets measured on a projection microscope (Reichert, Vienna, Austria).

The friability was determined by subjecting 10 g of spheres (710–1000 μm fraction) together with 200 glass beads (avg. diam.: 4 mm) to falling shocks in an Erweka friabilator (Erweka, Frankfurt, Germany) fitted with an abrasion wheel. After 10 min the yield fraction below 250 μm was determined.

A formulation was considered of an acceptable quality if it met the standards set by Baert et al. (1992) and by Vervaet et al. (1994) i.e. 90% of the spheres sized between 710 and 1400 μm, the E-value between 1 and 1.2 and the friability below 0.2%.

2.5. Photographs of the extrudate

Photographs of extrudate produced with the three different types of extrusion screens and containing β-lactose/Avicel® PH101/water (300:400:300 and 750:68:182 (w/w/w)) were taken with a stereomicroscope (Wild M8, Heerbrugg, Switzerland) at a magnification of 35.

3. Results and discussion

3.1. Influence of the impeller design

Fig. 1A shows the original Nica system configuration of the impeller (design A) whereas Fig. 1B shows the new high efficiency impeller (design B) produced and developed by Aeromatic Fielder Ltd. Compared to design A the new design has blades with a lengthened compression surface (leading edge) and a conical inner edge which runs closely with the feeder blade (modified to suit). These modifications should improve the feed and compression characteristics of the extruder and give an even pressure across the perforated screen. The underside of design B is relieved to produce an overhang of the under surface of the blades. This serves to continually sweep the wet mass away from the impeller drive. A product seal is fitted underneath the impeller disc (in addition to new drive shaft seals) and together these modifications should eliminate the need for the pressure relief holes fitted in the original Nica design which could result in (oversize) material by-passing the screen. The aim of this part of the study is to verify if the process has become more efficient using the modified impeller (design B) compared to previous trials by Vervaet et al. (1994) using the original configuration (design A).

Vervaet et al. (1994) reported that good quality pellets could be formulated with a maximal β-lactose content of 58% (w/w) (Fig. 2) using the design A impeller and extruding with a punched screen of 1 mm thickness. Using the same punched screen and the new high efficiency impeller (design B) the β-lactose content was increased to 67% (w/w) (Fig. 3), still producing pellets of an acceptable quality. A similar influence of the impeller design was seen for the insoluble compound dicalcium phosphate dihydrate. Formulations loaded with 43% (w/w) of DCP still yielded pellets of an acceptable quality when extruded with design B impeller in comparison with design A where (Vervaet et al., 1994) the limit range was 18% (w/w). The processing parameters were kept constant in both cases. The extension of the zone to formulations containing a higher loading of the model compound can be attributed to the modifications made to the impeller design, allowing a higher efficiency of the process and an improved interparticular adhesion due to the improved feed and compression characteristics of the extruder. This increased energy transfer into the mass results in the formation of fewer fines during spheronisation. For β-lactose the process became nearly as efficient as previously (Vervaet et

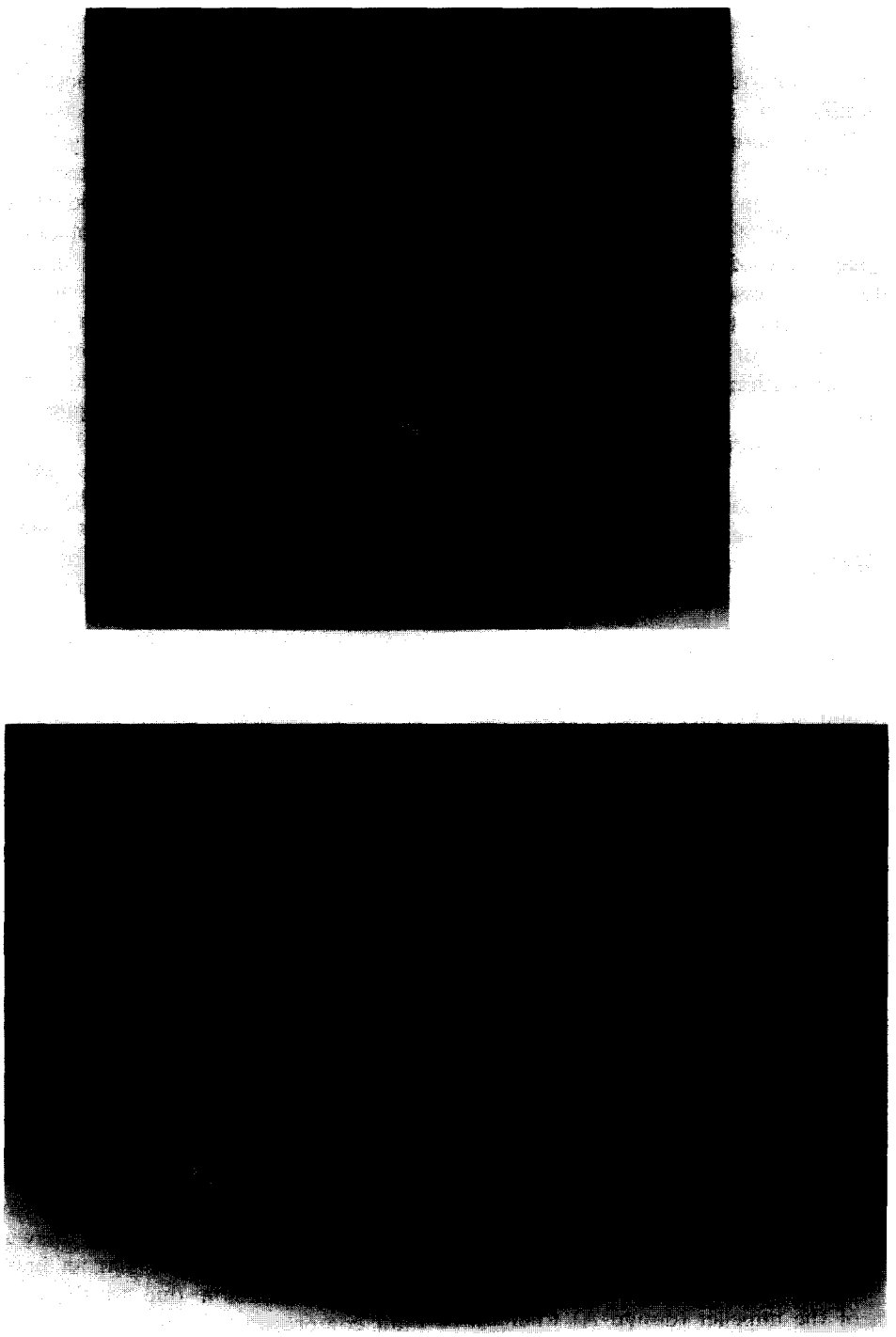

Fig. 1. (A) The original Nica system configuration of the impeller (design A). (B) The new high efficiency impeller (design B)

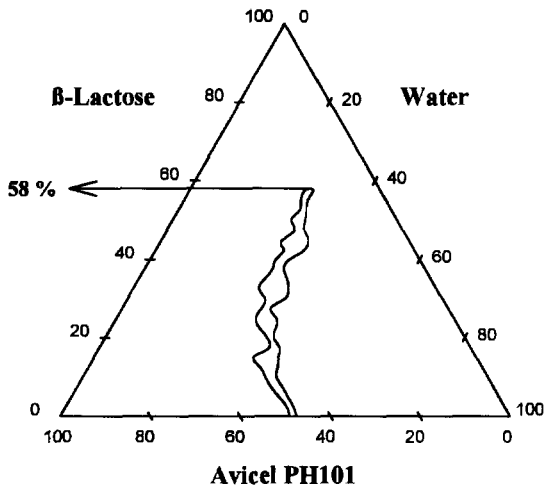

Fig. 2. Phase diagram indicating the zone where pellets of the desired quality were obtained for β-lactose/Avicel® PH101/water mixtures. Zone outlined with the punched screen using the original configuration of the impeller (design A).

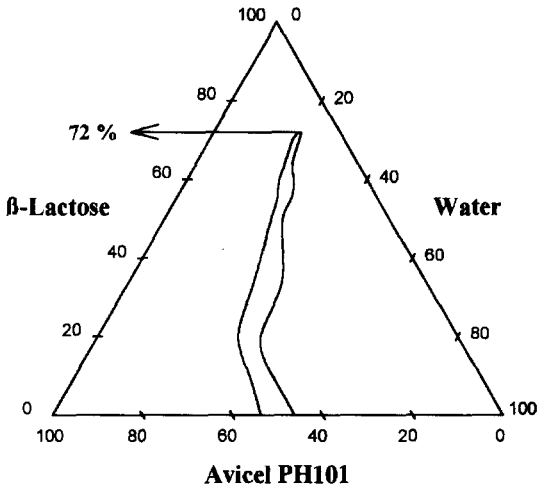

Fig. 4. Phase diagram indicating the zone where pellets of the desired quality were obtained for β-lactose/Avicel® PH101/water mixtures. Zone outlined with the drilled screen using the new high efficiency impeller (design B).

al., 1994) reported when a screen of 2 mm thickness was used (limit in β-lactose-content 68 (w/w)) without sharing the negative aspects of a lower throughput and a higher heat production.

For the insoluble model compound the loading was increased another 10% when the screen of 2 mm thickness was used (limit in DCP-content 52% (w/w)).

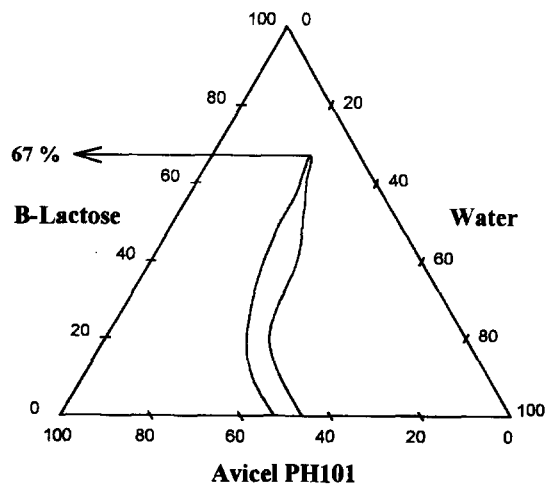

Fig. 3. Phase diagram indicating the zone where pellets of the desired quality were obtained for β-lactose/Avicel® PH101/water mixtures. Zone outlined with the punched screen using the new high efficiency impeller (design B).

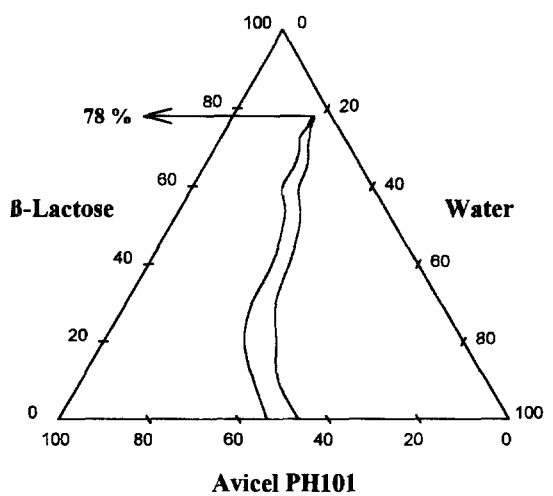

Fig. 5. Phase diagram indicating the zone where pellets of the desired quality were obtained for β-lactose/Avicel® PH101/water mixtures. Zone outlined with the profile screen using the new high efficiency impeller (design B).

Extruding at a rotational speed of 60 or 75 rev./min did not induce a shift in the particle size distribution to larger spheres as the modifications of the impeller design made the extrusion process independent of the extrusion speed. This observation shows that the new impeller design **B** became more efficient in comparison to the original impeller design where the efficiency increased at higher extrusion speeds (Vervaet et al. (1994)).

3.2. Influence of screen perforation geometry (using the new impeller design)

The use of a drilled or a profile extrusion screen did not cause a left or a right shift of the zone where pellets of an acceptable quality were obtained compared to the zone outlined with the punched screen. This indicated that the amount of water required to form good quality pellets was independent of the screen used. For both the drilled and the profile screen the zone extended to higher β-lactose concentrations compared to the punched screen as the maximal concentration increased from 67% (w/w) (Fig. 3) for the punched screen to 72 (Fig. 4) and 78% (w/w) (Fig. 5) for the drilled and the profile screens, respectively. These differences in maximal β-lactose concentration were due to differences in hole geometry resulting in different die fillings during extrusion of formulations containing high concentrations of the model compound. The formulations which were less plastic at a higher β-lactose concentration due to the decreased Avicel® PH101 concentration filled up the die less easily. The drilled hole being more regular shaped (Fig. 6B) compared to the punched one (Fig. 6A) enabled a good die filling resulting in a smooth extrudate at a higher β-lactose concentration. Extrusion with the profile screen promoted good die filling even at higher β-lactose concentration as the slightly conical holes of the profile screen (Fig. 6C) had a wider inlet and the wet mass was extra compacted inside these holes. This hypothesis was confirmed by photographs taken of the extrudate containing 75% of β-lactose. The profile screen produced a very smooth extrudate with little sharkskinning (Fig. 7A) whereas both the punched and the drilled (Fig. 7B) screens produced a loosely bound extrudate with many interruptions.

The DCP phase diagrams showed the same tendency when extruding with a drilled or a profile screen. Slightly higher concentrations of DCP could be used in the formulations compared to formulations extruded with the punched screen (43% (w/w) punched, 47% (w/w) drilled and 46% (w/w) profile screen). While extruding DCP as a model compound and using the profile extrusion screen it was not possible to reach a higher DCP loading compared to the drilled screen. This was probably due to the particle size of the insoluble DCP and the geometry of the perforation leading to bridging inside the perforations. DCP particles formed an arc inside the perforations which withstood the pressure exerted by the impeller resulting in a complete block of the screen.

4. Conclusions

This study shows that modifications made to the extruder design can affect the quality of pellet and that the perforation method of the extrusion screen and the perforation geometry are two factors to consider while optimising a formulation for a extrusion/spheronisation process.

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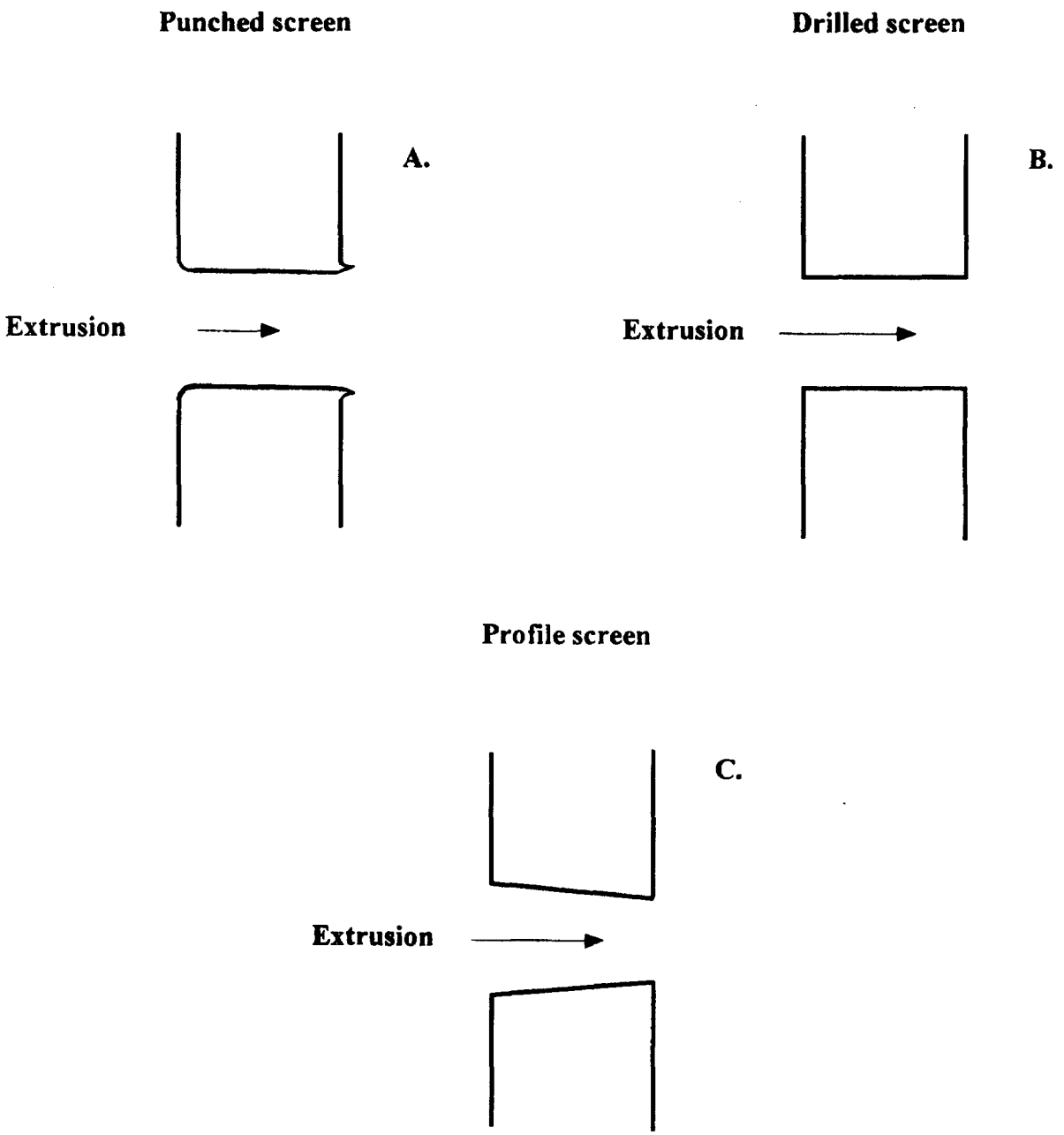

Fig. 6. Drawing of a screen perforation. (A) Punched screen. (B) Drilled screen. (C) Profile screen.

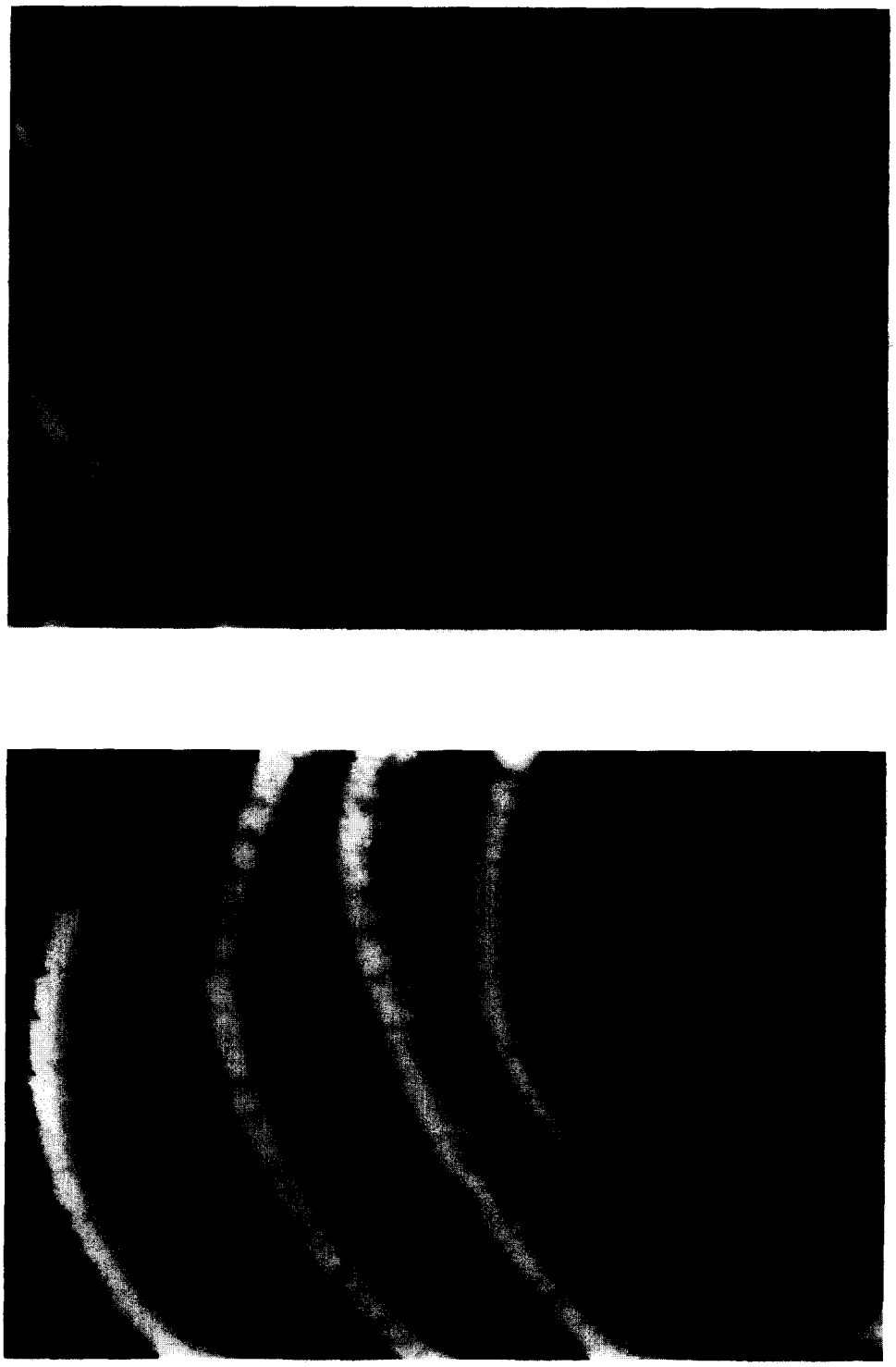

Fig. 7. Photographs of extrudate containing β-lactose/Avicel® PH101/water (750:68:182, w/w/w). (A) Produced with the drilled screen. (B) Produced with the profile screen.

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