DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 12(11-13), 1701-1713 (1986)

CONTINUOUS EXTRUSION USING A BAKER PERKINS MP50 (Multipurpose) EXTRUDER

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ABSTRACT

The Baker Perkins MP50 mixer/extruder has been used to produce paracetamol extrudates with a high drug loading. The extrudate had a high incidence of defects (ie surface roughness and shark skinning). Addition of hydroxypropyl methyl cellulose to the basic formula (of paracetamol/avicel/lactose) improved extrudability but did not significantly influence extrudate quality. The mixer/extruder offers significant advantages by reducing the number of pieces of equipment required for extrudate manufacture, but further formulation work or equipment modification is required for the formulations examined to extrude satisfactorily.

INTRODUCTION

Continuous processing is an activity not normally associated with the pharmaceutical industry, with its requirements for relatively small batch sizes, clear definition of product integrity and large numbers of unduly differing products. Nevertheless the potential advantages of reduced capital investment, space saving, ease of automations and reductions in labour costs

 0363-9045/86/1211-1701$3.50/0

make it an option worthy of consideration. The potential for continuous granulation has been reviewed by Greer (1).

Extrusion is generally carried out with one of two objectives. It is a particularly effective way of producing a relatively dense granule, such as may be suitable for tabletting, from low density material. It is also a significant process in the manufacture of controlled release pellets by extrusion/spheronisation (2). The Baker Perkins MP50 offers the major advantage of performing what at present are two unit operations on one piece of equipment, resulting in savings of space, and capital and operating costs.

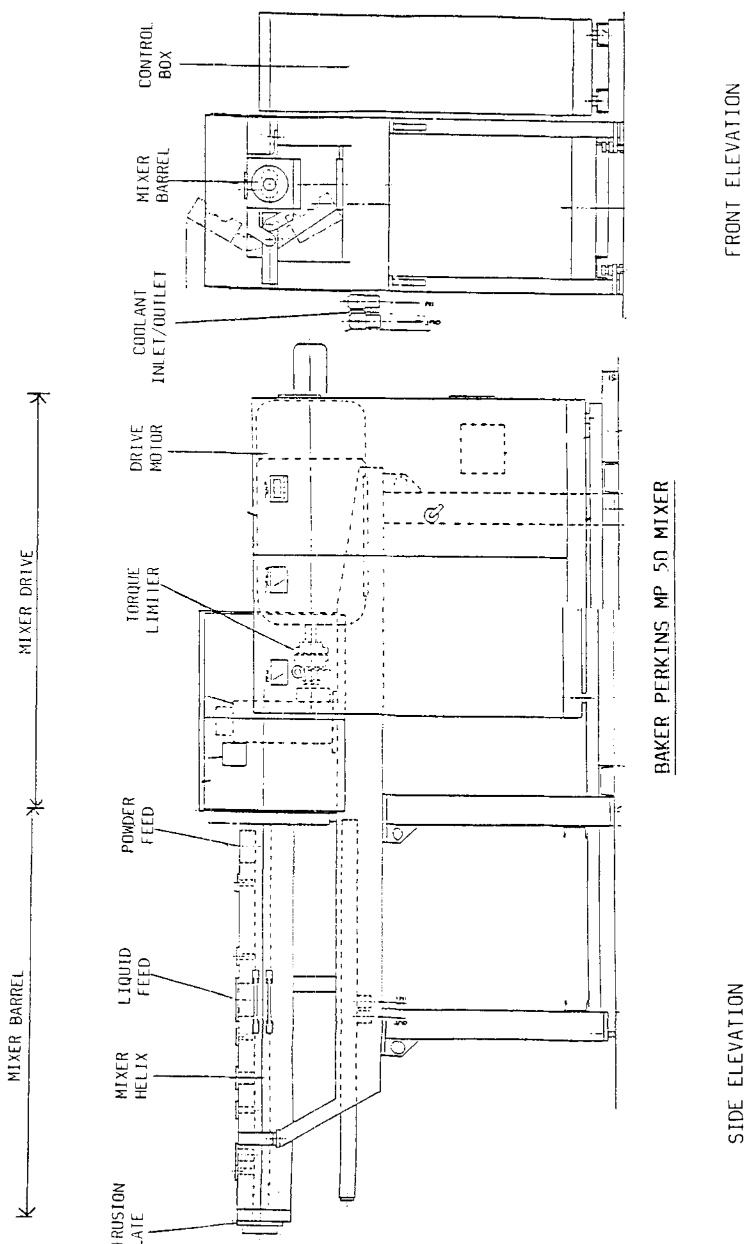
Harrison et al (3) have recently reported the influence of several parameters on the incidence of defects in an extruded product. Such defects are manifest as surface roughness (less serious) or "sharkskinning" (more serious). The latter term refers to cracks penetrating deeply into the core of the extrudate. Variables markedly influencing the incidence of defects were identified as the composition of the extrudate, its moisture content, the rate of extrusion and the length to diameter ratios of the die through which extrusion takes place.

The purpose of the present work was to evaluate the influence of extrudate composition and moisture content on the quality of extrudate obtained from the Baker Perkins MP50 extruder. In particular, the effect of adding a small amount of binder (HPMC) to a granulation of paracetamol, avicel and lactose was examined.

EQUIPMENT

The arrangement of the extruder and its ancillary equipment is shown schematically in Figure 1. The arrangement of the mixer helices and extrusion plate are shown in Figure 2.

Powder was fed into the machine using a continuous calibrated powder feed (KTron Type S-2 , Ktron-Soder Ag 5702, Niederburg, Switzerland). The powder is conveyed along the jacketed barrel of the mixer by the helical mixing



BAKER PERKINS MP 50 MIXER

FIGURE ONE

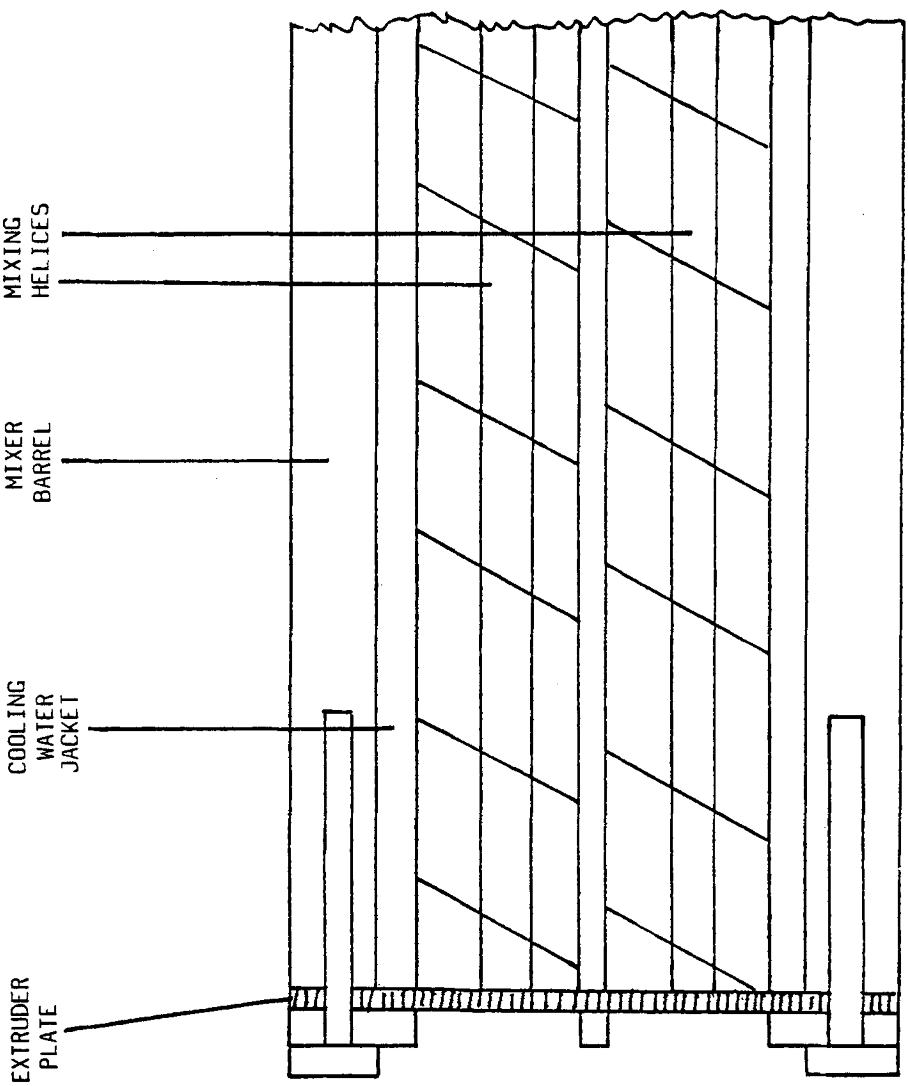


FIGURE 2

BAKER PERKINS MP50 MIXER BARREL

blades towards the extrusion plate. Water was fed into the mix part way along the barrel, by a Watson Marlow (Falmouth, UK) Type 601 peristaltic pump. Mixing continues until the material is pushed through the extrusion plate by the pressure generated from the mixing helix. Both the peristaltic pump and the powder feed were calibrated, with the binder/granulating solvent and the powder blend in use respectively. The extrusion plate consisted of a piece of stainless steel sheet 0.74 mm thick perforated with 0.94 mm circular holes. The holes constituted 23% of the area of the plate.

Cooling water at a temperature of 5°C was recirculated through the water jacket of the mixer barrel throughout the experimental procedures.

MATERIALS AND METHODS

Paracetamol was used as supplied by the manufacturers (Sterling Organics, Cramlington, UK) as were Avicel PH 101 (FMC Corporation, Marcus Hook, Pennsylvania, USA), lactose (100 mesh, DMV, Veghel, Holland) and hydroxypropyl methyl cellulose (Methocel E5, Colorcon, Orpington, Kent, UK). The weight median diameter of the Lactose was found to be 135μm by Alpine Airjet sieve.

Formula 1	%
Paracetamol	80
Avicel PH 101	10
Lactose BP/USP	10

Formula 2	%
Paracetamol	80
Avicel PH 101	9
Lactose BP/USP	9
HPMC	2

Dry mixing of 20kg batches of each formula was carried out for 2 minutes in a Baker Perkins "Dry Dispersa" 601 mixer at 650rpm. The powder blend was used to calibrate the Ktron powder feed.

Powder was fed to the machine at a constant rate (60kg per hour for Formula 1 and 70kg per hour to Formula 2). The liquid feed rate was changed

FIGURE 3

FORMULA 1, 20% WATER

in the range 15.3 - 23.4 kg/hr (Formula 1) and 16.5 - 23.4 kg/hr (Formula 2). This corresponded to 20.3 - 29.1% and 19.0 - 25.1% for Formulas 1 and 2 respectively. Ten gram samples of extrudate were collected at each moisture content examined.

The torque used by the mixer drive, and the temperature of the extrudate as it emerged from the extruder plate were recorded at each moisture content examined.

OBSERVATIONS AND RESULTS

Extrusion of Formula 1 was associated with partial screen blockage at all moisture contents and marked irregularities in the rate of extrusion. In

FIGURE 4

FORMULA 1, 25% WATER

contrast, Formula 2 extruded uniformly at all moisture contents. In both cases, the upper limit to the moisture content was accompanied by adhesion of the extrudate strands one with another, so that lumps were formed. It was not possible to reduce the moisture content below the minimum values reported as the load on the mixer became excessive (assessed using the torque indicator on the machine). This indicated that the formulations were inadequately lubricated at these moisture levels.

Photomicrographs of the extrudate produced at the lowest and highest moisture contents of Formula 1 (Figures 3 and 4 respectively) and Formula 2 (Figures 5 and 6 respectively) are shown below. The influence of moisture

FIGURE 5

FORMULA 2, 20% WATER

content on mixer torque and extrudate temperature are seen in Figures 7 and 8 respectively.

DISCUSSION

Effect of Moisture Content - Formula 1

Extrudate produced at all moisture contents showed a high incidence of defects, predominantly surface roughness and (relatively) mild shark skinning (Figures 3 and 4). Moisture contents in the range 20 to 25% w/w showed no significant differences in defect incidence. Examination of the photomicrographs of samples taken at intermediate moisture contents (not published) confirms this conclusion.

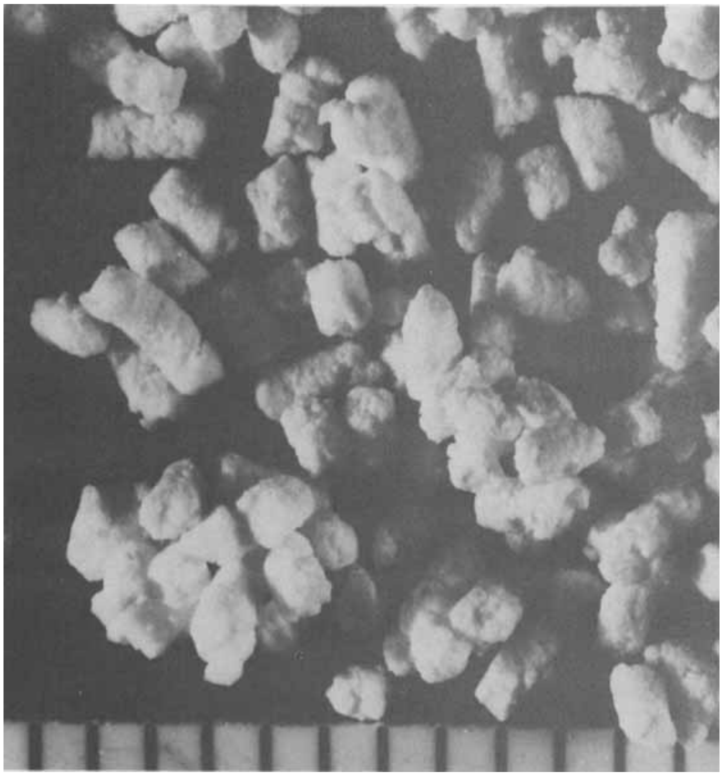


FIGURE 6

FORMULA 2, 25% WATER

The photomicrograph of the sample with a moisture content of 28% (Figure 9) shows an improvement in extrudate quality (reduced incidence of shark skinning, smoother extrudate) but also more extensive clumping together of the extrudate to form aggregates.

Effect of Moisture Content - Formula 2

Extrudate produced with moisture contents in the range 20 (Figure 5) - 23% showed a uniform incidence of severe shark skinning and surface roughness. At 24 and 25% moisture (Figure 6) some improvement in extrudate quality is evident but this again is associated with significant aggregation of the extrudate strands.

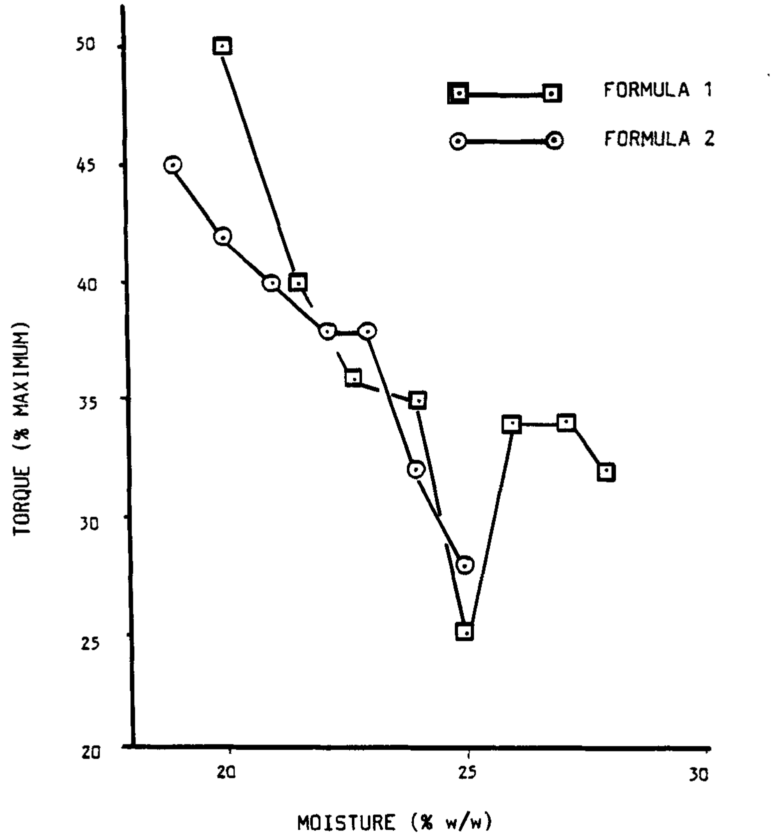


FIGURE 7

EFFECT OF MOISTURE CONTENT ON MIXER TORQUE

Comparison of Formulae 1 and 2

The influence of formulation on the quality of the extrudates produced was not regarded as significant at the moisture contents which is was possible to study. The quality of the extrudate would be unsuitable for spheronisation although it would be a possible granular product.

Effect of Formulation on mixer torque and extrudate temperature

The torque requirement of Formula 2 was significantly lower than that of Formula 1 (see Figure 7) despite the slightly higher extrusion rate used for

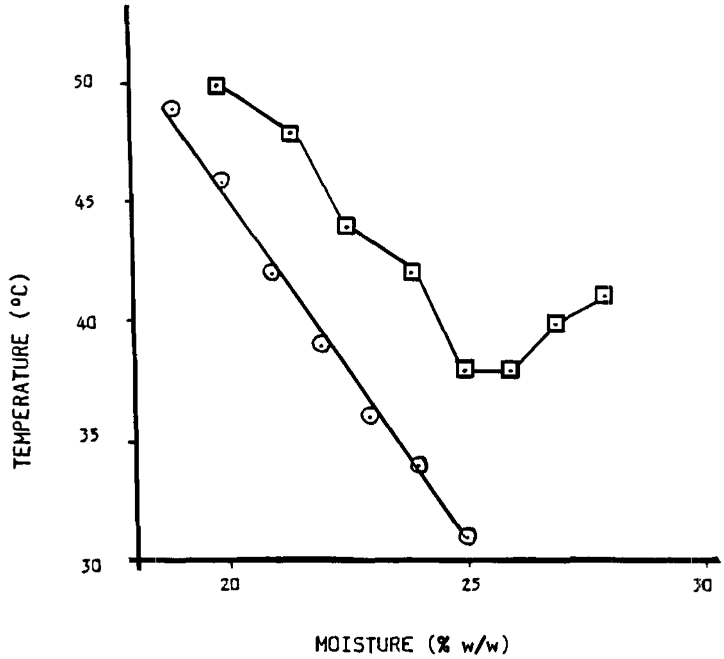


FIGURE 8

EFFECT OF MOISTURE CONTENT ON EXTRUDATE TEMPERATURE

Formula 2. This indicates that Formula 2's flow through the extruder plate was better than that of Formula 1. This hypothesis is supported by the lower extrudate temperatures recorded for Formula 2 (see Figure 8) which result from reduced frictional forces on extrusion, and the uniform flow of Formula 2 from the extruder, Formula 1 exhibiting partial blockage of the plate and intermittent flow.

General

From these data it is clear that the addition of HPMC to Formula 1 has had a significant influence on extrusion properties. This must result from an effect on the viscoelastic and or frictional properties of the extrudate. It would appear that HPMC helps to retain water at the extruder plate surface, reducing frictional forces between the extrudate and the plate. This effect is not reflected in the quality of the extrudate produced, although extrudates containing HPMC and produced with 25% moisture were of comparable quality to

FIGURE 9

FORMULA 2, 28% WATER

extrudate with moisture content of 28% produced without it. HPMC therefore appears to exhibit a water-sparing effect on the formulation.

These data appear to support the use of extrusion aids as recommended by Reynolds (2) and also recommendations to use grades of microcrystalline cellulose incorporating other cellulose derivatives as extrusion aids. The role of water in such systems is highly important.

The quality of extrudate produced from these formulae tested on the Baker Perkins MP50 was poor (in contrast with extrudate quality of other systems examined). This could result from formulation limitations, machine limitations or both. Two particular differences between the Baker Perkins MP50 and other extrusion systems are noticeable:-

a) The time from mixing to extrusion the BP MP50 is short. The mix at any one time in the mixer is only a few hundred grams and so residence times are short. This is a significant advantage of the machine as changes in granulation moisture content are reflected almost instantaneously. However, if the mixing process has a time dependent element (eg a hydration step) then this may not be adequately completed in the short residence time of a continuous mixer. Rearrangement of the mixing elements can be used to increase residence time.

b) The thickness to diameter ratios of the holes in the extruder plate is significantly shorter than that used in the some other systems. Short ratios have been associated with shark skinning (3). It is therefore likely that modification of the machine to increase the thickness of the extruder plate would improve the product in this case.

CONCLUSION

The formulations examined in this study were satisfactorily granulated Baker Perkins MP50, but the extrudate was unsuitable for spheronisation. Further work on:-

a) formulation optimisation

b) material residence time

c) die design

would be required to enhance the quality of the extrudate and to make full use of the flexibility of the extruder/granulator.

REFERENCES

(1) Greer, H. "Continuous Granulation". Paper presented 27th November 1984 at PHARMTECH '84,

(2) Reynolds, A. D. Manf. Chem. 41, 40-44, (1970)

(3) Harrison, P. J., Newton, J. M., and Rowe, R. C. J. Pharm. Pharmac. 37, 81-83 (1985)