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Scale-down of a high-shear pelletisation process: Flow profile and growth kinetics

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Abstract

For the predictive modelling of the high-shear pelletisation process it is necessary to have a better understanding of the underlying mechanisms. Therefore, pelletisation experiments were carried out with microcrystalline cellulose and lactose in a coffee grinder (small-scale) and in a Gral 10 ('large'-scale). A toroidal flow-pattern was observed and described for both apparatus. There was no effect of increased impeller speed on the velocity of pellets in the torus; only a change in angle with the tangential direction was observed. Moreover, the size of pellets decreased rapidly to a new value. This size increased again when the impeller speed was reduced to the initial (low) value. This suggested the existence of fast break-up and growth, resulting in a dynamic equilibrium depending on the impeller speed. Tracer experiments were used to investigate the turnover times of different sieve fractions. First order conversion rate constants for the pellets of different sieve fractions, calculated from colour concentrations at several processing times, were equal for both apparatus when plotted against the dimensionless diameter of the pellets (d/d_{50}). These results are a strong indication for the usefulness of small-scale experiments to retrieve a rapid insight into relevant mechanisms of growth of high-shear pelletisation.

Keywords: Pelletisation; Scale-down; Kinetics; Flow; Growth

1. Introduction

High-shear pelletisation processes are well established in the pharmaceutical industry (Knight, 1993; Vertommen et al., 1994; Landin et al., 1996). However, control of these processes is to a large extent still based on trial and error (Leuenberger, 1983; Vojnovic et al., 1995). What is needed, as recently mentioned by Ennis (1996), is a much better mechanistic understanding of agglomeration phenomena. Only then, will we be able to master this process to such an extent that we will be, for example, able to generalise the conditions that allow us to make narrow pellet

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size distributions, as obtained with microcrystalline cellulose (mcc).

To establish real mechanistic models, one has to take into account what happens at the scale of particles involved, and how this relates to transport processes, mechanical properties of excipients and operational variables like specific power input (P/V), relative swept volume (RSV), moisture content, etc.

High-shear pelletisation of mixtures containing mcc is an interesting process because very narrow particle size distributions can be obtained (80% within a range of 0.1 mm relative to an average value of 0.95 mm (Holm et al., 1996)). Furthermore, a very systematic toroidal flow pattern occurs (Holm et al., 1996). This leads to the question whether or not there is a relation between these two phenomena, and to what extent does mcc influence it. In the future, this should lead to conditions for high-shear pelletisation processes in which similar results (in particular a narrow particle size distributions) can be obtained with a broader range of excipients than mcc.

Because it will always be difficult to predict the behaviour of high-shear pelletisation entirely from first principles (particularly for the influence of the mechanical and surface properties of the materials involved), a combined mechanistic approach with small-scale experiments that are representative for production-scale conditions is necessary. In our case, a high-shear coffee grinder was used for small-scale experiments.

1.1. Previous work

Growth of pellets can be divided into four stages: initial nucleation with minor growth, exponential growth by coalescence, linear growth and equilibrium with zero net growth (Ramaker et al., 1997; Wauters et al., 1997).

During liquid addition, large primary nuclei are formed as soon as liquid drops reach the powder bed. Due to the impact of the impeller, the weak primary nuclei are crushed into several stronger and denser secondary nuclei. More densification of the secondary nuclei results in exponential growth by coalescence (Vonk et al., 1997). During kneading, the mean pellet size increases until a dynamic equilibrium is reached in which zero net growth occurs. The rates of growth and break-up of pellets become equal. In other words, although the mean pellet diameter is not changing anymore, growth and break-up of individual pellets still occur. The time of onset on the equilibrium depends on many variables like moisture content, relative swept volume and liquid distribution.

1.2. Theory

Break-up and growth of pellets take place at different locations within the mixer. Requirements for break-up and growth of pellets are collisions of any kind. Without any collisions, no break-up and growth occur. To obtain collisions, differences in velocity are needed. Break-up by fragmentation and abrasion occurs as a result of the action of the impeller and the chopper. Collisions between pellet–wall, pellet–impeller, pellet–chopper and pellet–pellet can cause break-up of the pellets. So, it is likely that break-up of pellets occurs at locations near the wall, impeller and chopper, where local differences are of major importance.

On the other hand, pellets grow at locations where the influence of impeller and chopper are less, but where some velocity differences still exist. So, growth of pellets takes place within the powder mass during mixing. To understand the mechanisms of growth and the growth profile of pellets, it is necessary to identify the flow pattern and the velocities of pellets during pelletisation in different high-shear mixers.

1.3. Froude number

Dimensionless numbers, like the Froude number, can be very useful during scale-up issues (Landin et al., 1996). Two forces acting on the pellets are of major importance for the flowing profile of the pellets. These two forces are the centrifugal force (mv^2/R) and the gravitational force (mg), where m is the mass of one pellet, g the gravitational acceleration constant, v the velocity of the pellet calculated as a fraction of the impeller tip velocity, R the radius of the bowl ($1/2$ D), D the diameter of the bowl, and N the

impeller rotational speed. The relationship between the centrifugal force and the gravitational force is given by the Froude number:

$$Fr_c = \frac{mv^2/R}{mg} = \frac{(\pi ND)^2/(1/2D)}{g} = 2\pi^2\frac{N^2D}{g} \quad (1)$$

$$Fr = \frac{N^2D}{g} \quad (2)$$

where Fr is the Froude number, and Fr_c is the critical Froude number.

Above a certain critical Froude number, the centrifugal force exceeds the gravitational force. This critical value is given by the constants left out at the Froude number-equation ($2\pi^2 \approx 20$). At a Froude number of 20, the centrifugal force and the gravitational force are equal. At a Froude number >20, the pellets are moving in a more fluidised pattern (e.g. torus profile), compared to the flowing profile at a lower Froude number, due to the higher centrifugal force acting on the pellets.

1.4. Aim

The aim of this study was to elucidate the flow pattern of pellets and also to analyse a number of mechanisms involved in the growth and break-up of pellets in a high-shear pelletisation process at small-scale experiments that are representative of large-scale production.

2. Materials and methods

2.1. Materials

Mixtures with equal amounts of microcrystalline cellulose (Pharmacel PH101, DMV, Veghel, The Netherlands) and α-lactose (Pharmatose 200 mesh, DMV) were used as starting materials. Amaranth, not having any effect on pellet growth, was added as a colouring agent during the tracer experiments (1 g/l binder liquid for the coffee grinder experiment, and 2 g/l binder liquid for the Gral experiment). Demineralised water was used as binder liquid.

2.2. Equipment

A Gral 10 high-shear mixer (Machines Collette, Wommelgem, Belgium) was used for the preparation of pellets. The impeller speed of the Gral was continuously adjustable until 660 rpm, the chopper speed could be varied between 0, 1500 and 3000 rpm. The temperature of water in the double-sided wall of the bowl was 25°C during the entire process. Binder liquid was added under gravity. The mean diameter of the liquid drops was 5 mm.

A Moulinex coffee grinder (Moulinex 980, Ireland) was used for small-scale experiments. The impeller speed was made continuously adjustable until 2×10^4 rpm using a transformer. The geometry of both apparatus and a number of their relevant properties are given in Table 1.

The sieving analyses were carried out with a set of sieves with openings of 150, 212, 300, 425, 600, 710, 850, 1120, 1400 and 2000 μm.

An UV/VIS-spectrophotometer (Philips PU8720, England) was used for colour concentration measurements during the tracer experiments.

2.3. Methods

Preparation of pellets in the Gral 10 was as follows: after 5 min of premixing, a precisely determined amount of binder liquid was added under gravity in 1 min and the mass was kneaded for 4 min. Subsequently, the wall-addition was

Table 1
Geometry of the two high-shear mixers and some of the relevant properties

	Gral 10	Coffee grinder
Volume bowl (l)	8	0.250
Diameter bowl (m)	0.245	0.08
Impeller radius (m)	0.115	0.033
Impeller speed (rpm)	400	$4.9 \times 10^3/11 \times 10^3$
Batch size (g)	800	24
Binder liquid (ml)	400	12
Relative swept volume (s^{-1})	12	14/31
Rotational speed torus (s^{-1})	0.7	1.6/1.5

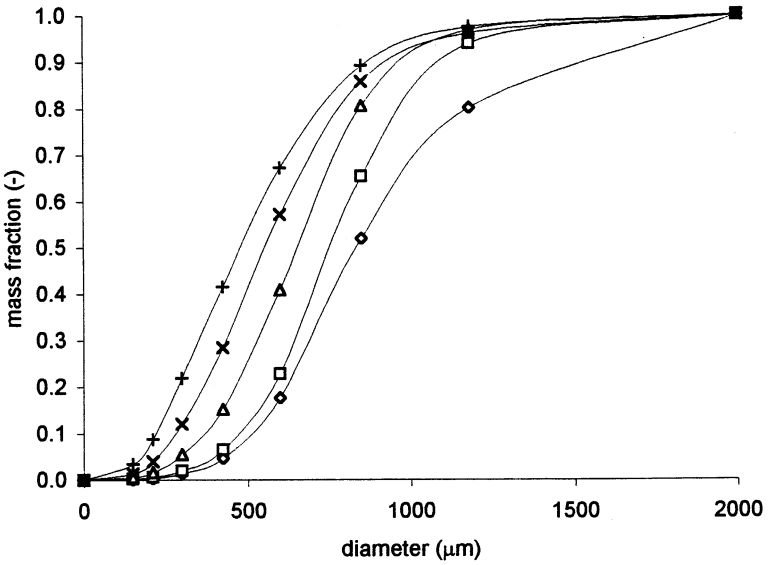

Fig. 1. Cumulative pellet size distributions at several impeller speeds for experiments performed in the coffee grinder. The impeller speed of ◇ was 20 rps, □ 82 rps, △ 138 rps, x 187 rps, and + 354 rps.

scraped from the wall, and the mass was kneaded for another 15 min. The total processing time was 25 min (including 5 min premixing). During the whole experiment, the impeller speed was set at 400 rpm. The chopper speed was set at 3000 rpm during the liquid addition and the first 4 min of the kneading stage; the chopper was turned off during the last 15 min of the kneading stage. All pellets were tray-dried at 60°C for 24 h.

In the coffee grinder, pellets were prepared in a similar way, but the time-scales were shortened to 30 s of premixing, 30 s of liquid addition and 120 s of wet massing. The impeller speed was set at 82 rps and at 187 rps for two different experiments. The liquid (12 ml) was added using a syringe.

During the tracer experiments, 5 (Gral experiment) or 10% (coffee grinder experiments) of the pellets were replaced by freshly prepared (wet) coloured pellets. All coloured pellets used in the tracer experiments, were prepared in the coffee grinder at a higher impeller speed (187 rps). The concentration of amaranth in each sieve fraction was measured at several processing times. After dissolving 300 mg of pellets in 3 ml water, the colour concentrations were measured spectrophotometrically at 522.5 nm.

Photos were taken from the pellets in the torus during the dynamic equilibrium stage. A stroboscope was used for the lighting of the process. The frequency of the stroboscope was adjusted to obtain two or more images of a pellet at one photo. The distance and the deviation of the pellets from the tangential line (= angle) were measured. The radial velocity, the tangential velocity, and the total velocity (v) were calculated from these data.

3. Results and discussion

3.1. Pellet diameter

The pellet diameter, measured as pellet size distribution and volumetric mean diameter (d_{50}), depends on several process variables like moisture content, impeller speed and processing time. The influence of the impeller speed on the final pellet size distribution is shown in Fig. 1. The effect of the impeller speed on the pellet size distribution was shown before by several authors (Knight, 1993; Schæfer and Mathiesen, 1996; Zhou et al., 1997). In contrast with their results, this figure

shows a decrease of pellet diameter at an increased impeller speed. We also found a dynamic equilibrium in growth, which has not been found by these authors. A combination of high impeller speed during process and a low filling degree of the bowl, resulting in a high relative swept volume probably cause these two differences.

The shift of the pellet size distribution towards a smaller mean diameter at an increased impeller speed can be explained by the higher destructive forces (higher tip-velocity) of the impeller. This causes two effects: first, the number of collisions is increased, and second the chance of successful collisions for coalescence is decreased, because of the low contact-time between the pellets. Break-up of pellets becomes more important compared to growth of pellets. In other words, the equilibrium between growth and break-up shifts towards a higher break-up, which leads to a lower mean pellet size.

The linear relationship between the impeller speed of the coffee grinder and the mean pellet diameter (d_{50}) is shown in Fig. 2. This relationship is levelled off at impeller speeds >185 rps. This may be caused by the more turbulent flow at higher impeller speeds.

The Froude number (Eqs. (1) and (2)), calculated with the mean pellet velocity at the whole torus (this is assumed to be 0.4 times the impeller velocity), the bowl diameter and the gravitational

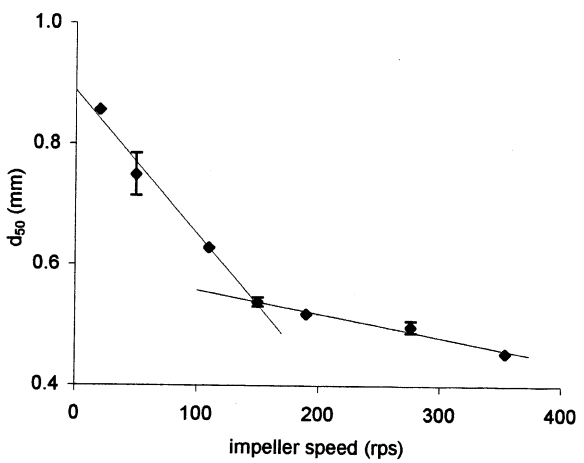

Fig. 2. Mean pellet diameter (d_{50}) as a function of the impeller speed for the coffee grinder experiments.

acceleration constant exceeds the critical value ($2\pi^2 = 20$) at an impeller speed of 125 rps ($((0.4 \times 125)^2 \times 0.08/9.813 = 20$). This indicates a greater influence of the centrifugal forces instead of the gravity forces at higher impeller speeds.

The mean pellet size can be controlled by the impeller speed. After preparation of a batch of pellets in the coffee grinder at 82 rps, the impeller speed was increased to 187 rps. This resulted in a 119 μm decrease of the mean pellet diameter (d_{50}). A decrease of the impeller speed to the starting value (82 rps) resulted in an increase of the mean pellet size with 188 μm. This indicated the existence of a dynamic equilibrium between growth and break-up of pellets. Furthermore, the effect of changed impeller speed on the mean pellet size is partly reversible. Therefore, the impeller speed can be used to control the mean pellet size.

3.2. Flow profile

The flow profile of the pellets, during the dynamic equilibrium, was investigated by measuring the displacement of pellets photographically. A torus of pellets was observed in the coffee grinder and the Gral. This torus can be characterised by the helical shape (Schæfer et al., 1993; Holm et al., 1996) due to a combination of two independent trajectories caused by centrifugal forces, impact forces and gravity. The pellet–pellet, pellet–impeller and pellet–wall collisions are responsible for all pellets to stay in this stable torus: even without the cover, the particles stay in the coffee grinder. No such stable flow pattern was observed for dry pellets. Most likely, this flow pattern is the result of visco-elastic properties of microcrystalline cellulose.

The total velocity of pellets in the torus of a coffee grinder is shown in Fig. 3. The velocity of pellets was lowest near to the wall of the bowl. Further from the wall, the total velocity of the pellets increased. No pellets were observed at the centre of the mixer; the bottom of the bowl could be seen clearly.

Surprisingly, no differences in velocities of the pellets (at the surface of the torus) were measured at a higher impeller speed. The angle (tangential difference) of the pellets is shown in Fig. 4. Near

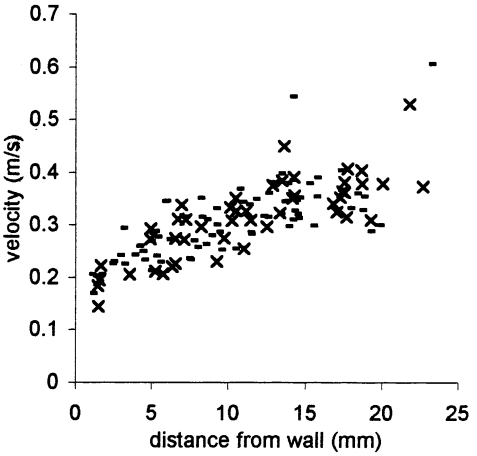

Fig. 3. Velocity of the pellets as a function of the distance from the wall of the coffee grinder; — represents the data at an impeller speed of 82 rps, x represents the data at an impeller speed of 187 rps.

the wall, the direction of the pellets was almost equal to the tangential line. Near the centre, the angle increased and the direction of the pellets was more inside (radial) orientated. At a higher impeller speed, the differences in the tangential direction became lower, while the velocity of the pellets remained unchanged. Only the velocities of the pellets at the upper side of the torus were measured because no method was available to measure the velocity of pellets at the bottom or in the torus.

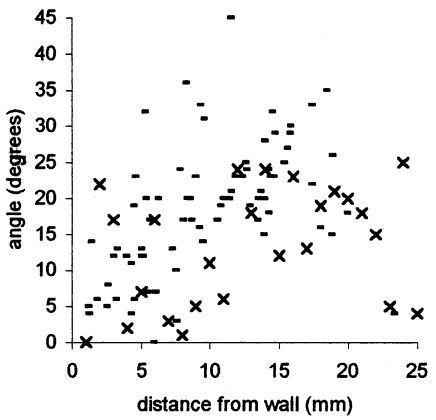

Fig. 4. Relationship between the tangential differences (= angle) of the pellets and the distance from the wall of the coffee grinder; — represents the data at an impeller speed of 82 rps, x represents the data at an impeller speed of 187 rps.

As a consequence of the higher impeller speed, more energy was dissipated. Because no change in pellet velocity was observed, more energy dissipation should lead to faster growth and destruction of all pellets, which will be further emphasised in Section 3.3.

The torus showed to be very stable. Disturbances due to the chopper (or little obstacles) only produced local changes in the direction of the pellets, and minor changes in velocity. The changes in the directions of the pellets caused more collisions between pellets. Thus, the turnover of the pellet mass will be faster due to the action of the chopper.

3.3. Tracer experiments

During equilibrium, the pellet size distribution was narrow and did not change with time. Nevertheless, growth and break-up of pellets still occurred due to the interactions between pellets in the torus, and between the impeller and the pellets. This can be explained by equal growth and break-up velocities, which result in zero net growth and a dynamic equilibrium. To prove this mechanism and to elucidate the rate at which growth and break-up occurs, experiments with coloured small pellets were performed. Fig. 5 gives the colour concentration of the different sieve fractions at several processing times for the coffee grinder. Fig. 5 shows a fast exponential decay of the colour concentration of the smallest sieve fractions and a fast increasing colour concentration of the largest sieve fractions. All concentrations converged to a constant value. The colour concentration-curve for the Gral experiment was similarly shaped, only the time-scales were prolonged. The colour distribution changed, within 30 s in the coffee grinder-experiment (and within 60 s for the Gral-experiment), from a heterogeneous state (only the smallest pellets were coloured) into a homogeneous state (all pellets were equally coloured). This indicated total turnover of the whole pellet population within 30 s for the coffee grinder experiment and 60 s for the Gral experiment.

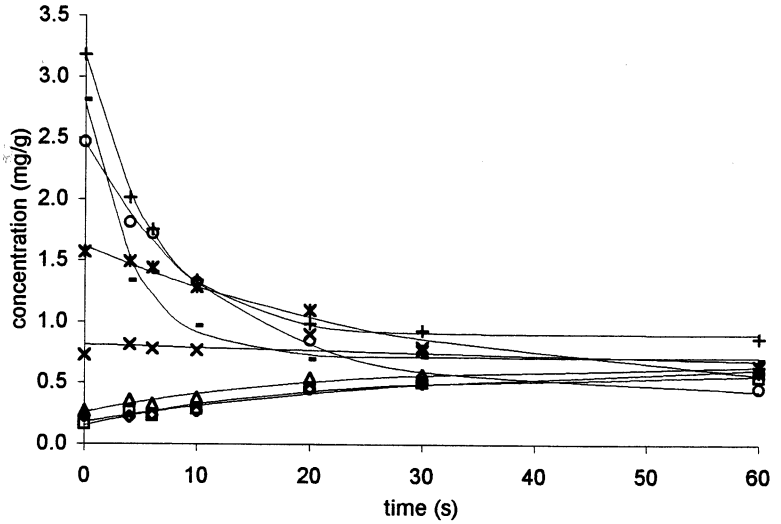

Fig. 5. Colour concentration for different sieve fractions at different processing times after colouring the small pellets. This experiment was performed in the coffee grinder at 82 rps; ◇ represents the sieve fraction with a mean diameter of 1.59 mm, □ the 1.015 mm sieve fraction, △ the 0.725 mm sieve fraction, x the 0.513 mm sieve fraction, * the 0.363 mm sieve fraction, ○ the 0.256 mm sieve fraction, + the 0.181 mm sieve fraction, and − represents the 0.075 mm sieve fraction. The lines are the model according to Eq. (3).

For each sieve fraction, the colour concentration as a function of time could be described with:

$$\frac{C - C_\infty}{C_0 - C_\infty} = \exp[-k \bullet t] \tag{3}$$

where C is the colour concentration (mg/g), k is the conversion rate constant (s^{-1}) and t is the processing time (s). Fig. 6 shows the conversion rate constants for the small- and large-scale experiments as a function of the dimensionless pellet diameter (d/d_{50}), whereas d_{50} is the volume mean diameter of the whole pellet mass, and d is the mean diameter of one sieve fraction.

First, the Gral experiment (squares) and the 82 rps coffee grinder experiment (triangles) are discussed. The conversion rate constants of the smallest pellets were five to seven times higher compared to the larger ones. This indicated fast growth of small pellets, and a fast formation of small pellets by break-up of larger pellets. The conversion rate constants of the larger pellets ($> d_{50}$) were almost constant. This indicated a similar mechanism of growth and break-up for those pellets at both scales.

Because of the different geometry of both apparatus, it was not possible to prepare pellets with exactly the same pellet size distribution. The conversion rate constant of the pellets however, showed to be independent of the scale of operation. So in this respect, both scales can be compared to each other.

An additional tracer experiment was performed in the coffee grinder at a higher impeller speed (187 rps). The colour concentration distributed similarly, only the time until homogeneous colour distribution was shortened from 30 (at an impeller speed of 82 rps) to 7 s (at 187 rps). The conversion rate constants for the different sieve fractions (Fig. 6, diamonds) were almost ten times higher, compared to the lower impeller speed experiment. This corresponds to the ratio of the power numbers (Landin et al., 1996) for both processes in the coffee grinder:

$$P \propto N^3 D^5$$

$$\frac{P_{high}}{P_{low}} \propto \left(\frac{187}{82}\right)^3 \approx 10 \tag{4}$$

The velocities of pellets in the torus of the coffee grinder (Fig. 3) were almost the same at 82

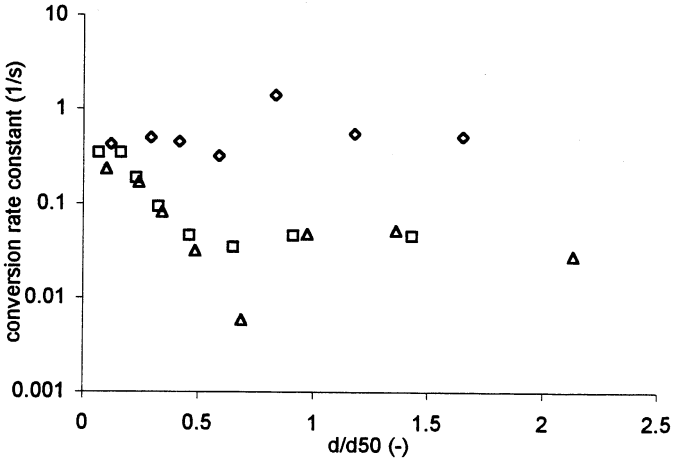

Fig. 6. Conversion rate constant as a function of the normalised pellet diameter; □ represents the data for the Gral experiment, △ the coffee grinder experiment at 82 rps, and ◇ the coffee grinder experiment at 187 rps.

and 187 rps. Additional power input at a higher impeller speed caused faster break-up of pellets. Although the velocity of the impeller was increased by a factor 2.3, the measured velocities of the pellets remained unchanged. This indicated larger differences in velocity between pellets and the impeller. Thus, more interactions between impeller and pellets occurred, which caused higher conversion rate constants for higher impeller speed experiments and therefore faster onset of equilibrium.

4. Conclusions

The flow profile of pellets during the equilibrium stage was characterised as a toroidal ring. As soon as pellets were formed this torus was seen in the Gral and the coffee grinder. The velocity of pellets at the surface of the torus was equal at different impeller speeds; the difference of the trajectory of the pellets from the tangential line was increased at a higher impeller speed. Because the velocity of the pellets did not change when the impeller speed was increased, an increase in velocity differences between impeller and pellets resulted in faster growth and destruction.

An increased impeller speed resulted in a decrease of the mean pellet size. This effect showed to be partly reversible. Therefore, the impeller speed can be used to control the mean pellet size during high-shear pelletisation.

Growth and destruction of pellets from different sieve fractions could be measured with tracer experiments. Conversion rate constants were derived from the exponential decay of the colour concentration at different processing times for each sieve fraction. Compared to the dimensionless diameter, similar conversion rate constants were found in the coffee grinder and the Gral. The conversion rate constants of the smallest pellets were higher (compared to the larger ones), which indicated faster growth of the smaller pellets due to the destruction of the large pellets.

At a higher impeller speed, the velocity of pellets at the upper side of the torus was unchanged. The velocity differences between impeller and pellets were increased, which resulted in faster turnover of the whole pellet mass. The conversion rate constants at 187 rps were about ten times higher compared to those at 82 rps. This ratio is equal to the third power of the ratio between impeller speeds, suggesting that P/V is important.

The fact that similar phenomena are observed in coffee grinder and Gral suggested that experiments with a coffee grinder can be a cheap and rapid method to elucidate relevant mechanisms in high-shear pelletisation.

List of symbols

C	colour concentration (mg/g)
d	diameter pellet (m)
D	diameter bowl (m)
Fr_c	critical Froude number (−)
Fr	Froude number (−)
g	gravitational acceleration constant (m/s^2)
k	conversion rate constant (l/s)
m	pellet mass (kg)
N	impeller rotational speed (l/s)
P	power (W)
R	radius bowl (m)
t	time (s)
v	velocity (m/s)
V	volume (m^3)

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