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Process variables of instant granulator and spheroniser: III. Shape and shape distributions of pellets

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Summary

The complete 2^6 study design was used to investigate the influence of the process variables of a continuously working granulator, and a spheroniser on the shape and shape distributions of pellets. Shape parameters were derived from size parameters measured by image analysis. Of seven shape parameters suggested, roundness and elongation most effectively distinguished pellets from each other. For a homogeneous pellet batch, 200 pellets need to be measured, but in the case of a heterogeneous batch, even up to 800 measurements were required to achieve reliable and reproducible results. The most important process variables affecting the shape of pellets were the size of the granule outlet in the granulator, the speed of the friction plate and the residence time: rounder pellets could be produced using larger granule outlet, faster speed of the friction plate and longer residence time.

Introduction

One of the main purposes of pelletization is to produce uniformly sized and shaped spherical pellets which can be successfully coated and, thus, are optimal for controlled release products.

The size of a pellet can be characterised, e.g., by its diameter or projected area (Allen 1990). Instead, the definition of pellet shape – which is also related to the size – is a less determinable characteristic. The evaluation of the shape of pellets in order to determine whether a certain pellet is acceptable seems to be an important and demanding question. Recently, various techniques for the determination of the shape of a pellet have been developed (Whiteman and Ridgway, 1986; Chapman et al., 1988; Lövgren and Lundberg, 1989).

The present study has two basic aims: to evaluate the applicability of different shape parameters in describing the sphericity of pellets, and to study the effects of the granulator and the spheroniser on the shape of pellets.

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Materials and Methods

Preparation of pellets

Mannitol (75%, Merck, Germany), microcrystalline cellulose (20%, Emcocel 50M, Edward

Mendell Co., U.S.A.), caffeine (5%, Boehringer Ingelheim, Germany) and distilled water (35 or 38% on the basis of dry weight, i.e., 25.9 or 27.5% of wetted mass, respectively) were used as starting materials, all of Ph.Eur. grade.

Pellets were prepared using the continuous granulation and extrusion/spheronisation method (Nica System AB, Mölndal, Sweden). The equipment, preparation of pellets and experimental design of this study have been described earlier (Hellén et al., 1993c).

Shape of pellets

The shape of pellets was studied by optical microscopy (Olympus Stereo Zoom Microscopy, SZH-ILLK, Olympus Optical Co., Tokyo, Japan) and image analysis (OPT/IA, Kontron Vidas +, Kontron Bildanalyse GmbH, Munich, Germany). The method employed has been presented earlier (Hellén et al., 1993a).

Altogether seven parameters (Eqns 1–7) indicating shape were derived from size data measured by OPT/IA (Hellén et al., 1993b). The purpose of these parameters was to emphasise the spherical (circularity, roundness), oblongated (elongation, modelx), elliptical (pellips) or rectangular (rectang) shape of pellets. The parameters were as follows:

$$\text{circularity} = \frac{4 \cdot \pi \cdot \text{area}}{[\text{perim}]^2} \tag{1}$$

$$\text{roundness} = \frac{\text{area}}{\pi \cdot \left[\frac{d_{\max}}{2}\right]^2} \tag{2}$$

$$\text{elongation} = \frac{d_{\max}}{d_{\min}} \tag{3}$$

$$\text{pellips} = \frac{\text{perim}}{\pi \cdot d_{\max}} \tag{4}$$

$$\text{rectang} = \frac{\text{area}}{d_{\min} \cdot d_{\max}} \tag{5}$$

$$\text{modelx} = \frac{\text{perim} \cdot d_{\max}}{4 \cdot \text{area}} \tag{6}$$

$$\text{roughness} = \frac{\text{perim}}{\text{cperim}} \tag{7}$$

From all shape distributions, means, standard deviations, 10%, 50% (median) and 90% fractiles, and 90–10% widths were calculated. All distributions were drawn as histograms using proper class widths (MathCAD 3.0 V, MathSoft Inc., Cambridge, MA, U.S.A.). The analysis of variance (ANOVA) as well as the Pearson correlation were used in studying the interactions between the independent process variables and the response variables (Systat 5.0 MS/DOS, Systat Inc., U.S.A.).

Results and Discussion

Shape of six individual pellets

The calculated shape parameters for the six pellets (A–F) representing different visual shape groups I–VI (VI refers to roundest pellet) are listed in Table 1. Photographs of these pellets have been presented in the preceding paper (Hellén et al., 1993d).

The circularity parameter seemed to be limited in the evaluation of the shape of pellets – this parameter could not distinguish the difference between the three roundest pellets, i.e., shape groups IV–VI (Table 1). The roundness parameter, instead, was very sensitive, ranging from 0.39 to 0.91 and classifying the pellets clearly according to visual observation; the elliptical pellet D possessed, however, a lower roundness value than pellet C. Like circularity and roundness, the pellips parameter increased as the shape of pellets became more spherical. The pellips parameter ranged from 0.80 to 1.01.

The elongation and modelx parameters behaved very similarly. Elongation values ranged from 2.73 to 1.06, and modelx from 2.05 to 1.12. The numerical value of both these parameters decreased systematically as the pellets became rounder. Very clear correlation between the elongation and $d_{\max}$ values of pellets (Hellén et al., 1993d) was found – even the numerical values were quite similar due to the fact that all $d_{\min}$ values were close to 1.00 mm, the diameter of the

TABLE 1

Shape parameters of six pellets A–F

	A	B	C	D	E	F
Visual shape group	I	II	III	IV	V	VI
Circularity	0.61	0.79	0.84	0.88	0.89	0.88
Roundness	0.39	0.55	0.67	0.66	0.82	0.91
Pellips	0.80	0.83	0.89	0.87	0.96	1.01
Elongation	2.73	2.00	1.61	1.55	1.24	1.06
Modelx	2.05	1.52	1.33	1.31	1.17	1.12
Rectang	0.84	0.86	0.85	0.81	0.80	0.76
Roughness	1.31	1.26	1.28	1.29	1.32	1.36

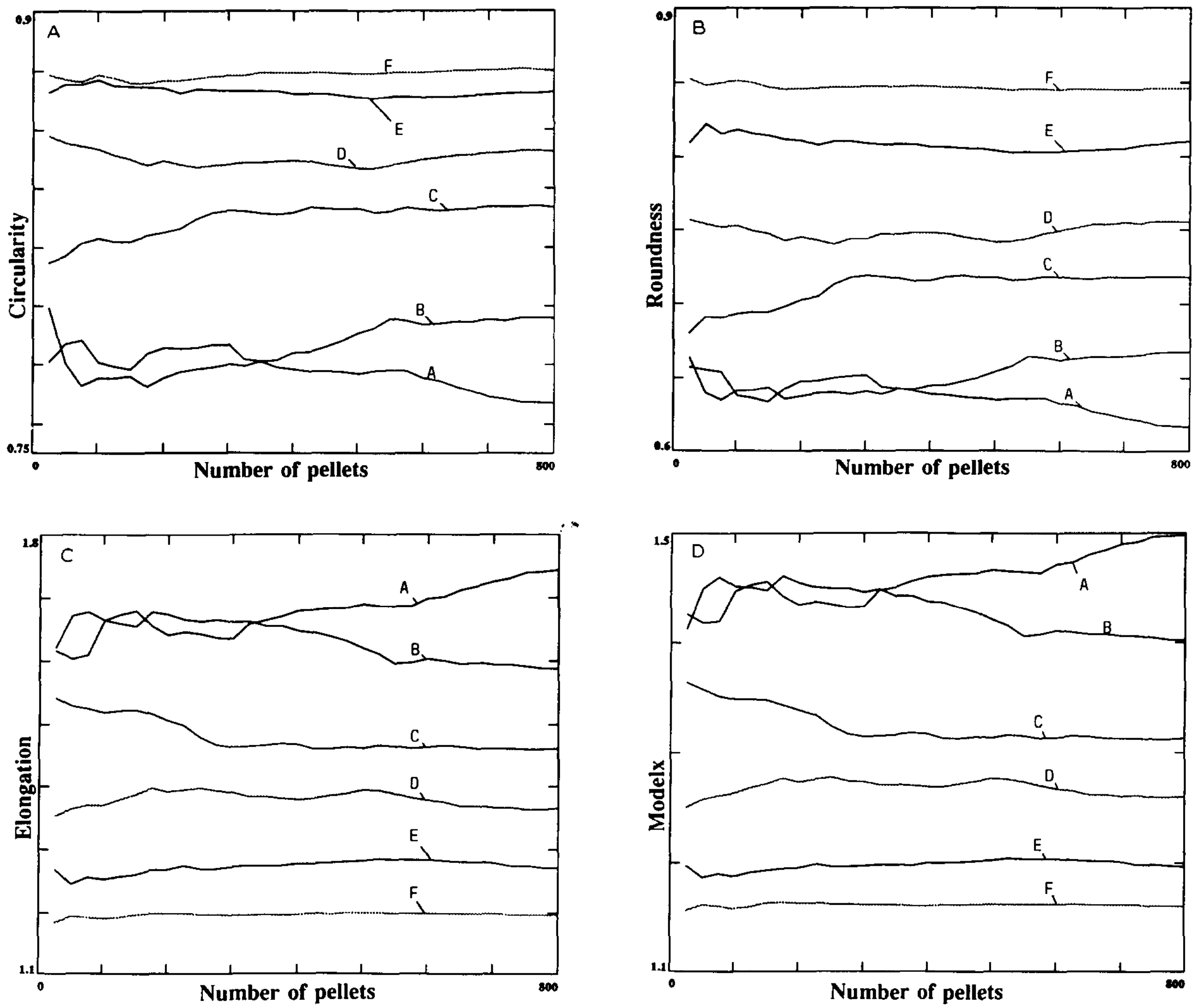

Fig. 1. The development of mean values of shape parameters (batches A–F) as a function of number of pellets: (A) circularity, (B) roundness, (C) elongation, (D) modelx.

dies in the extruder screen. The rectang parameter was somewhat limited – it was able to classify these six pellets only into two categories. Shape groups I–III had slightly higher rectang values; on the basis of the photographs presented earlier (Hellén et al., 1993d), these pellets really had a more rectangular shape.

The roughness parameter could not distinguish the different shapes or surface structures from each other. Hence, due to its insensitivity, the roughness parameter cannot be used as an indicator of shape or surface structure in the case of pellets (Hellén et al., 1993b).

According to these results and data reported earlier (Hellén et al., 1993b), roundness and elongation, but possibly also circularity and modelx parameters, are evidently applicable in pellet shape studies. Only these will be used in further pellet shape and shape distribution evaluations.

Shape parameters as a function of number of pellets measured

For the evaluation of number of pellets needed to give reliable and representative shape values for pellets, pellet batches was studied. The development of mean values (batches A–F) of four shape parameters is represented in Fig. 1A–D. The mean values have been calculated using 25 pellet intervals up to 800 pellets.

The circularity and roundness behaved almost identically (Fig. 1A, B). However, roundness proved to be a more efficient shape parameter

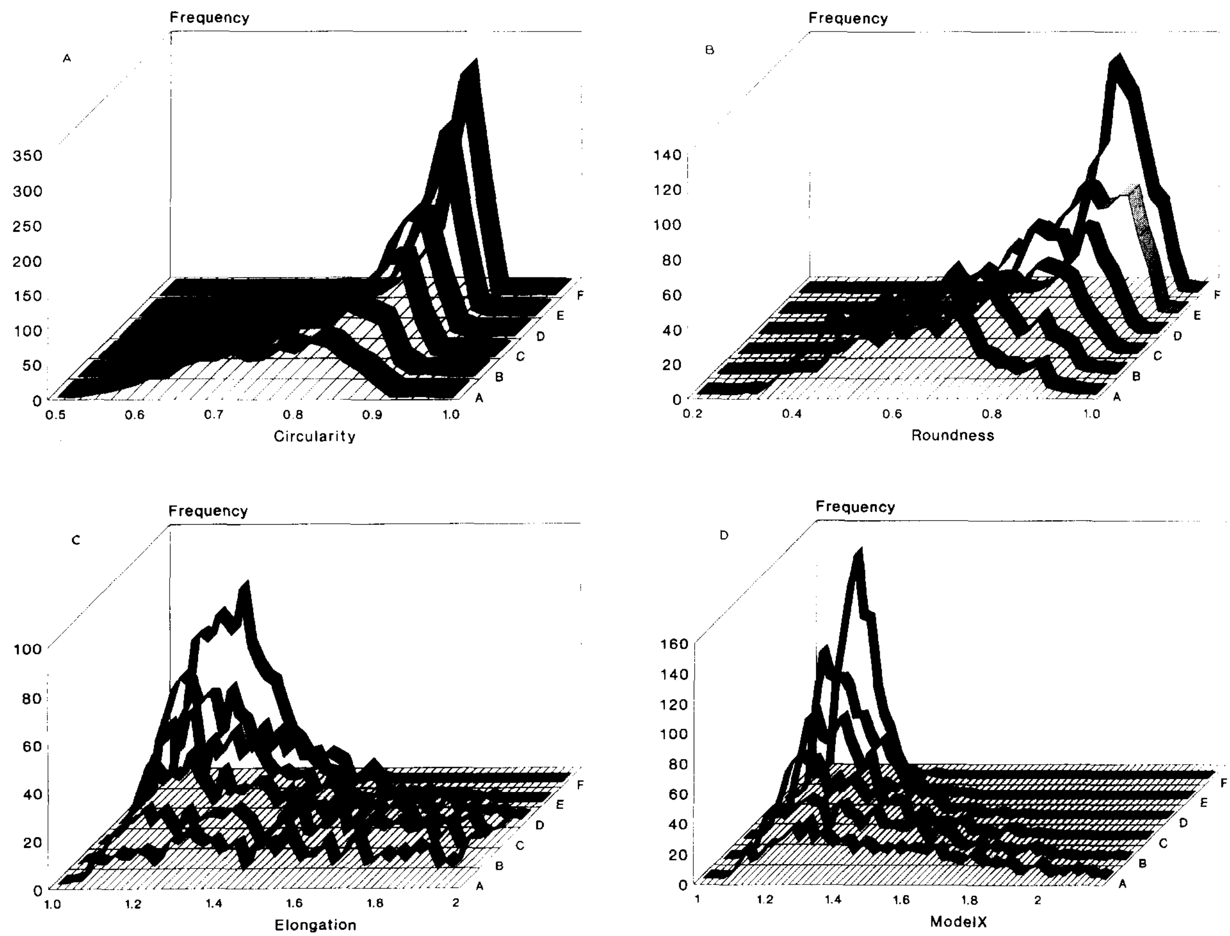

Fig. 2. Distributions of five shape parameters for batches A–F: (A) circularity, (B) roundness, (C) elongation, (D) modelx.

for pellet studies, since it could separate more clearly batches E and F consisting of round pellets. An adequate number of spherical pellets for circularity and roundness determinations would be about 300, or even 200 (E and F). The most elongated pellets seemed to require much more measurements, up to 800.

The parameters elongation and modelx also behaved identically (Fig. 1C, D), although the ability of elongation to separate the batches appeared to be better. The homogeneity of batch F was very good; actually no changes in mean values could be found. Instead, batches A and B, containing long, cylindrical pellets, were quite heterogeneous. Again, 800 measurements were needed.

Shape distributions

The only exact way to describe distributions is to present them as they are. Distributions of five shape parameters of batches A–F are presented in Fig. 2A–D.

The circularity parameter (Fig. 2A) satisfactorily separated the six pellet batches from each other. This very clear difference between the batches could not be observed on the basis of single pellet values. Fig. 2 also indicates that the width of the distributions might be a useful parameter in comparing different pellet batches – the width of the most heterogeneous pellet batch A was 0.22 (span 0.29), while that of the most homogeneous batch F was only 0.06 (span 0.07). The roundness parameter of the batches studied behaved mainly like the circularity parameter, but even more effectively especially in the case of the roundest pellet batches. The widths of distributions varied between 0.35 and 0.14, and spans between 0.58 and 0.16, respectively.

Elongation and modelx distributions also had quite similar shapes. This is slightly less evident in Fig. 2C and D, since the step lengths used in producing the frequency distributions were different. The comparison might have been easier if the distributions had been normalised. On the basis of the present results, it is quite difficult to say which one of the two parameters is more useful. The calculation of elongation is, however, easier, which supports the use of this parameter.

TABLE 2

Analysis of variance and Pearson correlation

	G1	G3	S1	S2	S3
Circularity					
10%	–	(+) [a]	(+) [a]	(+) [a]	(+) [a]
50%	–	(+) [a]	–	(+) [b]	(+) [a]
90%	–	(+) [a]	–	(+) [a]	(+) [a]
Roundness					
10%	(+) [b]	(+) [a]	(+) [a]	(+) [a]	(+) [a]
50%	–	(+) [a]	[c]	(+) [a]	(+) [a]
90%	–	(+) [a]	–	(+) [a]	(+) [a]
Elongation					
10%	–	(–) [a]	–	(–) [b]	(–) [a]
50%	–	(–) [a]	(–) [c]	(–) [b]	(–) [a]
90%	[b]	(–) [a]	(–) [a]	(–) [a]	(–) [a]
Modelx					
10%	–	(–) [a]	–	(–) [a]	(–) [a]
50%	–	(–) [a]	(–) [c]	(–) [a]	(–) [a]
90%	–	(–) [a]	(–) [a]	(–) [a]	(–) [a]

The effect of variables of the granulator – amount of water (G1), and size of the granule outlet (G3) – and the effect of the variables of the spheroniser – load (S1), residence time (S2) and speed of the friction plate (S3) – on the shape distribution characteristics of pellets are indicated.

[a] $p < 0.001$, [b] $p < 0.01$, [c] $p < 0.05$. –, no effect; (+), positive correlation; (–), negative correlation.

The widths of elongation distributions of batches A and F were 1.10 and 0.23, and the widths of modelx 0.65 and 0.12, respectively.

Effect of process variables on the shape of pellets

On the basis of preliminary analysis of variance studies, the speed of powder addition (G2) had no statistically significant effect on the shape and shape distribution characteristics of pellets. Hence, in final ANOVA and Pearson correlation studies values from 32 batches and two control batches were used.

The amount of water used as a granulation liquid (G1) affected the shape parameters only slightly (Table 2). Previously, the amount of granulation liquid had been found to have a pronounced effect on the sphericity of pellets – with a greater amount of water pellets were more spherical (Uvdal, 1986; Lövgren and Lundberg, 1989). The differences in results may due to the formulations used and consequently the plastic properties of the wet mass – most probably the plastic mouldability of wet masses used was not sensitive to the 3% difference in water content.

The most important process variables affecting the shape of pellets were the size of the granule outlet in the granulator (G3), the residence time (S2) and the speed of the friction plate (S3). With higher process variable levels the sphericity (circularity and roundness) increased and logically, the oblongation (elongation, modelx) decreased. According to the present and a preceding study (Hellén et al., 1993b), the formulation used containing mainly mannitol tolerates only light compaction during granulation and extrusion, but needs high energy input during spheronisation in order to produce spherical particles.

The prominent effect of speed of the friction plate can clearly be seen in Fig. 3A and B, where uneven batch numbers represent lower, and even batch numbers higher speed of the friction plate. Whenever a higher speed (900 rpm) was used, the circularity and roundness values were higher (Fig. 3A), and oblongation parameters systematically lower (Fig. 3B).

The load in the spheroniser (S1) affected the 10% fractiles of sphericity parameters and 90% fractiles of oblongation parameters significantly – with higher load the sphericity of less round and most elongated pellets increases. This evidently means that with higher load the shape distributions become narrower and pellet batches more homogeneous.

The shape and shape distributions of pellets were found to be very sensitive especially to spheroniser variables. The acceptable pellet batches with high roundness value, narrow distribution and good reproducibility were produced

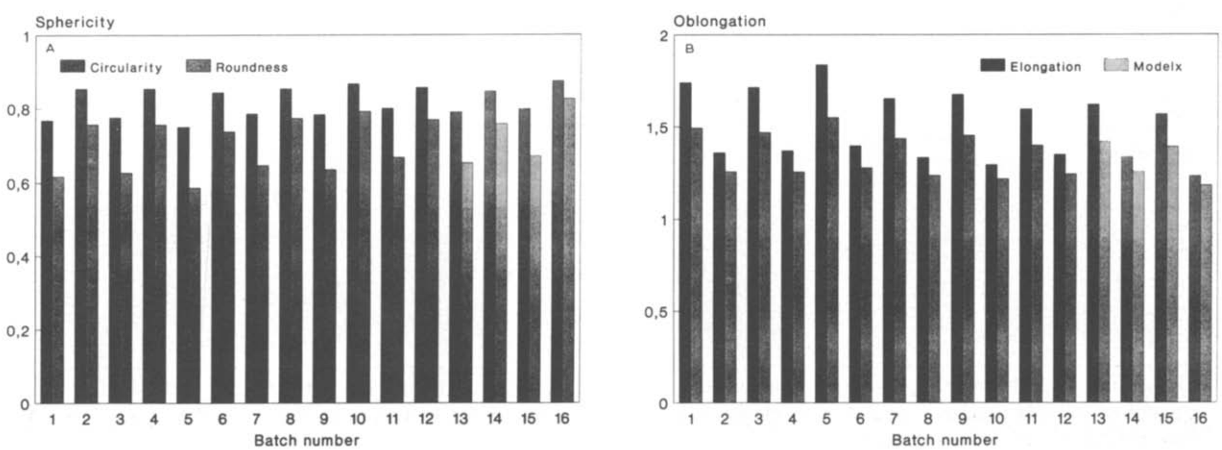

Fig. 3. (A) Circularity and roundness, (B) elongation and modelx median values of pellet batches 1–16.

using larger granule outlet, higher load, longer residence time and faster speed of the friction plate.

In future, further evaluations for the characterisation of wet mass properties will be performed in order to elucidate not only the process but also the material – the interactions between the formulation and the process are strong (Newton, 1990). Because of the prominent effect of the spheronisation stage on the physical properties of pellets, the changes in size and shape of pellets during spheronisation will be evaluated.

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