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A Shape Factor to Characterize The Quality of Spheroids

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Abstract—A shape factor e_R has been devised to describe how the form of spherical particles approaches that of a true spheroid, based on a two-dimensional image analysis. Both the deviation of shape from a circle towards an ellipse and surface irregularities influence the value of e_R. Using a set of model figures such as squares, triangles, diamonds and stars, it could be shown that e_R clearly differentiates between different polygonally symmetric figures, even in the case where common shape descriptors such as the aspect ratio provide equal values. The value of e_R is 1·0 in the case of a perfect spheroid, while ellipticity and surface roughness lead to a significant change in the value.

The number of multiple-dosage forms of oral, controlled-release products has increased over the last few years. Multiple doses consist of small spherical agglomerates, which provide many advantages in manufacture and in in-vivo application. Such in-vivo aspects include the reduction of the risk of a dose dumping (Sucker et al 1991), and the liquid-like behaviour during stomach emptying (Sugito et al 1990).

Generally, part of the manufacturing process includes a film coating procedure, although matrix systems can be formulated. The use of different coating materials allows targeted drug delivery, for example in the small intestine (Watanabe et al 1990) or in the colon (Milojevic et al 1993). The spherical shape provides ideal conditions for a uniform application of the film, if the surface of the particles is relatively smooth. Hence, not only the roundness of the particles but also their surface texture should be maintained in given limits to guarantee a reproducible manufacture of the dosage form. There are several methods of preparing multiple units, including extrusion/spheronization (Reynolds 1970), centrifugal granulation (Niskanen et al 1990) and melt granulation (Schäfer et al 1992).

For an industrial application, the method of describing the geometric shape and surface texture of particles must be sensitive enough to quantify the changes in either characteristic during the manufacturing process (Chapman et al 1988) preferably giving one number only. The most common number used for this purpose is the aspect ratio, i.e. the ratio between length and breadth of the particle (Beddow & Meloy 1980). However, a circle, square or other polygonally symmetric shape will all have an aspect ratio of 1·0, because in these examples length and breadth are equal. Other authors provided two-dimensional descriptive techniques (Wells 1988) or more or less mathematically complicated numbers based on measurements of the dimensions of the particles (Profitt 1982; Wang 1987; Nikolakakis & Pilpel 1988; Chapman et al 1988). The numbers suggested by Profitt do not provide a better quantification than the aspect ratio (Chapman et al 1988). The equations proposed by Wang (1987) can be used to simulate the shape and texture of polygonally symmetric particles. The inverse problem however, the evaluation of the constants of his equations from a particle, needs special computerized video techniques and fitting routines. The one-plane critical stability proposed by Chapman et al (1988) differentiates small changes in roundness, but even here a special computer system with a licensed routine are needed, and each pellet has to be measured individually.

Shape and surface texture distributions can be characterized using fractal geometry (Mandelbrot 1983). The distribution of the geometric shapes and surface irregularities of particles (Farin & Avnir 1992) and soil granules (Tyler & Wheatcraft 1992) could be related to their application properties. However, for fractals there is no exact number applicable for distinguishing between spherical, polygonal or unorganized particles.

Hence, there is still a need to provide a readily accessible and discerning description of roundness. The aim of the present work was to develop a shape factor that considers both the geometrical shape and the surface texture of spherical agglomerates such as spheroids, pellets and granules.

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Theory

The linear eccentricity of an ellipse is given by:

$$e = \sqrt{l^2 - b^2} \tag{1}$$

where l = length of the ellipse and b = breadth of the ellipse (largest distance perpendicular to the length axis).

For both a circle and a square (l = b) e = 0. For elliptical figures the value of e can take on any positive value and depends on the absolute values of l and b. Hence, a normalized value was developed by dividing the term $(l^2 - b^2)$ by l.

$$e_n = \sqrt{1 - \left(\frac{b}{l}\right)^2} \tag{2}$$

For a circle, $e_n = 0$ and for other shapes e_n can be up to 1.

The perimeter of a circle can be calculated from:

$$P_c = 2 \cdot \pi \cdot r \tag{3}$$

where r = radius of the circle.

The calculated perimeter, P_c, and the measured perimeter,

P_m, are equal if there is no irregularity of the surface of the circle. A surface roughness, however, leads to a value of P_m that is greater than the theoretical value. On the other hand, flat edges decrease the perimeter measured. Hence, the equation:

$$P_R = \frac{2 \cdot \pi \cdot r}{P_m} \quad (4)$$

is 1·0, if no surface roughness is present. For a square, the value of P_R is about 0·85.

Combining equations 2 and 4, a shape factor, which weighs both the deviation from the circularity and the surface roughness, can be used to evaluate the roundness of spherical particles:

$$e_R = \frac{2 \cdot \pi \cdot r}{P_m} - \sqrt{1 - \left(\frac{b}{l}\right)^2} \quad (5)$$

Theoretically, only a circle can have an e_R value of 1·0. For all other figures, the value is smaller than 1·0 and can be negative for very elongated or rough particles.

Having a noncircular figure, the radius of an equivalent circle must be determined, if equation 5 is to be used. Image analysis offers the possibility of finding the centre of gravity of any figure; distance measurements can be made from the centre of gravity to the perimeter in different directions. If an angle of 1° between every distance measurement is used, a mean radius can be calculated describing an equivalent circle:

$$r_e = \frac{\Sigma d_\alpha}{n} \quad (6)$$

where d_α = distance between the centre of gravity and the perimeter at an angle α and n = number of measurements (e.g. n = 360, if $\alpha = 1°$).

Equation 5 can be modified to provide a shape factor for spherical or elongated particles with or without surface roughness by substitution of the value r by r_e:

$$e_R = \frac{2 \cdot \pi \cdot r_e}{P_m} \sqrt{1 - \left(\frac{b}{l}\right)^2} \quad (7)$$

Experimental

Measurements were carried out using a Seescan Image Analyser (Seescan, Cambridge/UK), completed with a black and white camera (CCD-4 miniature video camera module, Rengo Co. Ltd, Toyohashi, Japan) connected to a zoom lens (18–108/2·5, Olympus, Hamburg, Germany), and the one-plane critical stability system described by Chapman et al (1988).

Results and Discussion

Shape of model figures

A set of model figures, which are not circular, was compared with circles to test whether the shape factor e_R is able to differentiate between spherical and irregular particles. The figures were drawn using Letraset shapes, and different sizes were used. Table 1 describes the figures, their dimensions and the values observed for e_R in comparison with the one-plane critical stability (OPCS) and the aspect ratio (AR). Even the circles are not completely circular. The image analyser was able to detect very small deviations from the ideal shape. Nevertheless, the e_R values from the circles are the only values above 0·9. The squares and the circles have similar values of AR, but the e_R for the squares is about 0·1 less than those for the circles. Figures such as triangles, diamonds or rectangles provide smaller e_R values than circles. The two flower shapes, which are described as polygonally symmetric figures by Wang (1987), show AR values near 1, and they are also characterized by low e_R values. The OPCS can also differentiate between the model figures, but the method is very tedious and time consuming. Hence, for the set of model shapes given in Table 1, the e_R proved to be able to differentiate between spherical and irregular figures and appears to be the most powerful of the three methods chosen.

Table 1. Comparison of different shape factors using model figures.

Figure	Dimensions (mm)	AR	e_R	OPCS
Circle	10 × 10	1·002	0·937	
	7·5 × 7·5	1·001	0·952	
	5 × 5	1·001	0·942	10·1
	3 × 3	1·002	0·926	
Square	10 × 10	1·001	0·854	
	7·5 × 7·5	1·004	0·850	
	5 × 5	1·015	0·850	41·5
	3 × 3	1·018	0·832	
Triangle (equilateral)	10 × 10	1·151	0·231	
	7·5 × 7·5	1·141	0·246	
	5 × 5	1·143	0·243	62·8
	3 × 3	1·134	0·280	
Diamond	10 × 12·5	1·258	0·221	
	7·5 × 9·5	1·252	0·248	
	6 × 5	1·269	0·198	52·5
	4 × 3	1·239	0·247	
Rectangle	14 × 10	1·096	0·426	60·8
	7·5 × 18	1·469	−0·001	69·4
	5 × 12	1·461	0·002	66·9
	3 × 9·5	2·839	−0·392	80·2
Flower (10 petals)	12 × 12	1·065	0·382	55·9
Flower (4 petals)	10 × 10	1·028	0·628	49·2
Star (6 points)	12 × 12	1·154	0·144	64·4
Star (8 points)	17 × 17	1·000	0·617	58·5

A set of related elliptical figures was generated using a computer, and the shape factor e_R and the values of AR were calculated. The following equations were used:

$$\frac{x^2}{a^2} + \frac{y^2}{b^2} = 1 \quad (8)$$

where a = longest distance between mean point and perimeter, b = shortest distance between mean point and perimeter and x,y = co-ordinates of a point at the perimeter.

In a two dimensional co-ordinate system, for a given x_i, the corresponding perimeter co-ordinate y_i can be calculated from:

$$y_i = \sqrt{\left(1 - \frac{x_i^2}{a^2}\right) \cdot b^2} \quad (9)$$

The distance between the mean point of the ellipse ($x_m = y_m = 0$) and any point $x_i y_i$ at the perimeter, c_i is defined by:

$$c_i = \sqrt{x_i^2 + y_i^2} \tag{10}$$

The distance between two points x_1y_1 and x_2y_2 at the perimeter can be estimated as follows:

$$d = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2} \tag{11}$$

For the computer simulation, the longest distance between the mean point and the perimeter was fixed to a value of $a = 4{\cdot}00$, and b was varied between 4·00 (circle) and 1·00. Table 2 summarizes the simulation results. If the circular figures, which appear to be round to the human eye (compare Table 1), were regarded as a comparison, an ellipse with an AR value of 1·02 or an e_R value of 0·94 may be called circular. Hence, looking at the values of AR, an ellipse with an a/b-ratio of 4·00/3·92 will be regarded as a circle. Comparing the e_R values, however, only the first value simulated, which is a circle ($a = b = 4{\cdot}00$), will be accepted. Hence, the shape factor e_R is far more sensitive to deviations from the circle than the AR. Because a square has an e_R of about 0·85 (compare Table 1), the limiting value for a circular two-dimensional shape to be accepted should in practice be 0·9.

The influence of surface roughness on e_R was simulated considering a circle that has a radius of 4 units. The roughness was generated by computing r_e (eqn 6) with $n = 360$, and both 180 of the single radii and 36 radii only were "shortened" (compare Table 3). The perimeter of the rough particle was estimated using:

$$c = \sqrt{(4 - r_s)^2 + \left(\frac{P_c}{360°}\right)^2} \tag{12}$$

where r_s = shorter radius, P_c = perimeter of the circle and c = distance between two neighbouring points at the surface.

It will be assumed that these shorter radii are distributed equally over the whole circle. The shape factor does not react to a rough surface with the same degree of sensitivity as to deviations from an ellipse, but a difference between the calculated and the measured perimeter of 0·6% leads to an initial decrease in e_R. A certain degree of ellipticity also causes a deviation between the perimeters, and therefore the shape factor decreases more rapidly.

Table 2. Computer simulation of shape factors of related elliptic figures with a longest distance between mean point (b) and perimeter of $a = 4{\cdot}00$.

b	AR	r_e	e_R
4·00	1·000	2·000	1·000
3·99	1·002	1·997	0·928
3·98	1·005	1·993	0·899
3·97	1·008	1·990	0·876
3·96	1·010	1·987	0·857
3·95	1·013	1·983	0·840
3·94	1·015	1·980	0·824
3·93	1·018	1·977	0·810
3·92	1·020	1·973	0·797
3·91	1·023	1·970	0·785
3·90	1·026	1·967	0·773
3·80	1·053	1·934	0·679
3·70	1·081	1·901	0·607
3·60	1·111	1·868	0·546
3·50	1·143	1·836	0·493
3·40	1·176	1·803	0·446
3·00	1·333	1·676	0·291
2·00	2·000	1·380	0·029
1·00	4·000	1·133	−0·138

r_e, mean radius.

Table 3. Computer simulation of the influence of surface roughness on the value of the shape factor e_R.

Set	s_r	r_e	P_m	e_R
1	3·99	3·995	25·3892	0·989
	3·98	3·990	26·1437	0·959
	3·97	3·985	27·3549	0·915
	3·96	3·980	28·9657	0·863
	3·95	3·975	30·9136	0·808
2	3·99	3·999	25·2353	0·996
	3·98	3·998	25·5371	0·984
	3·97	3·997	26·0216	0·965
	3·96	3·996	26·6659	0·942
	3·95	3·995	27·4451	0·915
	3·93	3·993	29·3159	0·856
	3·90	3·990	32·6416	0·768

Number of radii measured: 360; initial radius 4 units. Set 1: every 2nd radius shortened = 180 radii. Set 2: every 5th radius shortened = 36 radii. s_r, length of the shorter radius; r_e, mean radius of the circle, calculated (eqn 6); P_m, perimeter of the rough surface.

Practical granules

Two sets of spherical particles, which were prepared by extrusion/spheronization, were studied applying both the AR and the e_R concept. For comparison, the OPCS values are also listed. Eighty spheres of either sample were measured. The distributions of the parameters measured will be described by the median value, M, the mean deviation from the median, υ_M, and the variability coefficient v:

	Sample			%
e_R	1	$M = 0{\cdot}568$	$\upsilon_M = 0{\cdot}081$	$v = 14{\cdot}3$
	2	$M = 0{\cdot}416$	$\upsilon_M = 0{\cdot}115$	$v = 27{\cdot}6$
AR	1	$M = 1{\cdot}076$	$\upsilon_M = 0{\cdot}041$	$v = 3{\cdot}8$
	2	$M = 1{\cdot}138$	$\upsilon_M = 0{\cdot}080$	$v = 7{\cdot}0$
OPCS	1	16·1°		
	2	22·4°		

The samples cannot be regarded as spherical particles. They appear spherical, but they show surface irregularities and the tendency to be elliptical. The e_R values of either sample show a normal distribution. Hence, a test of significant difference in the mean values was carried out ($x_1 = 0{\cdot}555$; $x_2 = 0{\cdot}433$; $s_1 = 0{\cdot}113$; $s_2 = 0{\cdot}147$; $F = 1{\cdot}692$; $t = 2{\cdot}730$; $f = 158$). The samples are significantly different in shape ($P < 0{\cdot}05$). The AR values do not show normal distribution. The frequency distribution histograms show a curtosis to the left hand side. The variability coefficients of e_R are clearly higher than those of AR. This also reflects the sensitivity of e_R to small differences in shape in comparison with the AR. The low values of e_R tend to show a considerable departure from the ideal value of 0·9.

The spheres are projected as two-dimensional figures using the image analyser, and diffuse light reflection at the surface of the spheroids can cause small shadows, which produce a small apparent ellipticity in the image. To assess how much the image of a spheroid will be deformed, ball-bearings of the size of the spheres tested (Skefko Co. Ltd, Luton, UK) were analysed. The results ($e_R = 0{\cdot}766 \pm 0{\cdot}028$; $n = 10$) clearly show that even an ideal spheroid will not provide an $e_R = 1{\cdot}000$. One possible reason is, being a three dimensional image, the distance between the upper surface of the sphere and the camera is less than between the maximum perimeter and the camera. There is also diffused light reflection which alters the shape. The image analyser, therefore, perceives the maximum perimeter at a lower grey level and has some difficulty in identifying its true dimension. This results in an irregular definition of the perimeter, which creates an apparent surface roughness of up to 3% and an increased AR.

To provide a value for the shape factor, which may be used as a standard with which spherical granules may be compared statistically, a value of $e_R = 0{\cdot}75$ has been chosen. This is a practical value, which is obtained when good quality ball-bearings are measured (see above). Using this limiting value, a t-test was carried out to check whether the samples tested can be regarded as spherical agglomerates or not. The test values (sample 1: $t = 15{\cdot}46$; sample 2: $t = 19{\cdot}27$; $f = 79$; $P < 0{\cdot}05$) confirm, however, that they are irregular in shape.

Conclusion

The shape factor e_R introduced in this paper is able to detect small deviations from circularity and differentiates between more or less elliptical figures. Furthermore, its value for a circle is different from other polygonally symmetric figures such as a square or a flower. Hence, it can be regarded as more powerful than commonly-used parameters such as the aspect ratio to describe spherical particles.

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