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The evolution of pellet size and shape during spheronisation of an extruded microcrystalline cellulose paste

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ABSTRACT

The process by which cylindrical rods of soft solid paste extrudate are converted into round pellets on a spheroniser (Marumeriser™) plate was studied by interrupting spheronisation tests and measuring the size and shape of the pellets. Batches of 20 identical rods (20 mm long, 3 mm diameter) generated by ram extrusion of 47 wt% microcrystalline cellulose/water paste were spheronised at rotational speeds, ω, between 1200 rpm and 1800 rpm on a laboratory spheroniser. The time to complete spheronisation was found to scale with $\omega^{-3.6}$, which was close to the ω^{-3}dependency predicted by a simple collision model. Breakage occupied the first 10% of the process duration: rounding off was the rate-determining step. The evolution of pellet shape was classified into five stages, the duration of which was found to scale with spheronisation time. Pellet shape, quantified by aspect ratio, circularity, shape and angularity factors presented by Sukumaran and Ashmawy (2001), showed similar behaviour for all ω studied. A phenomenological model is proposed which identifies different routes for small and large rod breakage products.

Keywords: Breakage; Extrusion–spheronisation; Microcrystalline cellulose; Rounding; Shape; Pellet; Granulation

1. Introduction

Extrusion–spheronisation (E–S) is widely used in the pharmaceutical and other industrial sectors for manufacturing pellets with high sphericity and density compared to other granulation methods (Haring et al., 2008). E–S is a two-stage process (Wilson and Rough, 2007): first, the particulate solids are combined with a liquid (the binder) to yield a dense suspension or paste which is extruded through dies or screens to give cylindrical extrudates; these extrudates are then spheronised (or *marumerised*) on a rotating friction plate to produce pellets. The term pellet is used here to differentiate the granule from the constituent particles.

E–S requires the material to exhibit plastic (or viscoplastic) behaviour so that the products (extrudates and pellets) retain their shape in the absence of deforming stresses or collisions. The stresses generated during extrusion give rise to extrudates with high density, which break down on the friction plate and are rounded by plastic collisions between pellets, and between the pellets and the wall. The collisions can also cause attrition, generating fines, which can attach to larger pellets (labelled 'mass transfer' by Koester et al., 2012). Several physical pathways are therefore involved in E–S, which make identification of suitable formulations for successful E–S challenging, as outlined by the reviews by Vervaet et al. (1995) and Wilson and Rough (2007). In particular, not only must the formulation be able to exhibit plastic behaviour for extrusion but it must also be able to be broken down and rounded off during spheronisation. The inclusion of microcrystalline cellulose (MCC) has been found to provide this behaviour and MCC is therefore widely used as an E–S aid (the 'gold standard' according to Koester and Thommes, 2013). Dukic-Ott et al. (2009) outlined some of the challenges involved in pharmaceutical pelletisation without using MCC as the excipient.

Formulation development can be improved by two different approaches. One is to use optimisation techniques to

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Nomenclature

Roman

A	Projected area (m^2)
AF	Angularity factor (–)
AR	Aspect ratio (–)
b	Minor axis length (m)
C	Circularity (–)
D	Die diameter (m)
E_d	Deformation work per collision (J)
l	Major axis length (m)
m	Mass of pellet (kg)
n	Number of segments (–)
N_c	Number of collisions (–)
N_p	Number of pellets (–)
P	Perimeter (m)
R	Friction plate radius (m)
R^2	Correlation coefficient (–)
SF	Shape factor (–)
t	Time (s)
t_{end}	Time to complete spheronisation (s)
t_s	Time at which test is stopped (s)
t^*	Dimensionless time, $t^* = t_s/t_{end}$ (–)
V	Velocity of friction plate rim ($m\,s^{-1}$)
W	Plastic work per unit mass ($J\,kg^{-1}$)

Greek

α	Distortion angle, Fig. 3 (–)
β	Internal angle, Fig. 3 (–)
ϕ	Shape analysis sampling interval, Fig. 3 (–)
ω	Spheroniser rotational speed (s^{-1})

maximise the benefit of experimental trials, such as the response surface methodology reported by Desire et al. (2013). The second is to elucidate the physical mechanisms involved in E–S so that quantitative physical models can be constructed. These can then guide the interpretation of experimental data and, in due course, yield mechanistic tools which can be used to identify formulations *in silico*. The latter approach has been applied successfully in the fields of low- and high-shear granulation (see Salman et al., 2007; Vonk et al., 1997). This paper presents a short study of the fundamental steps involved in the spheronisation of MCC–water paste extrudates, and illustrates both the complexity of the process and the steps that need to be investigated both independently and in parallel.

Conine and Hadley (1970) proposed that the basic criterion for successful spheronisation is that the extrudate must be able to break up into sections that are plastic enough to be rounded by the frictional forces on the rotating plate and collisions with pellets and walls. Fig. 1 summarises the three phenomenological models for spheronisation in the literature.

Model A

Rowe (1985) reported that the cylindrical extrudates break into shorter lengths which collide with each other, the friction plate and the walls. The rods undergo plastic deformation which cause them to become rounded cylinders: these are subsequently rounded to a dumb-bell, then to an ellipsoid or egg-shape and finally a sphere.

Model B

Baert et al. (1993) suggested that rods are rounded by collisions with the walls and other pellets and become twisted,

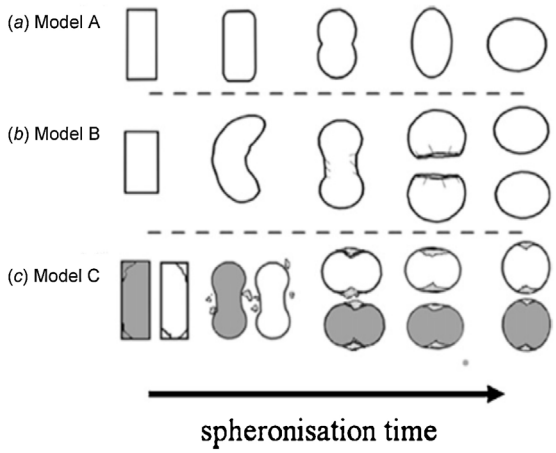

Fig. 1 – Spheronisation mechanisms according to (a) Rowe (1985); (b) Baert et al. (1993); (c) combined deformation and agglomeration mechanism (Liew et al., 2007; Koester et al., 2012).

eventually breaking into sub-pellets with rounded and fractured sides. The latter faces are folded together by the rotating and frictional forces on the friction plate to form the near-spherical pellet. This folding action was claimed to explain why some pellets contain a cavity.

Model C

Liew et al. (2007) studied the effect of extrusion on E–S and observed in their spheronisation tests that pellets pass through the dumb-bell stage and become spherical by agglomeration of fines in the mid-plane or 'waist' region of the pellet. Koester et al. (2012) also advocated this model, in which attrition generates fines which subsequently re-attach to larger pellets in an agglomeration step. The tendency to form fines is determined by the friability of the material and the operating conditions.

All three models emphasise the role played by collisions between pellets and between pellets and the spheroniser surfaces. Measurement of the distribution of pellet positions and pellet velocities has become accessible using modern instrumentation techniques. Bouffard et al. (2012, 2013) have shown that pellet trajectories can be tracked and modelled in pan granulation systems, which are closely related to pharmaceutical spheronisers. Koester and Thommes (2013) used particle image velocimetry (PIV) techniques to measure pellet velocities and flow patterns in a spheroniser. They reported that the pellet velocities were around one tenth that of the plate rim speed, and depended on the liquid content (which determines the cohesion between particulate material in the bed) and loading. This information can be combined with simulations of pellet breakage and plastic deformation (such as those reported by Sinka, 2011) to construct quantitative physical models.

Information about factors determining the key steps in spheronisation, *i.e.* whether Model A, B or C applies, is needed to link pellet scale processes to bulk behaviour. To this end, this paper reports a study of the evolution of pellet size and shape for a greatly simplified model system containing a small number of pellets. Features can be identified at the local level in a deterministic fashion rather than being inferred by analysis of data sets involving a large number of pellets. Tests were conducted with a 47 wt% MCC/water paste which has

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