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Spheronisation of a basket screen-extruded paste using screens of different hole diameters

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ABSTRACT

In order to gain a better understanding of wiping mode screen extrusion-spheronisation process, a 45 wt% MCC/water paste was extruded using a basket screen extruder and the extrudate size and shape evolution during spheronisation tests were investigated in this study. Following the regular formulation tests, 30 g of extrudates with random lengths were employed as a starting charge for each spheronisation test. Two screens with 1 and 2 mm diameter holes were used to generate extrudates of the two diameters.

It was found that the mathematical relationship between time to complete spheronisation (t_{end}) and spheroniser plate rotational speeds (ω) varied with extrudate diameters. For the 1 mm diameter extrudates, t_{end} scaled with $\omega^{-3.8}$, which was close to that predicted by a simple collision model, whereas the product of t_{end} and ω was relatively constant for the 2 mm extrudates. Projected images and SEM images of the dry pellets showed that the shape of 1 mm diameter material during spheronisation went through a dumb-bell stage, and the dumb-bells folded over together to form pellets. In comparison, there were few dumb-bells observed during spheronisation of 2 mm extrudates, and agglomeration was the dominant scenario by which fines attached to big segments to form ellipses and to be rounded into spheres. In the case of the 2 mm extrudates, the aspect ratio was changed mainly with the total number of rotations, and the trend showed little variation between different spheronisation speeds. Based on the observation, it was able to propose a phenomenological model to illustrate pellet shape evolution as well as a semi-empirical mathematical relationship to demonstrate the correlation between processing parameters at an optimal condition for each case. The former emphasised the differences in the shape change route of extrudate with different diameters. The later provided a quantitative guide for optimisation of a spheronisation process. The results suggested that the strain experienced by the paste during extrusion has played an important role in extrudate breakage at the early stage of spheronisation. The size of extrudate segments, after breakage, then determined their spheronisation behaviour during following processing.

1. Introduction

Pellets produced *via* extrusion-spheronisation(E-S) route show an almost spherical shape, a relatively uniform size, smooth surface, *etc.*, which could benefit further processing steps, such as coating and tableting, to be carried out with great ease. In particular, the pharmaceutical pellets generated by E-S have good flowability and could achieve high drug loading and controlled drug release [8,13,31]. E-S has been described by Wilson and Rough [31] as four steps, namely combination, extrusion, spheronisation and drying and finishing. Combination is a mixing step during which solid powders (including active pharmaceutical ingredient, excipient) are combined with a liquid binder to generate a homogeneous wet mass or paste. The paste is then compacted in an extruder and forced to flow through a single-holed die or a screen to form long cylindrical extrudates. They are subsequently loaded into a spheroniser to be cut, granulated and shaped into spheres. The spheroniser must be fitted with a grooved surface plate at the bottom of the spheroniser chamber in order to increase the friction, which promotes cutting and shaping when the plate rotates. In industries, both the 1 and 2 mm extrudates are commonly produced for spheronisation use since they are both able to generate dry pellets within a suitable size range (0.5–1.5 mm diameter) for tableting and for filling into capsules [14].

Optimisation of E-S has to find an optimal relationship between equipments and operation conditions to extrude and spheronise a particular formulation [31]. It could be achieved by trials, while this approach often costs a long time and wastes big amount of active pharmaceutical ingredients (APIs). Another approach is to establish the physical mechanism which governs the process and then construct physical-mathematical models [29]. These models then could guide the interpretation of experimental data and development of new formulations for E-S.

Many workers have investigated ram and single screw extrusion [4,10–12,23,26,30,32]. Quantitative physical models, such as that proposed by Benbow and Bridgwater [3], are available to characterise paste rheology behaviour during extrusion. A number of literatures report that the extrudate properties could be influenced by the paste

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properties, extruder geometry and mixing and extrusion operation conditions (*e.g.* strain shear rate) [5,33,34]. The above work suggests that differences in extrusion strain could cause variations in extrudate properties, while how these variations would make differences in extrudate spheronisation behaviour has not, to the authors' knowledge, been reported before.

Although there are three phenomenological models reported in the literature to illustrate how the cylinder extrudates become to spheres within a spheroniser, a widely accepted model has yet been established. The models are summarised as following:

(i) Breakage and rounding [25]
Collisions involving cylindrical extrudates create shorter rods which are rounded by plastic deformation and pass through dumb-bell and ellipsoidal shapes before becoming spheres. This is the mechanism also reported by Bryan et al. [6] for spheronisation of ram-extruded pastes.

(ii) Twisting [1]
Baert et al. used a gravity feed-gear extruder to produce extrudates. They propose that extrudate rods become twisted by collisions between the extrudates and spheroniser plate and walls. The twisted segments break into sub-segments with rounded and fractured sides which are then folded together to form spherical pellets.

(iii) Agglomeration [18,20]
Liew et al. used a radial basket extruder to generate 1 mm diameter extrudates. They report that extrudates break into short rods, and attrition of corners and edges generates small fragments, labeled fines, which re-attach to larger pellets in an agglomeration step. Koester and Thommes [18], who used a twin screw extruder, report that short extrudates passed through a dumb-bell shape, and fines tended to attach at the 'waist'. Bryan et al. [5] found that the tendency to form fines was determined by the paste properties: passing the 45 wt% MCC/water paste used in this work through a high shear mixing step gave a noticeably stiffer paste which tended to produce fines during spheronisation.

All of the above models have shown an essential role of collisions in spheronisation. This is later supported by Lau et al. [19] who investigated ram extrusion and spheronisation of a 47 wt% paste. They report that the time to complete spheronisation, t_{end}, appear to scale with $\omega^{-3.6}$, where ω is the plate rotational speed. The relationship given by Lau et al. is close to that given by a simple collision model (see Appendix A.1), $t_{\mathrm{end}} \propto \omega^{-3}$, implying that the plastic deformation during spheronisation requires a certain amount of work. Moreover, Lau et al. suggest that extrudate segments with a length (L) to diameter (D) ratio ≤ 1.5 would form sphere by direct rounding (*i.e.* model (iii)).

Most previous work [1,6,18,19] have investigated pellet size and shape evolution during spheronisation of extrudates obtained after gear, screw or ram extrusion, while in industries extrudates are usually generated by basket screen extrusion which is not only easier to feed but also allows a greater throughput. Although Liew et al. [20] proposed an agglomeration model after investigation of spheronisation behaviour of the basket screen-extruded pastes, their work did not provide a quantitative relationship between processing parameters and they only focused on studying of 1 mm diameter extrudates. Recently, Lau et al. [19] and Bryan et al. [6] investigated the shape evolution of ram-extruded paste during spheronisation, where they employed 20 extrudates with equal length as a starting charge for spheronisation. Although the findings of Lau et al. and Bryan et al. give important information to understand pellet shape evolution, their work is not able to give further insight into bulk behaviour in industrial and normal lab-scale tests where there are much larger amount of extrudates used for spheronisation and the initial length of the extrudates are usually not controlled.

This work investigated spheronisation of extrudates obtained using a basket screen extruder fitted with a screen of 1 or 2 mm diameter holes. A 45 wt% MCC/water paste, which is commonly used for investigation of the mechanism of E-S [6,32–34], was employed here as a model formulation. Spheronisation was performed on 30 g of extrudates whose initial length was not controlled. The objectives of the study are to determine: (*i*) t_{end} at different ω for spheronisation of a bulk of basket screen-extruded pastes with a given diameter; (*ii*) the relationship between t_{end} and ω for each diameter to identify the dominant factor in producing acceptable pellets; (*iii*) the effects of extrudate diameter on extrudate spheronisation behaviour (*i.e.* extrudate breakage and shape evolution route) by investigation of the material mass distribution and shape changes during the early stages of spheronisation. The results provide information for a better understanding of spheronisation of a basket screen-extruded paste and a guidance on optimisation of processing conditions.

2. Material and methods

2.1. Material

Microcrystalline cellulose (MCC, Avicel PH101) powder was obtained from FMC biopolymer™ (FMC Corporation, Philadelphia, USA). The moisture content of the as-received MCC powder was ~3 wt%. MCC is insoluble in water and most organic solvents. Particle sizing analysis was performed using a Beckman Coulter™ LS13320 laser diffraction particle size analyser (Beckman Coulter, Inc., USA), giving the MCC particle size ranges of 1.7–257 μm with a D[3,2] of 49.4 μm. Deionised water was used to prepare the suspension for the above particle sizing analysis and it was also used to prepare pastes.

2.2. Methods

2.2.1. Paste preparation

A 45 wt% MCC/water paste was prepared following a similar procedure to that reported by Zhang et al. [32]. An electronic balance (±0.01 g, PTF-A2000, Hua Zhi Scientific Instrument Co. Ltd., Fu Zhou, China) was used to measure the MCC powder and deionised water. A planetary mixer fitted with a K-shaped beater (Chef Classic KM353, Kenwood Ltd., Shanghai, China) was used to prepare the paste. MCC powder was loaded into the bowl, then deionised water was slowly added by pouring over a period of 1 min while the beater stirred at its minimum speed. Then the mixture was stirred for another 10 min, of which mixing was performed at a dial setting speed of 1, 2, 3 and 4 for 2, 3, 3 and 2 min, respectively. At end of each time period, mixing was paused and pastes built up on the walls were returned to the bowl using a wood spatula. The paste was then sealed into a plastic sample bag and held at room temperature for at least 1 h before extrusion, which allowed the water to equilibrate through the paste. The paste was discarded after 7 h.

2.2.2. Extrusion-spheronisation

Extrusion was performed on the 45 wt% MCC/water paste using a lab-scale basket extruder (ZLB-80, Cheng Hang Xin Rong Hua Manufacturer, Zhang Jia Gang, China). The screens and the blade were manufactured from stainless steel 304. Two screens with 1 and 2 mm diameter holes were used. The inner diameter and the thickness of both screens is 84 and 1 mm, respectively. The percentage of the area occupied by holes on the screen is 19.0% and 24.5% for 1 mm diameter hole screen and 2 mm diameter hole screen, respectively. All the extrusion tests were performed at a blade rotation speed of 52 rpm, generating a shear rate of 226 s^{-1} at a 1 mm nip between the blade and the screen.

A spheroniser (R-120, Chong Qing Li Pu Pharmaceutical Equipment Manufacturer, Co. Ltd., Chong Qing, China) fitted with a 120 mm grooved surface plate was used for spheronisation tests. Both the spheroniser plate and chamber are made from stainless steel 304. The plate has a cross-hatched surface with protuberances of pyramidal