



Abrupt disintegration of highly porous particles in early stage dissolution

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ABSTRACT

Dissolution of highly porous particles is a ubiquitous process in formulation chemistry. Scientific challenges remain unsolved due to the complex of interfacial properties and physical interactions between solid, liquid and gas phases. Two spray-dried powders consisting of sodium sulphate and linear alkylbenzene sulfonate (LAS) were used to investigate the abrupt disintegration mechanism focusing on the residual air in the highly porous particle during wetting stage. Four typical dissolution phenomena were identified through individual particle dissolution experiments using optical microscopy. The images suggest for the first time a link between abrupt disintegration phenomenon and air behaviour. We have examined the hypothesis that, as well as chemical changes occurring during wetting, physical processes can lead to disintegration. Tensile tests of individual particles in both dry and hydrated conditions show significant weakening of the particle strength during hydration. Mathematical simulation shows that fast penetration of water through the open-ended pores compresses entrapped air and increases the internal pressure. Hoop stresses generated by internal pressure are of the same magnitude as breaking forces, suggesting that abrupt disintegration in the early stage of dissolution is driven by air compression.

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1. Introduction

Physical and mechanical properties of spray-dried particles are a result of their porous structure. Controlled release of active ingredients in solid dosage forms is one of the key targets in pharmaceutical and biopharmaceutical industry [1]. Similarly in foods [2,3] and detergents [4], quick dissolution is desired for these porous particles. The dissolution phenomenon of them can be summarised as: i) wetting - water penetrates into the pores due to capillary force; ii) immersion - powder sinks into water; iii) disintegration - solid bridges between primary particles dissolve; and iv) dissolution - soluble primary particles dissolve [5]. Heavy study in orally disintegrating tablet in pharmaceuticals points out that disintegration is one of the effective paths to accelerate the whole dissolution process [6–11]. It could be realised through adding superdisintegrant into the tablets [12–16]. Other approaches include creating a variety of extra channels within the tablet for fast release using 3D printing technology [17].

On the controversy, very few papers have reported the study of disintegration of porous powders [18,19], especially the mechanism. Researchers tried to define disintegration according to their scenarios. From the macroscopic point of view, Forný et al. defined disintegration as solid bridges dissolving resulting in powder breakage, and illustrated

this mechanism schematically in the paper using spray-dried milk powder as research subject [20]. From the molecular point of view, Smrčka et al. defined three mechanisms: (i) *leaching* - the Active Pharmaceutical Ingredient (API) diffuse to solvent; (ii) *surface erosion* - solid bridges dissolve and individual primary particles detach from the granule surface; and (iii) *break-up* - granule breaks into various smaller particles abruptly [19,21]. The reason behind the vague definition is the diverse particle shape, size, surface area, pore structure, composition and strength. All these factors contribute to the complex dissolution process.

The dissolution phenomena of porous powders is related to their physical and chemical properties (e.g., particle size, density, porosity, and chemical composition) and the surrounding liquid (e.g., liquid surface tension, viscosity, density, temperature, and diffusion/convection). Hence, disintegration can be described differently. In this paper, we focus on the disintegration defined by Forný et al. which is similar to the third mechanism of Smrčka et al. In particular, we study the abruptly disintegration of porous particle in its early stage dissolution. This study has been limited in literature due to the existence of bubbles in the surrounding liquid, which affects the accuracy of optical observation and laser detection in bulk particle dissolution. Therefore, it is necessary to investigate through single particle approach using statistic study of individual particle mechanical strength and the force breaking them.

The mechanical strength of particles in both dry and wet powders has been reviewed by a number of researchers, including measurement methods and theoretical considerations [22,23]. However, given the

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inherent heterogeneity of particles, mechanical properties cannot be described by continuum properties. In most cases, the mechanical strength of a porous particle is affected by its tensile strength, yield strength, fracture toughness etc., and can be obtained using different loading conditions for example tensile, shear and compression [23]. Sophisticated analysis regarding the fracture of agglomerated powder mainly concerns the size and shape of primary particles [24,25], moisture in agglomerate [26,27], and the strength of connecting points between primary particles [25,27–29].

The force breaking particles comes from various states. In a compressed tablet, disintegration force comes from the interaction between water and disintegrant [30]. Detailed study shows that disintegration only happens when a certain amount of disintegration force is developed [31] and this force linearly depends on the amount of water absorbed by the tablet [30]. In a flow regime, particles experience numerous forces such as the collisional force between particles, the drag force from the frictional interaction between fluid and particles, and the shear force from viscous liquid moving around particle surface [32]. Among all these, only the shear stress has been related to particle disintegration [33].

The dissolution of a porous particle involves gas, liquid and solid, and capillary action plays a critical role in particle wetting. The generated capillary pressure across the meniscus caused by immiscible fluids (including liquid and gas) has been found to be highly related to pore size, liquid surface tension and pore surface energy [34–40]. And such an pressure can deform the walls of nano- and micro-channels [41,42]. In the present work, the mechanism of abrupt disintegration has been investigated using two spray-dried powders, focusing on the driving force and particle tensile strength. The sample powders were manufactured and provided by our industrial partner aiming at developing future detergent powders in developing countries. The investigated two samples have identical composition with only structural difference (e.g. porosity, pore size distribution, undissolved salt in the void space), so the effect of particle structure on dissolution can be distinguished from their composition. In this paper, particle structure was characterized by microscopic techniques and mercury porosimetry. Disintegration phenomena were identified by observing individual particle dissolving using optical microscopy. Numerical simulation of the particle internal force caused by compressed air during wetting stage was made, and compared to experimental results of the breaking force of both dry and hydrated particles measured by micromanipulation. The relationship between the calculated hoop stress and the measured tensile strength supports the hypothesis that the Young-Laplace pressure from the gas phase is a major factor for the abrupt disintegration of porous powders during dissolution.

2. Experimental methods

2.1. Materials

Two spray-dried powders (Batch code IM-14-000848 and IM-14-000849) supplied by Procter & Gamble were used. Sample 1 was made by mixing 29.1% of 45% linear alkylbenzene sulfonate (LAS) paste (LAS in water), 51.9% of sodium sulphate and 35% of water (including water from LAS paste); this mix was then pumped to spray-dry tower to form agglomerates at 220 °C using co-current hot air. Sample 2 was made by the same procedure but different formulation which was 16.9% of the 45% LAS paste, 30.4% of sodium sulphate and 62% of water (including water from LAS paste). This resulted in an identical composition ratio in the two dry powders but different porosities.

2.2. Particle characterization

Particle surface morphology was analysed using a scanning electron microscope (SEM) equipped with a backscatter detector (Hitachi TM3030, U.S.A) operated at 15 kV in low vacuum mode. Two

magnifications (50 and 200 times) were used. Internal structure was analysed using an X-ray Microtomography (XRT) system (Skyscan 1275, Bruker microCT, Belgium). Particles were scanned at 60 kV and 80 μ A. Scanning was performed by 180° rotation around the vertical axis with a rotation step of 0.2°. Images were reconstructed to provide axial cross-sections of their inner structure and pore size distribution on a single particle. Bulk density and porosity were measured using a mercury porosimeter (Micromeritics Autopore IV, GA) using intrusion pressures from 0.1 psi to 60,000 psi.

2.3. Experimental set up of dissolution test

Particles were first sieved into size ranges, <200, 200–500, 500–800 and 800–1000 μ m. 50 individual particles from each size range were put into water at 20 °C and monitored using the microscope (Leica Microsystem Z16, Germany) for the dissolution test. Dissolution temperature was controlled while the water container (a glass slide with a cavity) sat on a Peltier stage (Linkam Scientific Instruments Ltd. LTS120, United Kingdom). Image sequences were recorded at 5 frames per second and analysed using open source software ImageJ.

2.4. Experimental set up of tensile breaking

The breaking force of a single particle was determined by micromanipulation technique [43]. A glass probe with a diameter of 300 μ m mounted on a force transducer (Aurora Scientific Inc. 400A, 402A, Canada) was glued to one side of a particle by superglue (Loctite®, Ethy 1 2- cyanoacrylate). The transducer was fixed to a fine micromanipulator driven horizontally by a step motor. The other side of the particle was glued to another glass probe fixed on a manual micromanipulator. After the superglue dried, the particle was pulled apart with the glass probe travelling at 2.85 μ m/s and the signal from the transducer was recorded to a computer (process (a) (b) (c) in Fig. 1). 20 individual particles from each size range 200, 500 and 800 μ m, were tested in this set up when particles were dry. In a second approach, shown in Fig. 1 (a) (b) (d) (c), a 0.3 μ L water droplet was pre-loaded on a hydrophobic substrate and moved upwards to contact the particle for 3 s. The micromanipulation method was then used again to measure the breakage force, using same probe travelling speed. A room environment of 35% humidity and 20 °C temperature was presented. Further details of this technique are described elsewhere [43].

3. Results and discussion

3.1. Particle structure characterization

Spray-dried powders normally have hollow or semi hollow structures consisting of shell or film regions with different physical and chemical properties and a large central void space [44]. In Fig. 2, SEM images of powder samples 1 and 2 at lower magnification (Fig. 2 (a) and (c)) show that both two samples have a wide particle size distribution, from tens to hundreds of micrometres. Particles over 200 μ m are often agglomerates of smaller ones; this is a typical size range when spray-dried powders start to agglomerate [44]. Higher magnification (Fig. 2(b) and (d)) reveals that different sized holes appear on particle surfaces, from several micrometres to up to 200 μ m. Small spherical particles (<100 μ m) can be seen attached to the surface of sample 2, whereas significantly fewer attach to sample 1, resulting in different surface roughness.

In Fig. 2(e) and (f), XRT results of bulk particles cross-sections reveal that the particles have a hollow-shell structure (in agreement with literature [44]). In the images, white is solid and black is air. Higher magnifications of sample 1 show that a thin shell of about 10 to 50 μ m thickness wraps around pebble-looking undissolved salt crystals (Na_2SO_4), while in sample 2 a much thicker (about 10 to 100 μ m) shell forms a foam structure with almost no undissolved salts inside.

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