Chemical Engineering Science 125 (2015) 13–19

Contents lists available at ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

Attrition of paracetamol and aspirin under bulk shear deformation

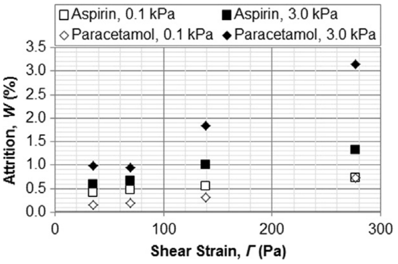
C. Hare*, M. Ghadiri

Institute of Particle Science and Engineering, University of Leeds, Leeds LS2 9JT, UK

HIGHLIGHTS

- Breakage of paracetamol and aspirin established for given stress and strain.
- Empirically determined at low stresses (0.1–3.0 kPa).
- Aspirin breaks more easily at onset of shearing.
- Paracetamol more prone to breakage at increased stress or strain.
- Surprisingly no preferential breakage along cleavage planes.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 25 April 2014
Received in revised form
12 September 2014
Accepted 14 October 2014
Available online 22 October 2014

Keywords:
Attrition
Breakage
Shear deformation
Particle
Chipping
Fragmentation

ABSTRACT

Particles are frequently exposed to shear stresses during manufacturing, which leads to breakage. This is particularly relevant to weak active pharmaceutical ingredients and is prevalent in pharmaceutical and food industries. The attrition of paracetamol and aspirin caused by shear deformation at very low stresses is investigated here. The extent of breakage of these particles is related to the prevailing shear stresses and strains. In contrast to the expected trend, smaller particles exhibited increased breakage rates. At the onset of shearing at low stresses aspirin particles experienced slightly more breakage than the paracetamol, however prolonged shearing resulted in greater breakage of paracetamol. Breakage occurred initially through chipping with some fragmentation, particularly more noticeable for aspirin, with an increase in abrasion after extensive shear strain for paracetamol. Empirical breakage relationships are proposed and when combined with process stresses and strain analyses the extent of breakage occurring in process equipment can be estimated.

1. Introduction

Particle processes invariably inflict unwanted stresses upon particles. These stresses could be caused by compression, impact, fatigue or shearing and can result in damage and breakage of the particles. One of the common causes in the unintentional breakage of particles (attrition) during processing is shear deformation. Shear stresses exist in the transition from stagnant to flowing material within a powder bed, and are prevalent in manufacturing, such as through agitation in a mixer, and in transport and release from storage.

It is highly desirable to produce particles with a specified range of sizes, shapes and surface properties to limit downstream processing problems and ensure the final product satisfies its end-use application. However, attrition causes a deviation from these characteristics, leading to material loss or reduced process efficiency. Dust may be produced by attrition, which can result in substantial triboelectric charge generation. In extreme cases, the dust generated from attrition can lead to an explosive atmosphere. Attrition is a particular problem in the pharmaceutical industry, as many pharmaceutical compounds are relatively weak and therefore prone to breakage. It is therefore of interest to understand the susceptibility of common pharmaceutical materials to attrition.

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* Corresponding author. Tel.: +44 113 343 2407; fax: +44 113 343 2384.
E-mail address: c.l.hare@leeds.ac.uk (C. Hare).

http://dx.doi.org/10.1016/j.ces.2014.10.027
0009-2509/

The stresses and strains present in shear bands formed in powder processes are highly dependent on the orientation of the particle–particle contacts, known as the bed fabric, and the material properties (Antony and Kuhn, 2004). A distribution of material properties is ubiquitous in powders (Salman et al., 1995), and particle rearrangements lead to an ever-changing bed fabric. Therefore, stresses fluctuate significantly throughout a particle bed, and even within a shear band (Liu et al., 1995). Stresses also fluctuate with time (Thornton and Antony, 2000). Due to these complexities in quantifying stress and strain within particle systems, it is difficult to establish a relationship of breakage with stress, strain and strain rate in processing equipment. For this reason, Paramanathan and Bridgwater (1983a, 1983b) developed an attrition shear cell to characterise particle breakage resulting from shear stresses. We use their approach in evaluating the attrition propensity of paracetamol and aspirin.

The attrition shear cell is shown in Fig. 1 and has been made by Ajax Equipment (Bolton, UK). Further details are given by Ghadiri et al. (2000). The strain, Γ, is estimated by the following relationship:

$$\Gamma = \frac{\theta}{360}\frac{\pi D_c}{h} f \tag{1}$$

where, θ, D_c, h and f are the degree of cell rotation, the mean cell diameter, the bed height and the grip factor, respectively. Early work suggested the breakage may be proportional to the work applied to the bed (Bridgwater, 1989) as Neil (1986) found that the internal angle of friction remained unchanged during shearing, thus the shear stress, τ, is proportional to the normal stress. Therefore the work applied to the bed is proportional to $\tau\Gamma$. The two-dimensional Discrete Element simulations of Potapov and Campbell (1997) supported this conclusion of Bridgwater (1989), as did the experimental work of Kenter (1992), in contrast to the experimental work of Neil and Bridgwater (1994). Potapov and Campbell (1997) suggested four possible reasons for their simulations showing anomalous behaviour in comparison to Neil and Bridgwater (1994): (i) the two dimensional nature of the simulation, (ii) the lack of gravity, (iii) the omission of the work required for the initiation of shearing and (iv) due to the properties of the simulated material. In most cases the breakage has been shown not to be proportional to the work applied to the bed. Neil and Bridgwater (1994) measured the attrition of 11 materials over a wide range of stresses and strains and found that the breakage could not be suitably expressed as a function of the input work. Instead, they proposed a new relationship:

$$W = K_N\left[\left(\frac{\sigma}{\sigma_{SCS}}\right)\Gamma^{\varphi}\right]^{\beta} \tag{2}$$

where, K_N is the proportionality constant, σ is the applied normal stress, σ_{SCS} is the material side-crushing strength, φ is the relative influence of strain to stress on attrition and β is the rate exponent. Ghadiri et al. (2000) also showed the above relationship fits better to the breakage of catalyst beads in a shear cell as compared to input work and the earlier model of Ouwerkerk (1991). Moreover they showed that the nature of a power law model implies that a range of values of α and β may all provide a suitably close minimum fitting error, hence not leading to a unique set of values. Due to the complexities of sheared powder beds this is the best model which is currently available, as particle breakage under shear deformation cannot yet be determined by first principles based on knowledge of the mechanical properties of the particles. Consequently, the empirical approach defined above is required to describe the breakage of a given material. Moreover this analysis is extremely useful in determining the extent of breakage arising in process equipment that causes breakage by shear deformation. Neil and Bridgwater (1999) showed that the relationship of attrition to strain (the product $\varphi\beta$ in Eq. (2)) was consistent for given materials in a shear cell, a fluidised bed and a screw pug-mill. Further to this, Hare et al. (2011) showed that the breakage rate determined in a shear cell can be combined with stress and strain rate analysis using the Distinct Element Method (DEM) to successfully predict the attrition in an agitated bed.

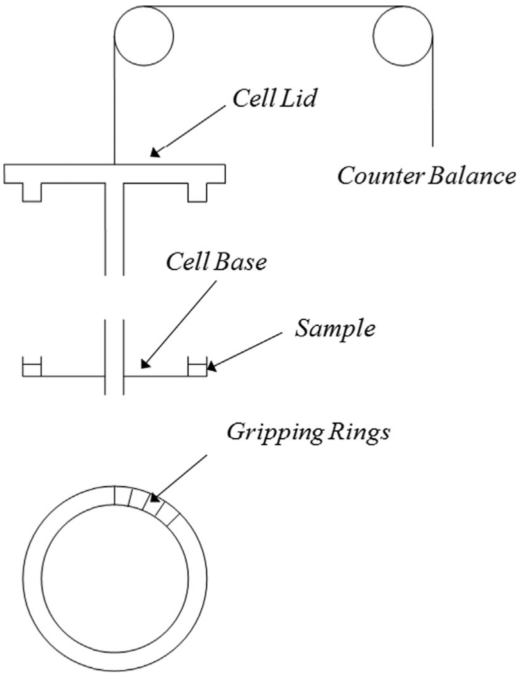

Fig. 1. Attrition shear cell (Hare et al., 2011).

In this work the attrition of paracetamol and aspirin are investigated using an annular attrition shear cell. The interest is to understand breakage of these particles at very low stresses of 0.1–3.0 kPa.

2. Materials and methods

The test methodology has previously been described by Ghadiri et al. (2000). Here we report our measurement and analysis for paracetamol (Form I) and aspirin (supplied by Kraemer & Martin Pharma Handels (Krefeld, Germany), and Weylchem (Mannheim, Germany), respectively). The following sieve cuts: 500–600 µm, 600–710 µm and 710–850 µm for paracetamol, and 355–425 µm, 425–500 µm and 500–600 µm for aspirin were used. Scanning electron micrographs (SEM) of these particles are shown in Fig. 2.

In each experiment the particles were sheared in the shear cell and subsequently sieved to assess breakage. Since the initial size was determined by sieving this method ensured the same shape descriptor was being measured after shearing. Sieving time and amplitude were selected to ensure that negligible attrition occurred due to sieving. The inner and outer diameters of the cell were 120 and 160 mm, respectively. The base and lid of the cell contained radially aligned saw-toothed gripping rings, with a depth of 1 mm, following the gripping criteria set out by Ghadiri et al. (2000). This provided sufficient grip for all size classifications tested. The material was weighed, prior to loading in the cell by pouring through a funnel. The bed was levelled using a T-piece to provide a bed with a relatively smooth surface and a known bed height. The bed height was controlled to be equal to approximately 5.5 times the median particle size (see Table 1), which corresponded to a naturally occurring shear band (Stephens and Bridgwater, 1978). Excess material was removed during the levelling process to achieve the conditions shown.