Influence of flaws and crystal properties on particle fracture in a jet mill

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A B S T R A C T

Jet milling is commonly used for reducing the particle size of active pharmaceutical ingredients. Unfortunately, this process is sometimes difficult to control as pre-existing flaws and mechanical properties affect the particle fracture behaviour in a mill. In this study the effect of pre-existing flaws on mechanical material properties of crystals of a model material, sodium chloride, from different sources have been investigated using optical microscopy, nanoindentation, and powder compaction. Subsequently, these properties have been correlated with particle fracture in a jet mill. The paper shows that particles that have a small average flake size possess the lowest constraint factor (i.e. the constraint factor is defined as the ratio of the hardness and the yield pressure and is an expression of the ductility of the material) whereas particles that have a large average flake size have a high constraint factor and hence behave more ductile. Moreover, the study shows that the rank orders of the mechanical properties are consistent with the rank order of the experimentally determined particle rate of breakage. Materials that have a relatively low hardness show the highest particle rate of breakage. The degree of particle fracture during jet-milling tends to decrease for particles that have a smaller flake density and behave more ductile. The paper shows that pre-existing flaws have an impact on mechanical properties and on particle fracture behaviour in a jet mill. It is concluded that the increase of the particle rate of breakage as a function of particle size is influenced by the number of flaws rather than by flake length.

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1. Introduction

In recent years and particularly in the pharmaceutical industry, product quality criteria have become more and more strict, leading to specifications like a narrower particle size distribution and hence closer control of particle size. Active pharmaceutical ingredients (APIs) used in pharmaceutical product development are rarely ready for use as crystalised drug substance. Frequently, the particle size needs to be reduced in order to meet the specific requirements. For example, the route of administration dictates the particle size distribution, like pulmonal delivery for which typically particle sizes in the range of 1–6 μm are required [1]. Milling operations in pharmaceutical industry are generally limited to two or three types of equipment e.g. jet mills, impact mills or conical cone screen mills where the main criteria of choice is the ability to obtain a certain product quality, in terms of particle size or specific surface area. Unfortunately, size reduction by milling has remained essentially an empirical science [2]. This is not due to either a lack of interest or research conducted since the number of references in the literature dealing with milling is overwhelming mainly as an effect of the needs to maximise production capacity and to minimise energy consumption in the mineral energy [3]. Moreover, fundamental particle breakage studies have attracted a great deal of attention of researchers over the last few decades [3,4]. Despite intensive use and research the detailed mechanism of jet milling is not yet entirely understood [6]. This leads to the situation that the milling conditions have to be determined for each material using pilot-scale trials. This is both material and time consuming [7]. It is believed that both particle deformation and fracture mechanisms play an important role in particle breakage and hence in milling performance. The particle fracture behaviour of a material in general depends on the mechanical properties of the material to be milled, processing conditions like stressing intensity, impact velocity, temperature, and the pre-existing imperfections and flaws in the material [8]. For instance, the fracture strength of particles of identical material and identical size differ because different flaws are present on the particle surface [8], Zügner et al. [6] reported that elastic plastic properties of the materials to be milled are important as these determine the resistance against particle fracture as well as the formation and propagation of cracks. In the theory of milling it is common practice to evaluate the particle fracture behaviour as an entangled effect of pre-existing flaws and cracks as well as mechanical parameters. Moreover, sometimes it is assumed that particle fracture behaviour is governed largely by pre-existing flaws. Currently, to the
Table 1

<table>
<thead>
<tr>
<th>Type</th>
<th>D(&gt;10%) [μm]</th>
<th>D(&gt;50%) [μm]</th>
<th>D(&gt;90%) [μm]</th>
<th>True density [kg/m³]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt 1</td>
<td>182</td>
<td>351</td>
<td>577</td>
<td>2150</td>
</tr>
<tr>
<td>Salt 2</td>
<td>225</td>
<td>391</td>
<td>555</td>
<td>2149</td>
</tr>
<tr>
<td>Salt 3</td>
<td>202</td>
<td>393</td>
<td>686</td>
<td>2149</td>
</tr>
<tr>
<td>Salt 4</td>
<td>201</td>
<td>411</td>
<td>625</td>
<td>2154</td>
</tr>
</tbody>
</table>

knowledge of the authors it is not clear whether either pre-existing flaws or material properties dominate particle fracture. The purpose of this paper is to investigate the effect of pre-existing flaws and mechanical properties on particle fracture in a jet mill in order to improve control of the milling process.

2. Material and methods

2.1. Material

Sodium chloride has been chosen as a model compound. The reason for this choice is that different sources and production methods give different inclusions in the form of vacuoles (that contain brine) and other lattice defects, which offers the possibility of controlled variation of defects in the material. At the same time, the particle size and shape remain largely unchanged. Therefore, sodium chloride is a suitable model compound for this study. Sodium chloride crystals are cubic in shape and were produced by evaporation of pickling brine saturated in natural rock salt. All materials used were produced by Akzo Nobel at different production areas: salt 1 from Stade (Germany), salt 2 from Hengelo (The Netherlands), an intermediate quality salt 3 Mariager (Denmark), and salt 4 from Stade which is chemically the purest salt. Table 1 shows the particle size distribution of sodium chloride and the true density of the four types of sodium chloride investigated.

2.2. Methods

2.2.1. Determination of yield strength

The yield pressure was determined as proposed by Heckel [9]. The porosity-pressure relation of the compounds was investigated using a high speed compression simulator (ESH, Brierley Hill, UK). This compression simulator enables the assessment of compaction behaviour with single tablets. A powder sample of 500 mg was compressed into a cylindrical compact with a diameter of 13 mm. Compression load and compact volume with time were recorded. The average punch speed was 3 mm/s. The compression profile was sinusoidal. It has been shown by Heckel [9] that the porosity (ε) is related to the compression pressure (P) by:

$$-\ln(\varepsilon) = K \cdot P_t + A$$  \hspace{1cm} (1)

The symbol A is a constant which is thought to be a measure of the relative density of the powder bed after particle rearrangement [10].

The linear part of the curve has slope K and this slope is related to the yield strength ($\sigma_y$) by:

$$\sigma_y = \frac{1}{3K}$$  \hspace{1cm} (2)

The yield pressure of a material is approximately equal to 3 times the yield strength [11]. Hence, the reciprocal of K can be regarded as numerically equal to the mean yield pressure:

$$P_y = 3 \cdot \sigma_y = \frac{1}{K}$$  \hspace{1cm} (3)

The true density of sodium chloride was determined with a gas pycnometer (AccyPyc 1330, Micromeritics) using nitrogen as test gas.

2.2.2. Indentation procedure

Reproducible nanoindentation measurements can be performed only on smooth and almost horizontal surfaces. The nanoindentation samples had to be processed in a special way, avoiding use of water which would dissolve the material. The crystals were embedded in epoxy (containing no water). Subsequently, the samples were dry-ground (i.e. using no lubricant) according to the DIN-norm using, consecutively silicon carbide abrasive paper with decreasing coarseness: Grit 800 (~0.5 mm), Grit 1200 (~0.1 mm), Grit 2400, and Grit 4000. After this, a polishing step of 75 s was carried out, using 0–1 μm diamond powder on a Dur-polishing cloth (Struers), using ethanol p.a. as a lubricant. As shown in Fig. 1 the procedure resulted in a polished crystal surface with a typical surface roughness (Ra) smaller than 0.5 μm.

In indentation, a sharp diamond pyramidal tip (an “indenter”) is pressed into the surface of the material, while the force on the tip and the penetration depth of the indenter into the material is measured. From the resulting force–displacement curve, together with subsequent observation of the probed surface, the static mechanical properties can be determined. Load-control nanoindentation tests (Nano Indenter XP, MTS Systems Co., Oak Ridge, TN) were performed on the embedded specimens using a Berkovich diamond indenter. The tests were performed in a vibration isolation cabinet at room temperature and stable humidity to ensure that the influence from thermal drift was minimal. The loading rate was $\frac{\text{d}P}{\text{d}t}/P = 0.075$ s⁻¹, and the maximum indentation depth was 1 μm. After reaching the maximum depth, the force was kept constant for 10 s, after which the unloading took place at $\frac{\text{d}P}{\text{d}t}$ = 0.075 s⁻¹.

From this protocol load-displacement curves were obtained and the Oliver and Pharr method [12] was applied to determine the elastic modulus and the hardness. Using the contact area $A_c$, and the contact stiffness $S$, which is the slope of the initial portion of the final unloading curve, assuming a purely elastic effect, the

Fig. 1. Micrographs of the polished crystals for nanoindentation; (a) optical interferometry plot (Zygo); (b) white light optical micrograph.
Fig. 2. Relation between material properties of sodium chloride particles of different origins.

Table 2: Mean mechanical material properties and constraint factor of sodium chloride particles of different sources (standard deviation in brackets)

<table>
<thead>
<tr>
<th>Material</th>
<th>$H$ (MPa)</th>
<th>$E$ (GPa)</th>
<th>$P_f$ (MPa)</th>
<th>$H/P_y$ (–)</th>
<th>$E/P_y$ (–)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt 1</td>
<td>308 (1.5%)</td>
<td>39.9 (1.4%)</td>
<td>86.8 (5%)</td>
<td>3.5 (6.5%)</td>
<td>459 (6.4%)</td>
</tr>
<tr>
<td>Salt 2</td>
<td>262 (10.3%)</td>
<td>30.8 (4.3%)</td>
<td>100.7 (5%)</td>
<td>2.6 (15.3%)</td>
<td>306 (9.3%)</td>
</tr>
<tr>
<td>Salt 3</td>
<td>266 (7.1%)</td>
<td>30.9 (6.2%)</td>
<td>105.6 (5%)</td>
<td>2.5 (12.1%)</td>
<td>293 (11.2%)</td>
</tr>
<tr>
<td>Salt 4</td>
<td>319 (0.4%)</td>
<td>40.5 (1.1%)</td>
<td>87.2 (5%)</td>
<td>3.6 (5.4%)</td>
<td>465 (6.1%)</td>
</tr>
</tbody>
</table>

Due to the wavelength of visible light and the numerical aperture of the microscope the resolving power is 1 μm. As a consequence the detection of flaws in particles is restricted to flaws larger than 1 μm.

3. Results and discussion

3.1. Mechanical properties of starting materials

The static mechanical properties of crystals have been probed using nanoindentation. The yield pressure ($P_f$) of each type of salt has been determined by making a Heckel plot [9] as described in the materials and method section. Table 2 gives the values determined by nanoindentation and powder compaction. The table also contains two dimensionless numbers which will be discussed later.

It is noted that different sources of sodium chloride salts have different mechanical properties which was not expected a priori. Table 2 shows that salts 1 and 4 can be assigned as salts having a relatively high hardness and high Young’s modulus of elasticity, while, salts 2 and 3 are materials with a relatively low hardness and low Young’s modulus of elasticity. Clearly, the mechanical properties are different.

2.2.3. Determination of particle rate of breakage

The milling experiments were performed in a 100 AFG fluidized bed opposed jet mill (Alpine, Augsburg, Germany). This kind of mill is specifically designed for continuous milling. To perform batch milling experiments the particle feed was closed and the classifier speed was set to the maximum speed (22,000 RPM) to limit the amount of fines leaving the mill chamber. Milling pressure was set at 5 bar which is a normal milling pressure for this type of mill. Experiments were performed by introducing 200 g of powder into the mill and turning on the milling gas for a given time period (20–80 s). For each experiment, the processing conditions were kept the same allowing differentiation between material properties. After milling, the whole powder content of the mill was removed for particle size analysis. Dry dispersion laser diffraction measurements were performed with a Malvern Instruments model Mastersizer S (Malvern, UK). The Fraunhofer model was used for deconvolution of the diffraction pattern.

2.2.4. Determination of flaws

To check for flaws, impurities and crystal defects the particles were investigated with an optical microscope (Jenaval, Zeiss, Jena, Germany). The method has been described in detail elsewhere [13].

Table 3: Flaw density and average flaw size of the different types of sodium chloride particles (particle size 300–425 μm) adapted from [13]

<table>
<thead>
<tr>
<th></th>
<th>Salt 1</th>
<th>Salt 2</th>
<th>Salt 3</th>
<th>Salt 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flaw density [flaws/m²]</td>
<td>$6.05 \times 10^9$</td>
<td>$13.8 \times 10^9$</td>
<td>$8.98 \times 10^9$</td>
<td>$6.81 \times 10^9$</td>
</tr>
<tr>
<td>Average flaw size (μm)</td>
<td>7.3</td>
<td>5.3</td>
<td>5.7</td>
<td>6.8</td>
</tr>
</tbody>
</table>
operational parameters. If these parameters are kept constant, instrumentation of the mill allows adjustment and control of the stressed by impact. As a result particles are reduced in size. The

3.2. Milling experiments

In a fluidized bed opposed jet mill the particles to be ground are stressed by impact. As a result particles are reduced in size. The instrumentation of the mill allows adjustment and control of the operational parameters. If these parameters are kept constant, differences in particle size of the milled material are due to differences in properties of the feed material. The milling behaviour can be quantified by the particle rate of breakage function \( S \), also called selection function or breakage probability \([19,20]\). The rate of breakage function \( S \) is the probability of a particle with a certain size to break per unit time. The experimental particle rate of breakage is determined by means of Kapur’s \([21]\) simplification of the batch grinding equation. The approach of Berthiaux and Dodds \([20]\) has been followed, that states that the particle rate of breakage function can be calculated using Kapur’s approximation of the batch grinding equation using short grinding times. Fig. 3 shows the experimentally determined particle rate of breakage functions of the four types of sodium chloride salts investigated.

Fig. 3 shows that the particle rate of breakage is a function of particle size and this is consistent with theory \([8,22]\). It is commonly accepted that due to the presence of flaws in particles, the particle strength increases with decreasing particle size \([22]\). The low probability of finding a large flaw in a small particle explains the observed increase in the strength of smaller particles. Furthermore, each type of sodium chloride shows a distinct particle rate of fracture. This difference is not explained by the variation in the experimental set-up, since processing conditions were kept the same. Fig. 4 shows the particle rate of breakage \( S \) of the sodium chloride particles of different sources of size 350 µm as a function of their average flaw size \( c \). This figure illustrates that different types of materials show a distinct particle rate of fracture behaviour that correlates with the average flaw size. Linear regression analysis gives the following relationship between the particle rate of breakage \( S \) and average flaw size \( c \):

\[
S = -0.0030(\pm0.0004)c + 0.052(\pm0.003) \quad (8)
\]

The numbers in brackets in Eq. (8) gives the 95% confidence interval.

A similar but inverse correlation can be found when the rate of breakage is plotted as a function of flaw density. Combining the particle rate of breakage data of Fig. 3 with the mechanical properties of Table 2 shows that materials with a relatively high average flaw size are more

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**Fig. 3.** Particle rate of breakage of sodium chloride particles of different origins. Milling pressure was 5 bar. The error bars indicates the 95% confidence interval.

**Fig. 4.** Particle rate of breakage of particles with a size of 350 µm versus the average flaw size of the different sources of sodium chloride particles.

**Fig. 5.** Wing crack propagation in a particle where 2r is the flaw length and 2b is the bridge distance between two flaws (adapted from Wong et al. \([24]\)).
ductile during milling. Moreover, it is observed that sodium chloride particles (salts 2 and 3) that possess the lowest constraint factor and that have a relatively small average flaw size show the highest rate of breakage during milling. In contrast, sodium chloride particles (salts 1 and 4) with the highest constraint factor have a relatively large average flaw size and show the lowest rate of breakage during milling.

The discussion so far indicates that mechanical properties and flaw size or flaw density determine particle breakage behaviour. It is unclear however, whether the impact of flaw size is dominant or that of flaw density because the data are entangled. The next step is an attempt to separate these effects.

3.3. Particle strength of particles containing cracks and flaws

In this section the particle strength is calculated based on the interaction between flaws. Inglis [23] showed that flaws play a dominant role in particle fracture as the local stresses generated at the tips of the flaws are much higher than the loading stress. During stressing of particles wing cracks grow from these flaws near the tips of the initial flaw, where the tensile stress is a maximum, and then propagate at sharp angles from the pre-existing crack direction to become parallel to the direction of axial compression [24]. These cracks propagate and start to interact with neighbouring cracks and this leads to crack coalescence and finally, macroscopic, particle fracture. Nemat-Nasser and Horri [25,26] investigated the mechanism of crack interactions and they showed that flaw length is one of the parameters controlling the failure pattern of specimens.

Fig. 5 shows crack coalescence between two pre-existing flaws of length 2c. To calculate the particle strength of sodium chloride particles as a function of the number of flaws the model of Ashby–Halam [27] was employed. They derived an expression for the stress intensity factor \( K_{IC} \) at the tip of the wing cracks, which nucleates from a pre-existing inclined flaw of length 2c when a particle is stressed (as illustrated in Fig. 5) and when crack interaction and crack coalescence occurs. Reworking their model results in:

\[
\sigma = \frac{K_{IC}}{\sqrt{IC}} \left( \frac{\sin 2\alpha - \mu \cos 2\alpha}{(1 + L)^3} \right) \left( \frac{0.234}{\sqrt{3}} \frac{1}{(1 + L)^3} \right) + \left( 2\epsilon_0 \pi c \right)^{1/3} \]

where \( \sigma \) is the particle strength, \( K_{IC} \) is the critical stress intensity that characterizes the crack resistance (0.5 MPa/m for sodium chloride [28]), \( \psi \) is the angle measured from loading direction to the direction along the shear crack surface (i.e. \( \psi = 90^\circ - \alpha \) in which \( \alpha \) is the flaw angle, i.e. inclination of the flaw), \( L = \ell / c \) the normalized length of the wing cracks (\( \ell \) is the length of the wing crack as shown in Fig. 5 and 2c is the crack length of Table 4), \( \mu \) the friction coefficient on the surface, and, finally, \( \epsilon_0 \) is the initial crack density \( \epsilon_0 = c^2 N_o \), where \( N_o \) is the number of flaws per unit area of Table 3. In this study it has been assumed that the friction coefficient \( \mu \) is 0.6 [24–26] which is a commonly used value. Table 4 lists the values used to calculate the particle strength \( \sigma \) of sodium chloride particles with a particle size of 350 µm.

Since it was not possible in this study to determine the stress intensity factor \( K_{IC} \) experimentally, and since \( K_{IC} \) is a function of the flaw size [29] too, it is not possible to predict the precise particle strength of the four different sources of sodium chloride particles. However, keeping all parameters constant except the average flaw size (\( c \)) and the flaw density \( (N_o) \) it is possible to calculate the influence of these parameters individually on the particle strength. Fig. 6 shows the influence of both the flaw density and the average flaw size on the predicted particle strength of the four different sources of sodium chloride particles using Eq. (9) and the values of Table 4.

Fig. 6 shows that both the flaw density and flaw size influences the particle strength but in an opposite manner. Since during milling a difference in the particle rate of breakage is observed between the same types of materials (Fig. 3) it is hypothesized that the reduction in particle strength is due to the increase of the number of flaws introduced in the crystal during milling rather than an increase in flaw length. In addition, Fig. 4 shows that the particle rate of breakage decreases with increasing average flaw size. Since the salts which have a relatively low average flaw size are rich in small flaws, i.e. a high flaw density is correlated with a small average flaw size, this implies that the (apparent) relation between particle rate of breakage and average flaw size is basically a relation between particle rate of breakage and flaw density. Both observations are in agreement with each other and, therefore support the conclusion that the increase of the particle rate of breakage as a function of particle size is influenced by the number of flaws present in the crystal rather than flaw length.

4. Conclusions

In this study the effect of pre-existing flaws on mechanical properties of crystals of a model material, sodium chloride, from different sources have been investigated. These mechanical properties have been correlated with particle rate of fracture in a jet mill. The paper shows that particles that have a small average flaw size or high flaw density possess a relatively small constraint factor whereas particles that have a high average flaw size have a high constraint factor and hence behave more ductile. On the basis of an existing model the conclusion is that flaw density plays a more significant role than the average flaw size. The study shows that the rank orders of the mechanical properties where consistent with the rank order of the experimentally determined particle rate of breakage. Materials that

Table 4

<table>
<thead>
<tr>
<th>KIC (MPa/m)</th>
<th>μ (-)</th>
<th>Ψ (°)</th>
<th>L (-)</th>
<th>c (m)</th>
<th>Nflaw (flaws/m²)</th>
<th>εflaw (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt 1</td>
<td>0.5</td>
<td>0.6</td>
<td>45</td>
<td>7.3·10⁻⁷</td>
<td>6.05·10⁻⁶</td>
<td>16.8</td>
</tr>
<tr>
<td>Salt 2</td>
<td>0.5</td>
<td>0.6</td>
<td>45</td>
<td>5.3·10⁻³</td>
<td>13.8·10⁻⁶</td>
<td>38.1</td>
</tr>
<tr>
<td>Salt 3</td>
<td>0.5</td>
<td>0.6</td>
<td>45</td>
<td>5.7·10⁻⁹</td>
<td>8.98·10⁻⁹</td>
<td>25.2</td>
</tr>
<tr>
<td>Salt 4</td>
<td>0.5</td>
<td>0.6</td>
<td>45</td>
<td>6.8·10⁻⁷</td>
<td>6.81·10⁻⁷</td>
<td>18.9</td>
</tr>
</tbody>
</table>

Fig. 6. Predicted particle strength of sodium chloride particles as a function of flaw density and average flaw size (particle size 350 µm).
have a relatively low hardness show the largest particle rate of breakage. The degree of fracture tends to decrease for particles that have a smaller flaw density and hence behave more ductile. The paper shows that pre-existing flaws have an impact on mechanical properties and on particle fracture behaviour in a jet mill. It is concluded that crystal’s flaw size and density of flaws has an impact on the mechanical properties and subsequently, on fracture behaviour of particles in a jet mill. More precisely, it is concluded that the increase of the particle rate of breakage as a function of particle size is influenced by, among processing conditions and material properties, the number of flaws rather than by flaw length. Therefore, unit-operations like crystallization which has an impact on impurities and flaws in crystals, influences also the fracture behaviour of particles in a jet mill.

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References