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Comparison of various milling technologies for grinding pharmaceutical powders

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Abstract

This paper examines fine grinding techniques in current use in the pharmaceutical industry. Experimental results are given for fine grinding of vitamin C, chosen as a model substance representative of pharmaceutical products, using eight different grinding mills chosen amongst those in current use in the pharmaceutical industry. The results are evaluated in terms of product quality expressed as particle size and distribution and also in terms of operating criteria applicable in the pharmaceutical industry such as ease of setting up, ease of cleaning, and investment cost. The main conclusion reinforces and quantifies current practice of using pancake mills that are preferred for ultra fine grinding as they are simple to use, can treat high feed rates and are easy to clean.

Keywords: fine grinding; pharmaceutical industry; pancake mill

1. Introduction

In recent years and particularly in the pharmaceutical industry, product quality criteria have become more and more draconian, imposing specifications involving finer particles and closer control on the mean particle size, or the width and cut-off of the particle size distribution. Additional requirements are for the particle shape and surface properties of powders, which go towards the end use consumer requirements.

The past 10 years have also seen the development of new grinding technologies as well as significant improvements to existing methods. Nevertheless, size reduction by grinding has remained an essentially empirical science, but one needing a better understanding so as to meet new technical and economic requirements.

The theory of grinding has mainly been developed in the mineral industry as a response to needs for maximising production capacity and minimising energy use for low value added products (Prasher, 1987). On one hand, literature gives many examples of experimental investigations with different types of mill and numerous types of mineral powders for validating models of grinding as a

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unit operation applicable in such circumstances. On the other hand, there is a paucity of literature results for the food and pharmaceutical industries. This is partly due to the fact that products from natural sources are more variable, making investigation difficult to generalise, and partly due to the fact that in high value added industries, experimental results are often considered confidential. Accordingly, the scarce published data often conceals the nature and properties of the powders used, thus making it even more difficult to generalise the results.

Grinding operations in the pharmaceutical industry are generally limited to three or four main types of equipment, the choice between which is usually based on experience and limited by the fact that more fundamental approaches have been developed for the mineral industries. It is difficult to take into account the properties of organic materials and the process needs of the pharmaceutical industry. In this industrial area, the main factor of choice is the ability to give a certain product quality, in terms of fineness of particle size or specific surface, without causing physical or chemical changes such as amorphisation. Further criteria are the ease of determining operating parameters and ease of cleaning so as to eliminate contamination which are both specially important in multi-product installations. Finally investment costs must be borne in mind though they could be secondary in the case of high value added products.

The experimental investigation presented here is based on comparative grinding tests using vitamin C, a low-cost model pharmaceutical product for which much information is available in the literature. This

substance is non-toxic, easy to remove by conventional cleaning and readily available at a reasonable price, making it suitable for pilot plant tests. It is a good analogue of many pharmaceutical powders where fine particle size is required to improve dissolution, chemical reactivity and the homogeneity in powder mixtures, etc.

2. Methods

2.1. Types of mill used

Two families of grinding mill have been tested: air jet mills and impact mills. The main details of the equipment used are given in Table 1.

2.2. Powder used

Vitamin C is used in this investigation as a non-toxic model pharmaceutical product having mechanical properties typical of organic powders. It is available in large quantities at a reasonable price and does not pose problems of cleaning the equipment. The main physical properties are as follows: Crystalline particles with size $X_{10}=27.8\text{ }\mu\text{m}$, $X_{50}=122.8\text{ }\mu\text{m}$, $X_{90}=295.2\text{ }\mu\text{m}$, Blaine specific surface= $0.06\text{ m}^2/\text{g}$, bulk density= 0.9 g/ml .

2.3. Characterisation equipment and methods

The ground powder produced in the various tests has been characterised by the methods given in Table 2.

These measurements indicate that: the median diameter determined by the Insitex in line laser

Table 1
Types of mill used in the study

Type of mill	Air jet			Impact				
Model	Spiral jet Pancake Mill	Oval ring Mill	Fluidised bed with integral selector	Simple rotor pin mill	Simple rotor pin mill	Double rotor pin mill	Pin mill with selector	Fixed hammer mill
Maker	Alpine	Fluid Energy Aljet	Alpine	Forplex	Alpine	Alpine	Micron system	Forplex
Size	100 mm		0.8 L	100	160	250		100
Reference	AS100		AFG100	BLX			MS20	BLX

Table 2

Measurements made on ground products

Property	Method	Instrument	Pertinence
Particle size distribution	Laser diffraction	Malvern	Product quality control with respect to specifications
		Insittec	In line continuous measurement of product quality. Ensures traceability, correlated to Malvern
Specific surface	Permeability	Blaine	Robust, simple to use Correlated to the median diameter IPC
Density/flow	Tap density		Described in the European Pharmacopoeia Correlated to the median diameter IPC

diffraction instrument is not identical to that determined by the Malvern laser diffraction instrument but the two methods are well correlated by a straight line relation such that

$$X_{50 \text{ Insittec}} = 1.3534 X_{50 \text{ Malvern}} - 1.5549$$

This result has also been confirmed by other results with different products.

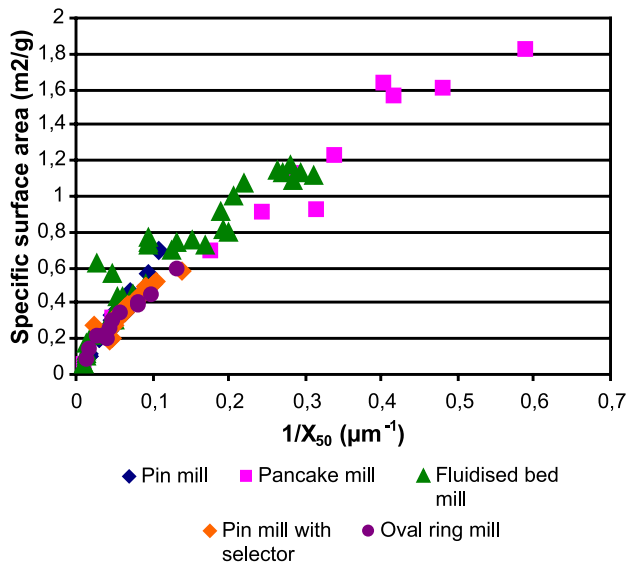


Fig. 1. Specific surface as a function of the reciprocal of the median diameter: Pin mill, Pancake mill, Fluidised bed mill, Pin mill with classifier, Oval ring jet mill.

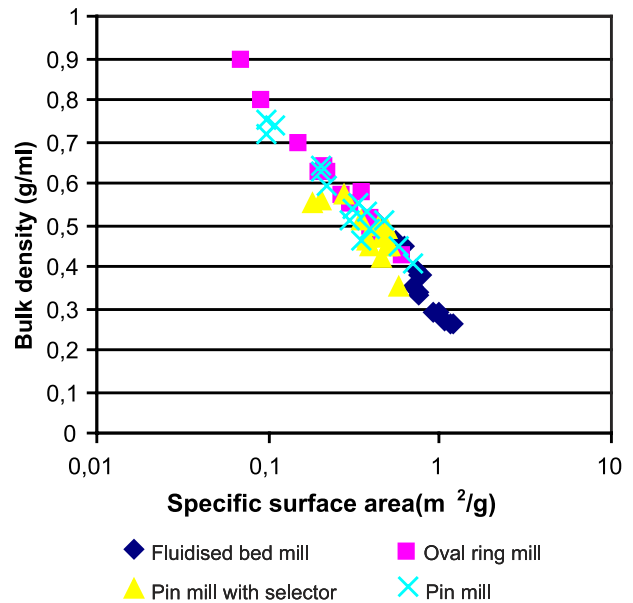


Fig. 2. Bulk density as a function of the specific surface.

For all grinding methods, the specific surface of the ground product is inversely proportional to the median diameter. See Fig. 1.

For all grinding methods the bulk density of the products decreases as the specific surface increases (see Fig. 2).

These results confirm the coherence of the different methods used for characterising the ground products.

3. Experimental procedures

3.1. Air jet milling

3.1.1. Spiral jet “pancake” mill

The mill comprises a flat cylindrical grinding chamber with a ring of air nozzles each set at an angle to the circumference of the chamber. These jets form a so-called grinding circle and a free vortex, which plays the role of a selector by pushing the un-ground particles outwards and sucking the fine ground particles to the centre of the chamber. After leaving the grinding chamber the product goes through a cyclone to separate the coarse particles (recovered in a container) from the fine product (recovered in the filter).

A priori, the main operating parameters are as follows:

- The gas pressure used for grinding and the solids feed rate determine the specific energy used for grinding (E_{sp})

$$E_{sp} = \frac{E_c}{Q_{solid}} \propto \frac{P}{Q_{solid}},$$

where E_c is the kinetic energy of the gas used for grinding, Q_{solid} is the solids feed rate and P the absolute pressure of the gas used for grinding.

- The geometry of the nozzles
- The number of nozzles
- The angle the nozzles make to the tangent at the circumference

To evaluate the grinding performance these latter three parameters were kept constant and the grinding pressure and the solid feed rate were varied. The results shown in Fig. 3 indicate that the specific surface of the ground product is mainly influenced by the specific energy used for grinding.

3.1.2. Oval ring mill

The oval ring mill has an oval vertical grinding-chamber divided into two parts.

A lower part where grinding takes place and an upper part where classification occurs. Particles are introduced in the lower part of the mill using a Venturi feed system and breakage is caused by the air jets projecting particles at one another. In the upper-part, centrifugal force pushes the coarse particles to the outside of the chamber to be recycled in the grinding section. The fine particles go to the inside of the grinding chamber ring where they exit and are collected in a filter.

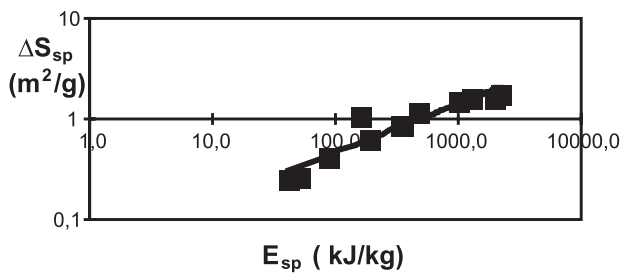


Fig. 3. Specific surface created as a function of the specific energy used for grinding in the spiral jet pancake mill.

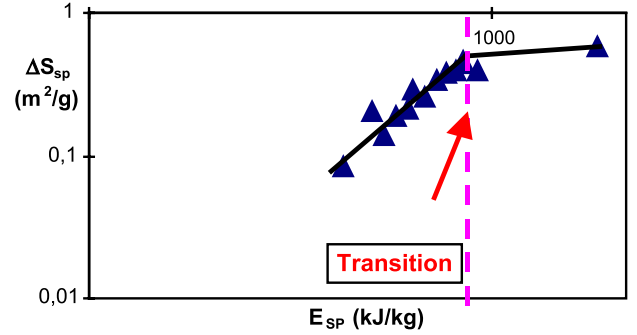


Fig. 4. Created specific surface as a function of the specific energy used for grinding in the oval ring mill.

A priori, the main operating parameters in this type of mill are the same as those important in the spiral jet pancake mill described above. Experimental results are given in Fig. 4 and show that the specific surface of the ground product depends essentially on the specific energy used for grinding. In addition, there are two regimes.

A low-pressure regime dominated by fragmentation, and a high-pressure regime dominated by attrition where pressure has a less marked effect.

3.1.3. Fluidised bed air jet mill with integral classifier

This mill has a cylindrical grinding chamber of diameter 100 mm fitted in its lower part with a cone having three 2 mm air jets pointing at each other. Fragmented particles are carried to a “squirrel cage” type turbo selector, the speed of rotation of which can be varied between 18,000 and 20,000 rpm, which is located in the upper part of the mill chamber.

Solid is introduced in the mill by a screw feeder, the product leaving the mill through the selector is collected in a cyclone and the transport air is further filtered to recover ultra-fine particles. The air jets form a fluidised bed of particles in the chamber and grinding occurs by projection of particles against one another. These particles are then carried upwards by the current of air to the turbo selector which only allows particles less than a certain size, determined by the speed of rotation, to leave the grinding chamber. Particles larger than the cut size are excluded by centrifugal force and return to the grinding section. The mill used in the tests also has an Insitex on line laser diffraction instrument, which gives continuous determination of the particle size distribution and also a measure of the solids flow rate from the attenuation of the light beam.

A priori, the important operating parameters of this type of mill are: The air pressure at the grinding nozzles, the solids feed rate, and the speed of rotation of the turbo selector.

Experiments performed by varying these parameters show:

- The specific surface of the product depends on the air pressure used for grinding (P) and the speed of rotation of the selector (N). As shown in Fig. 5, these two parameters seem to be linked together and similar results are obtained by keeping constant

$$\frac{P}{N^2} \propto \frac{\text{drag force}}{\text{centrifugal force}}$$

- In the range used here (1 to 10 kg/h) the solids feed rate has little influence on the specific surface of the product. The particle size is essentially controlled by the classifier that compensates the feed rate effects by recycling coarse particles in the grinding zone of the mill. It should be noted that with some products this mechanism can affect the particle morphology whilst still respecting size specifications. Moreover, the recycling of coarse particles causes an increase in the mill hold-up. This behaviour is also observed up to a feed rate flooding value when overflow of the classifier occurs. This importance of the influence of the classifier explains the pertinence of the (P/N^2) parameter to describe the experimental results.
- The Insitac on line measuring system showed that the instantaneous product particle size X_{50} and X_{90}

vary considerably during operation but that the X_{10} is more stable.

- In addition, it is found that the time required to establish a continuous operating regime depends on the solids feed rate and indications are that there is a solids hold up in the mill of about 240 g.

3.2. Impact mills

3.2.1. Pin mills

A pin mill comprises two disks fitted with overlapping pins. One of the disks (stator) is stationary the other (rotor) rotates with a high peripheral speed of up to 150 m/s. Product is introduced by a feed screw in the centre of the mill and leaves by the periphery to a collecting filter.

The main operating parameters varied in the experimental programme were the speed of rotation and the solids feed rate. In addition, the feed solids particle size was varied by making several passes through the same mill and the effect of the size of the mill was examined by using three different mills.

Fig. 6 shows that for the sizes of mill used, the specific surface of the product varies linearly with the square of the peripheral speed up to a value of 150 m/s. Above this value there is a change in slope. This indicates that the square of the peripheral speed is the main factor for scale up.

It is found that the solids feed rate has only a very minor effect on product quality that with respect to the speed of rotation. It is also found that, after two passes

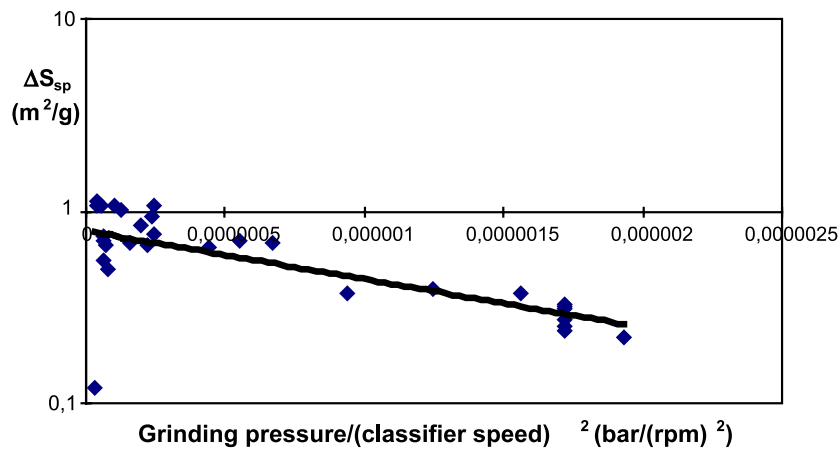


Fig. 5. Specific surface created as a function of the factor P/N^2 for the fluidised bed air jet mill.

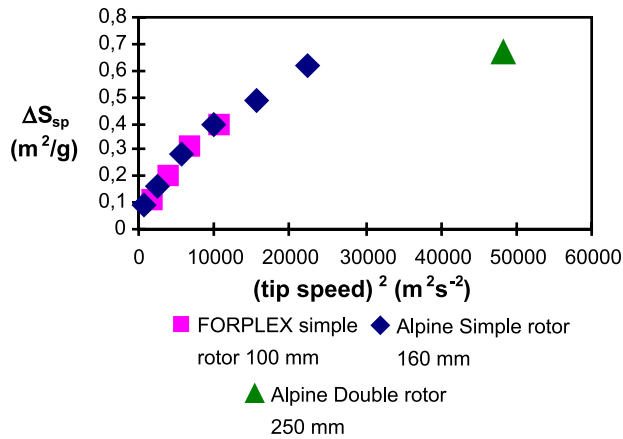


Fig. 6. Specific surface created as a function of the square of the peripheral speed for three sizes of pin mill: * Pin mill, * Double rotor pin mill.

through the mill, the product quality remains essentially constant.

3.2.2. Fixed hammer mill

In the case of a fixed hammer mill the feed is to the centre of the mill where it is thrown at a selector grid by the centrifugal force created by the rotating blades.

The particles are ground by successive impacts on the blades or between the particles and the grill. Peripheral speeds are in the range 50 to 100 m/s. Fixed hammer mills require high air ventilation to eliminate heat created by grinding. A priori the important operating parameters are, the peripheral speed of the rotor, the solids feed rate, the air flow rate and the characteristics of the selector grill: size and shape of the holes and free area of the holes.

The parameters varied in the experimental programme were the solid flow rate, the speed of rotation of the rotor, the type of grill and the hole size. Results given in Fig. 7 show that the specific surface of the ground product depends essentially on the square of the speed of rotation and that the type of grill has an important influence on product quality. For example, a punched hole grill gives the highest specific surface but the size of the holes has very little effect on grinding performance. It is also found that the solids flow rate has little influence on product quality as determined by the specific surface.

3.2.3. Pin mill with dynamic selector

The type of pin mill with dynamic selector used is a Micron System MS20 model, which has a pin mill coupled to a dynamic selector with solid feed through a pair of synchronised valves. A fan is fitted upstream from the mill to create a strong air flow through the grinding chamber of 100 to 320 m³/h. Final product is collected in a bag filter with cleaning system and a product recovery container. The mill used has a cylindrical chamber and a grinding rotor with eight teeth (diameter 6 mm, height 15 mm) turning at up to 10,000 rpm depending on the speed of the selector. The selector has 12 blades and rotates at up to 5000 rpm. Solid is introduced by the valve system to the circumference of the grinding chamber and ground product is carried by the air flow towards the selector ring where centrifugal force throws the coarse particles back into the grinding chamber and the fines are carried to the collector filter. The main operating parameters are the speed of the grinding rotor, the speed of the selector rotor, the solids feed rate and the air flow rate.

The experimental programme showed that product quality is essentially governed by the performance of the selector. The specific surface depends on the air pressure (P) and the speed of rotation of the selector (N). Fig. 8 shows that these two parameters seem to be linked together and similar results are obtained for similar values of the group:

$$\frac{P}{N^2} \propto \frac{\text{drag force}}{\text{centrifugal force}}$$

It is further found that the speed of rotation of the grinding rotor has little effect on the specific

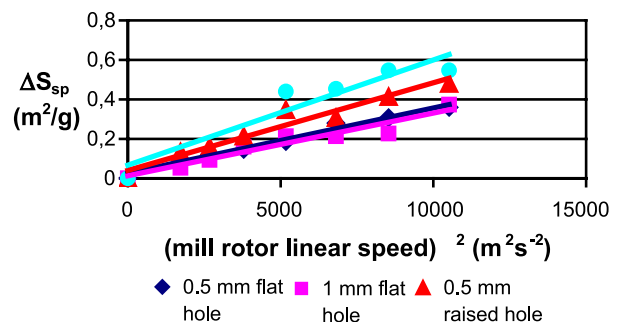


Fig. 7. Specific surface created as a function of the square of the speed of rotation in fixed hammer mills for different grid types.

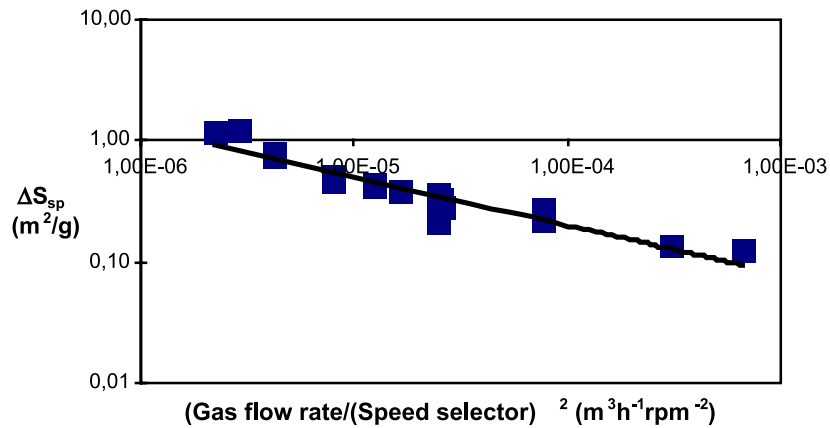


Fig. 8. Specific surface created as a function of the factor (air flow rate/(classifier speed)²) in a pin mill with dynamic selector.

surface of the product and that the solids flow rate has practically no effect on the product specific surface, which does however vary with the speed of rotation of the classifier. Repeated passages through the mill show that there is practically no change in product quality after the first passage through the mill. Up to a maximum value of the feed rate this phenomena are consequences of the importance of the classification process and coarse particles recycling to determine the output size of the product.

4. Summary of the main results

The main results of the study may be resumed as follows:

Product quality from an air jet mill depends mainly on the specific energy used (ratio of kinetic energy of the gas to the solids feed rate).

Product quality from a fluidised bed type air jet mill is mainly controlled by the performance of the turbo selector.

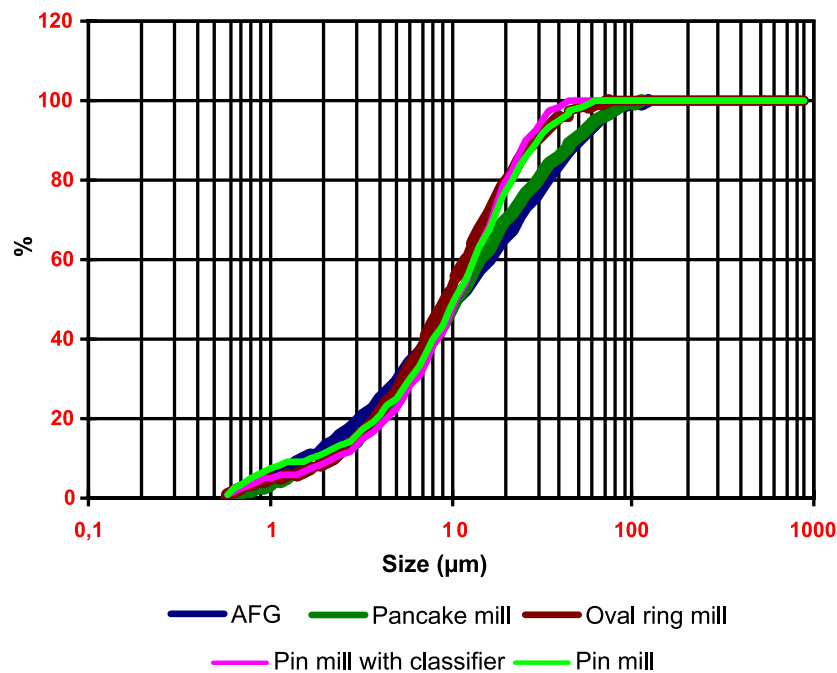


Fig. 9. Particle size distributions of products from five different types of mill.

Product quality from an impact type mill (pin mill, hammer mill) is mainly determined by the speed of rotation of the grinding rotor.

Product quality from a pin mill coupled with a selector is mainly governed by the performance of the selector.

5. Comparison of the different types of mill

The different types of mill can be compared on the basis of:

- The specific surface of the product, the width of the particle size distribution expressed as the span defined as:

$$\psi = \frac{X_{90} - X_{10}}{2X_{50}}$$

where X_{90} , X_{50} and X_{10} are the quantiles at 90%, 50% and 10%, respectively.

- The ease of use with respect to the production capacity of the mill,
- Cleaning,
- Investment costs.

Comparison shows that pancake mills give the smallest particle with the highest specific surface ($S_0 > 1.7 \text{ m}^2/\text{g}$ that is $X_{50} < 2 \text{ }\mu\text{m}$).

The two types of mill having integral selectors, that is the fluidised bed air jet mill and the MS20

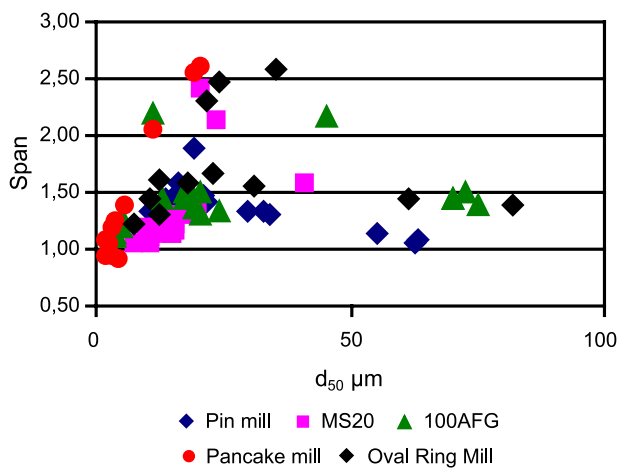


Fig. 10. Span of the size distributions from five different types of mill.

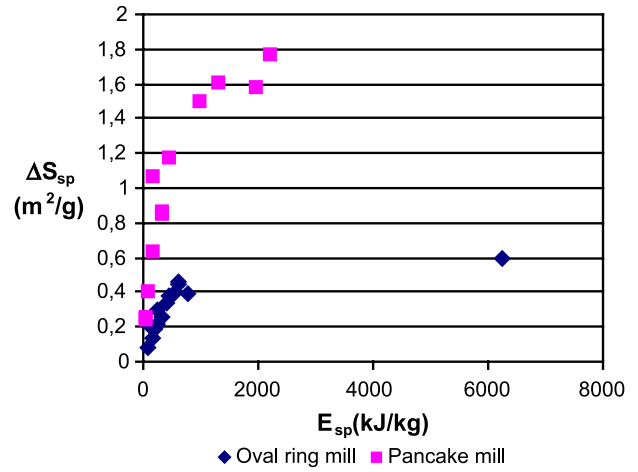


Table 3
Summary of conclusions

Type of mill	Product specific surface (m ² /g)	Maximum feed rate	Cleaning	Operation	Price (kF)
Pancake mill	1.77	10 kg/h	Easy	Mechanically simple, little or no maintenance	200
Oval ring mill	0.59	30 kg/h	Easy	Mechanically simple, little or no maintenance	200
Fluid bed+selector	1.12	7 kg/h for $N < 7000$ rpm 2.5 kg/h for $N > 7000$ rpm	Difficult	Mechanically complex, requires regular maintenance	1000
Pin mill (100 mm)	0.41	25 kg/h	Less easy	Requires regular maintenance	250
Fixed hammer mill	0.52	25 kg/h for $d_{\text{grid}} \geq 0.3$ mm 7 kg/h for $d_{\text{grid}} < 0.3$ mm	Less easy	Requires regular maintenance	250
Pin mill+selector	1.22	75 kg/h	Difficult	Requires regular maintenance	500

For fine or coarse grinding the oval ring mill and the pin mill are comparable. The MS20 can be useful if tight size distributions are required. Finally, the fluidised bed air jet mill does not seem to be well suited to grinding organic powders. This type of mill does not have any particular qualities with respect to particle size and distribution, has only a

low capacity, is rather expensive, and not very easy to use.

Reference

Prasher, C.L., 1987. *Crushing and Grinding Process Handbook*. John Wiley, London.