1 Aspects of milling

1.1 Introduction

The invention of making powder was one of the earliest inventions in human history. For example, food has to be ground since people gave up their nomadic lifestyle. The agriculture development for food purposes is a basis for human progress and history to civilization when mankind developed tools to reduce particles in size. Therefore, milling is a very old discipline originating from milling agricultural products to flour. People have been milling grains for over 75,000 years and the Greeks are thought to have been the first to create a commercial mill. Already during the stone-age people ground wheat between two stones and this method is basically not very different from the method of milling by milestones in a windmill or watermill. The windmill made its appearance at the end of the twelfth century. In a windmill or watermill the bottom stone was fixed and the top stone was balanced on a spindle which could be raised or lowered, making the space between it and the bottom stone as narrow or as wide as the miller wanted. Both stones were corrugated, and as a result during movement of the top stone, the wheat between the two stones was scraped. The wheat to be milled entered the mill by a hole in the top stone and was carried out towards the edge, leaving it as flour. Most villages had a mill to grind cereals, but this power-source could be turned to other uses. Mills were adapted to other industrial uses, such as paper-making, lead-melting and wood sawing (1). The most dangerous of these was gunpowder-making. Early descriptions of grinding and other process steps as practiced in the sixteenth-century can be found in the work of George Bauer, better known by the Latin version of his name Georgius Agricola (2). Figure 1-1 shows a stamp mill for crushing ores in which the mill is driven by water power.

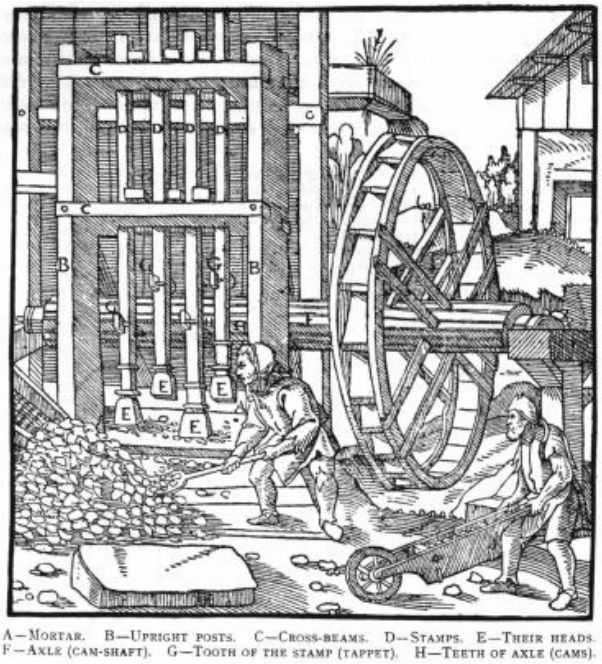

Figure 1-1 Stamp mill for the liberation milling of ores (Adapted from Agricola (2)).

Minerals are ground to liberate the ore which can be separated by means of mineral processing. During a period which is known as the Industrial Revolution a large change took place in the development of machine tools. The Industrial Revolution was the major technological, socio-economic and cultural change in late 18th and early 19th century that began in Britain and spread throughout the world (3). During that time, an economy based on manual labour was replaced by an economy dominated by industry and the manufacture of machinery. While certain machine tools existed long before then, there is no doubt that the development of machine tools as we know today is closely linked to the first several decades of the Industrial Revolution, from about 1775 to about 1830. Prior to that time, practically all machinery, or what little of it existed, was made of wood, and nearly all machine tools were geared to work in softer materials (4). However, it was not until the late 17th century that clockmakers, builders of scientific instruments, and furniture and gun makers began the

changeover from wood-working lathes to ones capable of machining tool steel. They had a need for a variety of gear cutting, grinding, precise screw-cutting machines to fabricate their products. The development of precise machine tools for these purposes paved the way for the industrial machine tools of the late 18th and early l9th centuries. In 1795, Oliver Evans revolutionized milling in America. In his book (5), 'The Young Millwright and Miller's Guide', Oliver Evans described the first fully automated mill. Not only did the water power do the grinding process, but it also powered the cleaning and sifting processes as well. The effects of this technology were far reaching. It reduced the number of people needed to work the mill from six or more to just one or two. Flour and other grain products became cheaper to make and to buy. The technological aspects were also felt in other industries. It began with the mechanisation of the textile industries and the development of iron-making techniques. In the textile industry automated mills soon followed. The development of all-metal machine tools in the first two decades of the 19th century facilitated the manufacture of more production machines for manufacturing in other industries which made possible the construction of the steam engine and the machines it had to power. In response of new industries which arose and modern methods of production that spread to older sectors as well, new tools and modifications to old tools were required. Also, machine tool builders produced new equipment notably milling equipment. Today, many of our products are manufactured in automated mills ranging from minerals like for instance ores and coal, chemicals, agriculture products, foods, and pharmaceuticals. The fineness to which a material is ground has a marked effect on its production rate and demand of energy. From the point of view of energy utilization, size reduction is an inefficient process as only between 0.1 and 2.0 percent of the energy supplied to the mill appears as increased surface energy in the solids (6). Concern about the rising cost of energy has led to publication of a report of the National Materials Advisory Board (7). This showed that the United States industries use approximately 32

billion kWh of electrical energy per annum in size-reduction operations. More than half of this energy is consumed in the crushing and grinding of minerals, one-quarter in the production of cement, one-eighth in coal, and one-eighth in agricultural products (6). Therefore, research in the field of milling originally was aimed at reduction of the energy consumption of mills. This was especially relevant to the mineral and ore industry. Early attempts to study the milling behaviour of compounds led to an emphasis on empirical rules of size reduction. Several laws have been proposed to relate size reduction to a single parameter, the energy input to the mill. In the 19th century the two earliest laws were proposed by Rittinger (8) and Kick (9). In 1952 a third law of size reduction was proposed by Bond (10). However, none of the energy laws apply well in practice, and they have failed to give a starting point for further understanding milling. Due to the inadequacy of these grinding "laws" and the enormous literature on size reduction this led to the belief that milling was considered to be an art which only could be learned by years of experience (11). From the perspective of process control this is an undesirable situation. This situation is specifically undesirable in fields where product control is critical. In these areas the focus in understanding milling shifted from energy reduction to quality of milled product. This is particularly the case in pharmaceutical industry and hence, there has been significant emphasis on the characterization and control of active pharmaceutical ingredient (API) (12) in the last two decades. The logical evolution of this trend is to characterize and control the particle size of the API throughout pharmaceutical processing. This is reflected in the framework of process control which is a topic of increasing attention, for example via the Process Analytical Technology initiative of the Food and Drugs Administration (FDA) (13). Furthermore, in the pharmaceutical industry the development of new drug products is not only related to the discovery of new drugs, but also to the pharmaceutical development of an effective pharmaceutical dosage form. Depending on the intended route of administration and

several properties of the drug a specific particle size of the API is required. The particle size of the API can significantly influence the manufacturability (e.g. content uniformity of granulate), stability, and the bioavailability of a drug. For example, the dissolution is influenced by the particle size of the API since the dissolution rate is directly proportional to the surface area of the drug which in turn increases with decreasing particle size as described by the Noyes-Whitney equation (14). Micronisation of particles is often a successful strategy for increasing the dissolution rate. Moreover, the particle size of the API influences the homogeneity of the granulate during high shear granulation. For example, Van den Dries et al (15) showed that the degree of demixing of the drug substance during high shear granulation depends on the difference in particle size of drug substance and excipients. The foregoing points at the importance of the drug substance particle size. Hence, during milling control of the drug substance particle size (distribution) is essential. Jet milling is a well established technique for milling of pharmaceutically active compounds. This type of mill will be addressed more in detail in the next section.

1.2 Methods of size reduction

Depending on the size of the particles required a size reduction method is selected. In general, it is found that a smaller particle size can be achieved by wet grinding compared to dry grinding (16). Wet grinding is also considered when both the feed material and the desired end product are suspensions. This thesis focuses on grinding in the dry state for application in solid oral dosage forms like tablets and capsules. If a maximum flexibility of product particle size is desired a jet mill with a separate air classifier is suitable, for example a fluidized bed opposed jet mill. Fluidized bed opposed jet mills have been applied in pharmaceutical industry over the last 10 years (17). Figure 1-2 shows a schematic view of a fluidized bed opposed jet mill.

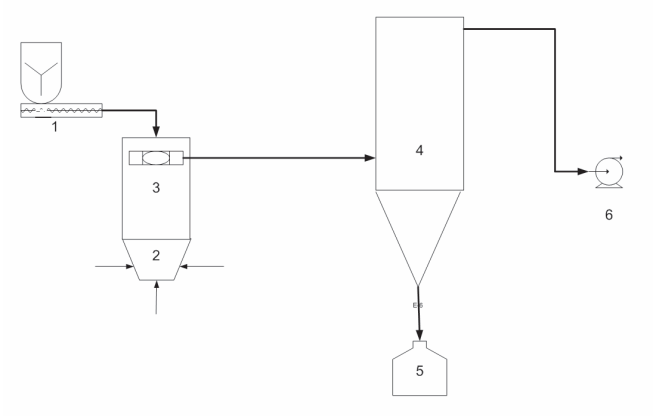

Figure 1-2 Schematic view of the fluidized bed opposed jet mill (100 AFG Hosokawa Alpine, Germany). (1= dosing screw, 2 = mill, 3 = classifier, 4 = filter, 5 = product bin, 6 = blower)

The fluidized bed opposed jet mill is a closed system which consists of two stages, i.e. milling of particles and classification of milled particles. In jet mills, which are also called fluid energy mills, expanding air jets entrain and accelerate the particles which are dispersed into the mill chamber. The feed material enters the mill via a dosing screw. The milling gas enters the mill via three nozzles which are situated at the bottom of the milling chamber resulting in three jets of compressed gas. The type of milling gas applied will not change significantly the particle size distribution. Subsequently, the powder particles in the mill are accelerated to a high velocity. Due to inter particle collisions and particle-wall contact particle size reduction takes place. The milling gas also produces a fluidizing effect transporting the particles to the classification zone were the particles are classified. The classification step is important in defining the upper cut size of the product. For the classification of particles in a fluidized bed opposed jet mill an air classifier is used. Particles that are larger then the cut-size will be returned to the milling zone (18) whereas particles that are sufficiently small in size pass

through the rotating vanes of the classifier wheel. Subsequently, the milled particles are collected by the filter. Since the objective is usually product quality in terms of particle size and particle size distribution, the fluidized bed opposed jet mill is a suitable mill to realize a required particle size distribution.

The previous section showed that depending on the dosage form a preferred particle size of the API is required. Therefore, during milling control of the particle size (distribution) of the API is essential. Unfortunately, batch-to-batch variations in terms of particle size are encountered during milling, even when the same processing conditions are employed. Because milling conditions are kept constant, the conclusion is that alterations in particle properties must play a role. Cleary, the process lacks control which is an undesired situation because process control is essential. This implies that a better fundamental understanding of the various mechanisms involved during breakage of particles is needed. The next section gives an overview on the current understanding of the various mechanisms involved during particle fracture.

1.2.1 Current state of research

1.2.1.1 Particle breakage

Milling is a unit operation which has no sound underlying theory comparable to that which exists for other unit operations. The design of milling equipment for a given application is based on accumulated experience of the manufactures. It is not for lack of either interest or investigation that a quantitative theory of milling does not exist. In contrast, the number of references in the literature dealing with milling is overwhelming. In this section a brief review of the present understanding of particle fracture is given.

Milling is an energy intensive and highly inefficient process in the sense that considerably more energy is consumed by the process than is actually required to break the particles (19).

The fineness to which particles are ground has a strong impact on its production rate and hence energy requirements. Therefore, originally, research in the field of milling was aimed at reduction of the energy consumption of mills.

Two early theories which describe the energy requirement as a function of particle size have received much study. Rittinger's law (8) stated that the energy consumed during a size reduction process is proportional to the new surface produced, where the specific surface energy is a material characteristic. Rittinger concluded that the energy consumed in a size reduction process, E, is inversely proportional to the product size. The relationship is expressed as:

$$E = c\left(\frac{1}{x_p} - \frac{1}{x_f}\right) \tag{1}$$

were c is a constant and x_p and x_f are the product and feed particle diameters, respectively. Kick's law (9) states that for geometrically similar size reduction, the energy required per unit volume is constant which is expressed as:

$$E = c\log\left(\frac{x_f}{x_p}\right) \tag{2}$$

The energy laws have a limited applicability and neither law is utilized to any extent. Bond (10) proposed a model which is a compromise between Rittinger's and Kick's models. This relationship is expressed as:

$$E = W_i\left(\frac{10}{\sqrt{x_p}} - \frac{10}{\sqrt{x_f}}\right) \tag{3}$$

were x_p and x_f are, respectively, the screen size of the product and feed particles through which 80% passes, and W_i is the so-called "Bond work index". The Bond work index may be found experimentally from laboratory milling tests. This relationship is widely used for the

design of milling circuits because a large body of information on W_i values exists (20). However, none of the energy laws apply well in practice, and they have failed to yield a starting point for further development of understanding milling and are mainly of historical interest.

A more detailed understanding of the fracture of particles became possible by theoretical stress analysis in spheres. In 1882 Hertz (21) considered the stress distribution when two homogenous bodies with ellipsoidal surfaces contact each other. His theory enables calculations of the normal stresses in the contact circle, the entire deformation of the sphere, and also the duration of sphere/sphere-impact (22). The Hertzian theory disregards the shape of the body and takes into account only the local radius of curvature of the impacting bodies at the point of contact. In 1904 Huber (22) then used the Hertzian pressure distribution in the contact area and derived equations for the stress field in the contact region. The Hertz-Huber-theory describes the stresses in the vicinity of the contact area and in the absence of cracks. However, almost al particles contain dislocations, flaws, and cracks. Moreover, the Hertz-Huber theory is a static theory and not applicable for dynamic loading conditions (23). The measured fracture strengths for most brittle materials are significantly lower than those predicted by theoretical calculations based on atomic bonding energies. This anomaly is explained by the presence of very small, microscopic flaws or cracks that always exist under normal conditions at the surface and within the interior of a body of material (24). These flaws affect the fracture strength because an applied stress may be amplified or concentrated at the tip. The magnitude of this amplification is depending on crack orientation and geometry. This is illustrated in Figure 1-3 which shows a plate with an elliptic hole having a long axis a and short axis b loaded remotely by a uniaxial stress σ_0. The hole is considered to be small relative to the size of the plate. If this plate is mechanically loaded the stress at the cross section containing the hole is increased relative to the remote loading stress σ_0. The

stress is not distributed uniformly over the reduced cross-section, but concentrated, primarily at the edges of the hole at the ends of the long axis and depends on the ratio of the long axis *a* and short axis *b*. At the edge at the end of the long axis the radius of curvature is given by $\rho=b^2/a$.

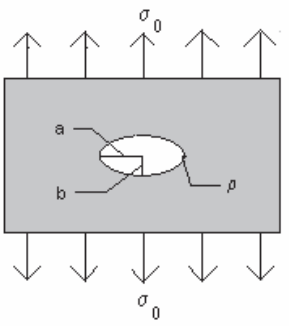

Figure 1-3 Plate with an elliptical hole having a long axis *a* and a short axis *b* loaded remotely by an uniaxial stress.

In 1913 Inglis (25) investigated the stress field around an elliptical hole in a plate and derived an equation for the stress at the end of the long axis of the elliptical hole as shown in Figure 1-3:

$$\sigma = \sigma_o \left(1 + \frac{2\,a}{b}\right) = \sigma_o \left(1 + 2\sqrt{\frac{a}{\rho}}\right) \tag{4}$$

Inglis showed that the presence of flaws in a material could lead to stress concentration in a material under stress. The field of Fracture Mechanics emerged during World War I by the English aeronautical engineer, Griffith, to explain the failure of brittle materials (24). Griffith proposed that all brittle materials contain a population of small cracks and flaws that have a variety of sizes, geometries, and orientations. Fracture will result when, upon application of a tensile stress, the theoretical strength of the material is exceeded at the tip of one of these

flaws. This leads to the formation of a crack that readily propagates. If no flaws were present, the fracture strength would be equal to the theoretical strength of the material determined by the atomic bond strength. Griffith formulated the concept that an existing crack will propagate if the total energy of the system will be lowered due to a release of what is termed the elastic strain energy, some of the energy that is stored in the material as it is elastically deformed. Furthermore, during the crack extension process, new surfaces are created at the faces of a crack, which gives rise to an increase in surface energy of the system. Griffith developed a criterion for crack propagation of an elliptical crack, as shown in Figure 1-3, by performing an energy balance consisting of a decrease in elastic strain energy within the stressed body as the crack extends, counteracted by the energy needed to create the new crack surfaces. He demonstrated that the critical stress (σ_c) required for crack propagation in a brittle material for an elliptical crack with a length (a) is described by:

$$\sigma_c = \left(\frac{2\,Y\,\gamma_s}{\pi\,a} \right)^{\frac{1}{2}} \tag{5}$$

Where Y is Young's modulus of elasticity and γ_s is the specific surface energy. Equation 5 applies only to brittle materials for which there is no plastic deformation during fracture. Griffith's work was ignored for over twenty years. Currently, the theory of Griffith is commonly accepted and allows the estimation of the theoretical strength of brittle solids and also gives the correct relationship between fracture strength and flaw size. In 1944 the Griffith concept was related to brittle fracture of metallic materials for the first time by Zener and Hollomon (26). However, most metals and many polymers do experience some plastic deformation during fracture. During World War II the group of Irwin at the U.S. Naval Research Laboratory (NRL) developed a modified form of Griffith's approach. In 1948 Irwin (27) suggested that the Griffith-type theory for ideally brittle materials could be modified and applied to both brittle materials and metals that exhibit plastic deformation. A similar

modification was proposed by Orowan (28). Irwin defined the 'energy release rate' or 'crack driving force', G, as the total energy that is released during cracking per unit increase in crack surface area. It was proposed that a material's resistance to crack extension (R) is determined by the sum of the surface energy γ_s and the plastic strain work γ_p (both per unit crack surface area that accompany crack extension. Consequently, in this case the crack resistance is:

$$R = 2\left(\gamma_s + \gamma_p\right) \tag{6}$$

Irwin also recognized that for ductile materials the energy required to form new crack surfaces is generally insignificant compared to the work done in plastic deformation i.e. $\gamma_p >> \gamma_s$. This is due to the fact that not only new surface is created during fracture, but also energy dissipation occurs, for example plastic deformation, phase transitions, and electrical phenomena, e.g. different electric charges on the crack surface, triboluminscence, and emissions of electrons can result in energy dissipation, and an increase in effective crack formation energy (29). The magnitude of this energy is different for different types of materials. Therefore, equation 5 is adjusted by replacing γ_s by R, where R represents the fracture energy associated with all energy dissipation processes that accompany crack extension (30):

$$\sigma_c = \left(\frac{2\,Y\,R}{\pi\,a}\right)^{\frac{1}{2}} \tag{7}$$

Here σ_c is the critical fracture stress or the fracture strength. As long as $\sigma < \sigma_c$, the crack growth needs more energy than the specimen can deliver and crack propagation does not occur. If $\sigma > \sigma_c$ the specimen delivers more energy than needed for crack extension and unstable crack growth occurs. Although Irwin's modification includes a plastic energy term, the energy balance approach to crack extension is still limited to defining conditions and presents problems for many practical situations. Owing to the practical difficulties of the

energy approach Irwin and his colleagues reformulated it in terms of stress, rather than energy (31). In the middle 1950s their work (31) resulted in a newly material property, which is called the stress intensity factor (*K*), and is now universally accepted as the defining property of fracture mechanics. The stress intensity factor is related to the applied stress and the crack length by:

$$K = \sigma\sqrt{\pi\, a}\;\; f\left(a/W\right) \tag{8}$$

where *f (a/W)* is a dimensionless parameter that depends on the geometries of the specimen and crack. For an infinite plate with a central crack of length 2*a*, *f(a/w)* =1 (30). Irwin showed that the energy approach is related to the stress intensity (*K*) approach by equation 9 which is valid for any geometry:

$$G = \frac{K^2}{Y} \tag{9}$$

The material property governing fracture may therefore be stated as critical stress intensity, K_c, or in terms of energy as a critical energy release rate (G_c). The understanding of particle fracture made progress when in 1957, Professor Rumpf started to build up the Institute of Mechanical Process Engineering at the University of Karlsruhe. At that time size reduction was a well established domain in engineering. Rumpf then had the idea to combine experience in engineering with the scientific methods of physics (32). This was the basis for a sound scientific research in the field of particle fracture. A more detailed understanding of the size reduction process became then possible through experiments on single particles, where the force and energy input to the particle could be measured related to the resulting particle size distribution (33, 34). Their conclusion was that particle fracture occurs in three steps. First, initiation of a crack, second, growth and acceleration of the crack, and third, branching of the crack at high speeds (32). During particle fracture consumption of elastically stored energy

takes place by a running crack, and usually this energy consumption is much higher than the specific surface energy. The difference between the offered elastic energy and the specific surface energy leads mainly to irreversible deformations at the tip of the crack. The result of these deformations is heat (35). The temperatures at the tip of a fast running crack are very high. At a distance of 30 micron from a fast running crack in iron a temperature increase of 130 K was measured. Temperatures of several thousand centigrades were determined experimentally by the analysis of the electromagnetic radiation, emitted from the tip of fast running cracks in brittle, transparent materials (32).

Rumpf (34) derived a similarity law of comminution. Starting from the simplifying assumptions of both geometrical similarity of the particles undergoing size reduction and similarity of the states of stress and strain, a relationship was obtained between initial particle size and energy investment for a distinct material. Using dimensional analysis the similarity law was extended to cover different materials and different initial flaw size distributions.

Weichert (36, 37) investigated the relation between the amount of energy needed to fracture a particle and particle size. To describe the fracture behaviour of spherical particles Weichert applied Weibull statistics for the flaw size distribution, Hertz theory of the stresses and fracture mechanics for the crack propagation. Weibull statistics describe the failure probability of a particle assuming that the strength of a particle is determined by the weakest link present in a particle. The application of fracture mechanics and the combination of Weibull-statistics with Hertz-Huber-theory gave a physical explanation for the observed dependence of breakage probability and fragment size distribution on milling energy and particle size.

Ghadiri et al (39,40) used nano-indentation to determine the hardness of single crystals. To study particle breakage, the individual particles were fired on a target plate at different impact speeds. Using this approach Ghadiri developed a model to predict the fractional loss (ζ) per

impact of semi-brittle materials in the chipping mode, where material removal occurs from the corner of the particle in the form of chips:

$$\xi = \alpha \frac{\rho U^2 \, x \, H}{K_c^2 \, \Phi^2} \tag{10}$$

where α is a proportionality constant that is independent of material properties, ρ is the particle density, Φ is a constraint factor, *i.e*. the ratio of the hardness to yield stress, U is the impact velocity, x the particle size, H is the hardness, and K_c is the critical stress intensity. Lecoq et al. (41) investigated the relation between the impact energy and the fineness of the impacted solids by single impact tests. Upon subsequent stressing the particles by impacts it was found that below the attrition threshold no breakage occurred, no matter what the number of impacts was. Above the attrition threshold size reduction occurred until a defined number of impacts depending on the type of material. Upon further impacting the particles did not break anymore. In a mill, particles are subject to forces that cause particles to break. The type of mill and the processing conditions employed determines the kind of forces applied to the particles. This, together with mechanical material properties, determines the resulting particle breakage. Professor Peukert (42) indicated that the milling process can be described by the process function representing the mill function and the material function. The mill function represents the type of mill and processing conditions, e.g. milling pressure which affects the number of stressing events. The material function describes the reaction of the particles to the stresses exerted by the mill. Based on similarity considerations and a fracture mechanic model Peukert and Vogel (42, 43, 44) derived an analytical function for the probability of breakage:

$$P_B = 1 - \exp\{-f_{mat} \, x \, k \, (W_{m,kin} - W_{m,\min})\} \tag{11}$$

were f_{mat} is a material property which characterises the fracture behaviour of the particles, x is the particle size, k is the impact number, $W_{m,\,kin}$ denotes the mass specific kinetic impact

energy of the particles, and $W_{m,\,min}$ is a specific threshold energy for a particle of size x, which has to be exceeded by the specific kinetic impact energy in order to cause particle breakage. The main result of this fracture model is the dependency of the breakage probability P_B on the product of initial particle size x, mass specific impact energy, and material parameter f_{mat}. The influence of stress intensity (impact energy), stress number, initial particle size and material are separated. The two material parameters could be determined by single particle impact experiments with narrow size fractions of the feed material. The procedure using narrow feed size fractions can be simplified using material with a certain particle size distribution. In order to determine the material properties and the impact number the population balance has to be inverted. Both the population balance and the inversion were experimentally validated by single impact tests and labscale tests using a small sieve hammer mill. The breakage behaviour of five different polymers, limestone and glass is described by a single master curve representing the selection function as a function of the total net impact energy. Despite the progress in predicting quantitatively the breakage behaviour still milling tests have to be performed if a new material has to be ground in order to determine the impact number and the material parameter f_{mat}.

Taylor et al. (45) tried to identify a physical property of a material in order to be able to predict the fracture behaviour of an API during milling. They correlated the brittleness index, which is defined as the ratio of hardness and stress intensity, to fracture behaviour. They found that materials that fragment extensively have a high brittleness index and vice versa. As the method provides an indication of the fracture behaviour and a guide to classify materials in: easy to break, moderately easy to break, difficult to break, the method gives an indication of the fracture behaviour of materials in a mill.

1.2.1.2 Particle deformation and strength

When a load (i.e. stress) is applied on a particle it deforms. During particle deformation three basic types of material behaviour can be distinguished i.e. elastic, elastic-plastic, and visco-elastic behaviour (46). This distinction can best be described with a stress-strain relation (Figure 1-4).

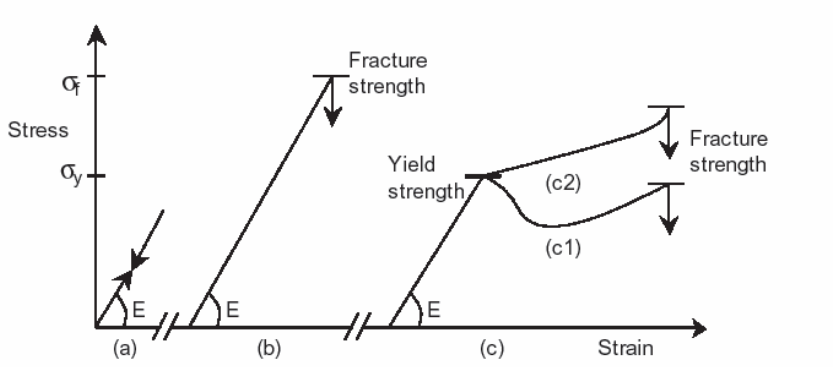

Figure 1-4 Macroscopic stress-strain relations: a. reversible elastic deformation; b. brittle behaviour; c. ductile behaviour (c1. normal plastic flow; c2. strain hardening) (Adapted from van Veen (47)).

The first stage of deformation is elastic deformation. Due to the resistance of a material against deformation (strain), the stress inside the particles increases. If the applied stress is released before the deformation reaches a specific critical value, the particle deforms elastically, i.e. the deformation is reversible and the particle returns to its original shape upon removal of stress. During elastic deformation the stress and strain are linearly proportional and is characterised by the elastic or Young's modulus. If particles fragment into smaller particles after only elastic deformation they are called brittle materials. The stress at fracture is the fracture strength (Fig. 1-4b). Another group of materials are the ductile or plastic materials. After a critical stress (Fig. 1-4c) the particles yield and start to deform plastically,

i.e. the stress applied is not longer proportional to the strain, and permanent or plastic deformation occurs.

Some brittle materials show ductile behaviour when the particles have a particle size smaller than a critical value. This critical particle size means that when a particle is smaller than d_{crit}, crack propagation is impossible under compressive forces. Particles appear to behave ductile and are squashed flat when attempts are made to comminute them by crushing. Kendall (48) derived an equation to calculate the critical particle size at the brittle-ductile transition:

$$d_{crit} = \frac{A\,Y\,R}{\sigma_y^2} \qquad (12)$$

where Y is the Young's modulus, R the fracture energy, σ_y the yield stress and A is a constant depending on the geometry and loading system. Whether particles behave ductile or brittle depends on the material. Roberts and Rowe (49) demonstrated that the stress necessary to cause particle fracture increases when the particle size decreases, whereas the stress causing plastic deformation of a material is independent of the particle size (Figure 1-5). When the fracture stress reaches the level of the yield strength, particles with diameters lower than the critical diameter will yield instead of break.

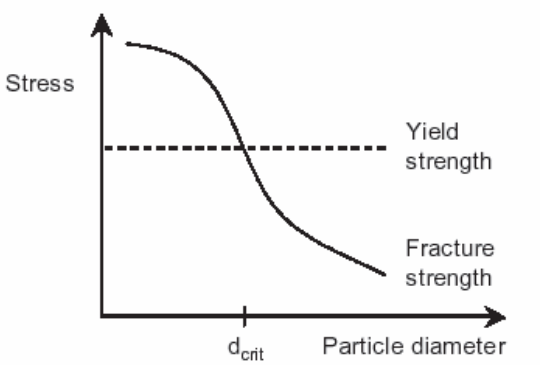

Figure 1-5 Schematic representation depicting the effect of particle size on yield strength or fracture strength (49).

An important material property in processing materials is the particle strength. The term particle strength is defined as the quotient of the force acting on the particle at the breakage point divided by a nominal cross-section of the indent load (50). Unfortunately, due to practical reasons it is impossible to determine the particle strength of small particles using a tensile stress-strain curve. The only method is to determine a compression curve, but this is not without problems either. Because of the irregular shape of the real particle and inelastic effects, the stress field can not be calculated. Another limitation is the applicability of the data. Usually a compression curve is measured at a low compression rate. As a result the data obtained is quasi static. In a mill however, the impact occurs at a high rate. By measuring the so-called hardness the strength of a material can be characterized without having to perform a stress-strain measurement, since the hardness is assumed to be proportional to the fracture strength. The first who studied hardness by the indentation method was Réamur in 1772 (51), followed by Hertz in 1882. The method consisted of pressing a hemisphere of the material under test into a steel plate to the point of appearance of cracks or plastic strain. In size reduction, a well known type of characterization of hardness is the Mohs hardness scale (52). Mohs proposed a scale of ten minerals such that each mineral is able to scratch the one above it. Table 1-1 shows the comparative ten-stage Mohs scale which is still used owing to its great testing simplicity.

Table 1-1 Mohs scale**.**

1. talc	*2. gypsum*	*3. calcite*	*4. fluorite*	*5. apatite*
6. orthoclase	*7. quartz*	*8. topaz*	*9. corundum*	*10. diamond*

Other methods to determine the hardness are indentation test methods where an indenter with a defined shape is pressed into the material under a certain load. The indenter is usually made of diamond. The geometry of the indenter is usually pyramidal, either with four faces

(Vickers indenter) or with three faces (cube corner or Berkovitch indenter). From the dimensions of the obtained indent in the sample the hardness is calculated. A further development of static methods of hardness testing was a method devised by Brinell (53), which consisted of driving a steel ball into the material to be tested for hardness under a pressure of 29.4 kN for about 30 seconds. Brinell hardness is defined as the ratio of load to surface of round indentation. In the Vickers test a square based diamond pyramid is used as the indenter, which can be used to determine the hardness of extremely hard materials (54). In the Knoop test (51) a diamond indenter is used but its shape is such that it forms an elongated pyramidal impression. This test is useful for studying the effect of crystal orientation on hardness. The Brinell, Vickers and Knoop indenters give hardness values which in most cases are close to one another (54). The Rockwell method is based on measurement of two stage penetration of a diamond indenter or a steel ball into a flat, well polished surface of the material to be tested (51). The equation most commonly employed in pharmaceutical compaction research is the Heckel-equation (55). This equation assumes a linear section of the relationship between the logarithm of the relative density under pressure and the applied pressures:

$$-\ln(\varepsilon) = K \,.\, P + A \tag{13}$$

The linear part of the curve has slope K and this slope is related to the yield strength by:

$$\sigma_c = \frac{1}{3 \,.\, K} \tag{14}$$

The yield pressure of a material is approximately equal to 3 times the yield strength. Hence, the reciprocal of K can be regarded as numerically equal to the mean yield pressure (49):

$$P_y = 3 \cdot \sigma_c \tag{15}$$

Based on the Heckel equation the hardness of materials can be estimated with the equation originally proposed by Tabor (54) and modified by Marsh (56):

$$\frac{H}{P_Y} = 0.07 + 0.6 \cdot \ln \frac{Y}{P_Y} \tag{16}$$

Often it is assumed that the ratio H over P_y has a value of 3 (49). As Heckel attributed the linear section to plastic deformation, equation 13 is in principle only appropriate to examine the densification behaviour of plastic materials. Nevertheless, Roberts et al. (57) modified the yield pressure P_y to the deformation stress σ_d, which is a plastic deformation stress, a fracture deformation stress or a combination of both, in order to calculate the deformation stress of particles with a brittle or even unknown fracture behaviour.

1.3 This thesis

The influence of material properties on particle breakage behaviour in a mill is widely recognized. However, there is no method that allows prediction of the grinding behaviour of particles based on material properties. This lack of information is reflected in the disappointing experience that each milling test with a new or unknown powder has to start from the beginning. The applicability and the physical meaning of models that describe the milling process can be improved considerably when material properties are included in these models. Therefore, the goal of this thesis is to investigate the effect of material properties on milling behaviour and to predict the degree of particle size reduction. Furthermore, it aims to identify a set of material parameters which are most critical for milling. Additionally, this thesis aims to give methods to predict the values of these parameters. According to the nature of the goals this thesis is divided in 4 parts. The first part (chapters 2 and 3) treats the relation between material properties and particle breakage kinetics in a fluidized bed opposed jet mill. The second part (chapter 4) is an extension of the influence of material properties on particle

breakage kinetics and discusses the effect of the pre-existing flaws in crystals on milling behaviour and milling kinetics. The third part (Chapter 5) describes the relation between crystal morphology and crystal hardness. The fourth part (chapter 6) is basically an extension of chapter 4 and describes the influence of multiple pre-existing flaws on the strength of a particle.

1.4 References

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