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THE EFFECT OF MILL VARIABLES ON A GRANULATION MILLING PROCESS

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ABSTRACT

An instrumented mill was used to evaluate the milling of a pharmaceutical granulation. The effects of changing mill speed, screen hole size, impeller type, and impeller-screen clearance on milling time and work, as well as particle size reduction were investigated. Screen hole size had the largest effect on milling time and work as well as particle size reduction, while impeller type had the largest effect on overall milling performance. A new impeller design was tested and found to enhance milling efficiency by improving both particle size reduction and mill output rate.

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INTRODUCTION

Milling is the mechanical process of reducing the particle size of solids. It is a common unit operation in the production of many pharmaceutical dosage forms. The use of improper milling conditions can often lead to undesirable changes in the milled material, including polymorphic transformations, increased rates of degradation, and the build-up of static charges (1-5). These changes are often the result of prolonged mill residence times or the use of excessive mill energy.

The determination of the time and energy requirements of a milling operation has been shown to be a reliable means of obtaining the optimum milling conditions for a particular mill and material (6). Improvements in mill design can also be evaluated using these observations. The objective of this investigation was to analyze the effects of a number of mill variables on the milling of a pharmaceutical granulation. An instrumented mill was used to examine the changes in the time and energy of milling brought about by the different combinations of mill variables. The degree of particle size reduction obtained with the different mill variable combinations was also examined. In addition, a more complete analysis of the effect of the mill variables on milling efficiency was obtained by combining the results of particle size reduction with those of milling time and work into two milling performance indices.

EXPERIMENTAL

Instrumented Milling System

The mill used in this study was a laboratory model Quadro Comil[1]. The milling chamber of the Comil consists of a vertically mounted rotating impeller surrounded by a screen in the shape of a truncated cone. The impeller is shaped such that its edges are in close proximity to the screen. Impeller rotational speed is adjustable between approximately 900 and 2500 revolutions per minute.

To obtain data on the time and energy of milling, the mill was equipped with three sensors. These sensors measured impeller shaft speed, torque on the impeller shaft, and the weight of material exiting the mill. The signals from the three sensors were input to a microcomputer controlled data acquisition system. Data from each of the sensors was collected at 100 samples/second. From the readings of impeller speed and torque, the work performed by the mill could be calculated. Milling time was established as the time

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1. Comil, Model 197-112, Quadro Engineering, Waterloo, Ontario, Canada.

required for a given weight of material to pass through the mill.

Mill Variables

The mill variables examined were impeller type, clearance between the impeller and the screen, mill speed, and screen hole size.

The three impellers used in the study had the same general shape, but differed in the shape of their sidearms. The action profiles of the three impellers as well as their general shapes are shown in Figure 1. Impeller 1601 has 0.25 inch diameter round sidearms, while impeller 1607 has flat faced sidearms. Preliminary studies had shown that while impeller 1601 produced a higher rate of material throughput, impeller 1607 caused greater particle size reduction. Impeller 1612 was proposed in order to obtain an increase in both particle size reduction and material throughput. While impeller 1612 possessed the outward angled face similar to the outward curving face of impeller 1601, it also possessed the sharp angles and flat face of impeller 1607.

The clearance between the impeller and the screen was changed through the use of washers which could be placed on the impeller shaft prior to the attachment of the impeller to the mill. With the screens and impellers used in this study, a 0.150 inch thick washer

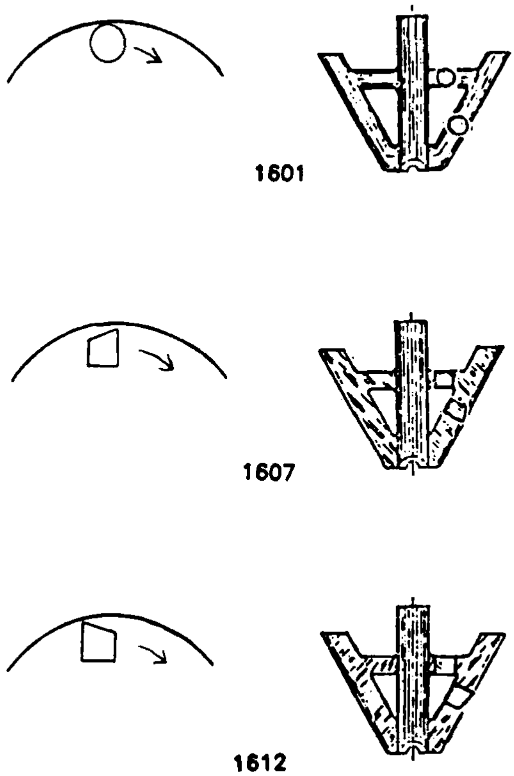

Figure 1. Action profiles and general shape of the three impellers used in the mill variables study.

provided the closest possible clearance without the impeller rubbing on the screen. Washers with thicknesses of 0.125 inch and 0.075 inch were also used. These washers provided increases in impeller-screen clearance of 0.0125 inch and 0.038 inch respectively.

Mill speed was shown to be an important variable in previous studies (7,8). The speeds used in this study were 1500, 1750, and 2000 rpm. This relatively narrow range of speeds was chosen so that the effect of mill speed would not overshadow the effects of the other variables.

The type of screen used has been shown to be a very important determinant in the milling process when using the Comil (8). The importance of screen hole size to the performance of other types of mills has also been demonstrated (7). The screens used in this study were chosen such that they varied only in hole diameter. Other screen variables such as screen thickness, hole shape, and percent open area were kept as constant as possible.

<u>Dependent Variables</u>

A number of factors were used to evaluate the performance of the mill at the different levels of mill variables previously described. These factors included the time of milling, the work of milling, and the reduction in mean particle size. The mean particle size of each milled sample was obtained by sieve analysis. This value was then subtracted from the mean particle size of the pre-milled granulation to determine the reduction in mean particle size.

To assess the effects of the mill variables on overall milling performance, the data obtained on the time and work of milling were combined with that of particle size reduction. This was achieved through the calculation of two milling performance indices. The milling work index, M_w, was calculated by dividing the particle size reduction obtained for a particular combination of mill variables by the milling work value as shown in Equation 1.

$$M_w = \frac{\text{Particle Size Reduction}}{\text{Milling Work}} \qquad \text{Eq. 1}$$

Likewise, the milling time index, M_t, was calculated by dividing the particle size reduction obtained for a particular combination of mill variables by the milling time value as shown in Equation 2.

$$M_t = \frac{\text{Particle Size Reduction}}{\text{Milling Time}} \qquad \text{Eq. 2}$$

By utilizing aspects of particle size reduction, milling time, and milling energy these milling performance indices provide a quantitative measure of overall milling efficiency and performance.

Granulation

The material milled was a commercially available granulation[1] containing aspirin with 10% starch. A 16 to 30 mesh (1190 um to 595 um) sample weighing 375 grams was used for the milling test.

RESULTS AND DISCUSSION

Reduction in Mean Particle Size

The reduction in mean particle size was used to evaluate the extent of milling produced by each

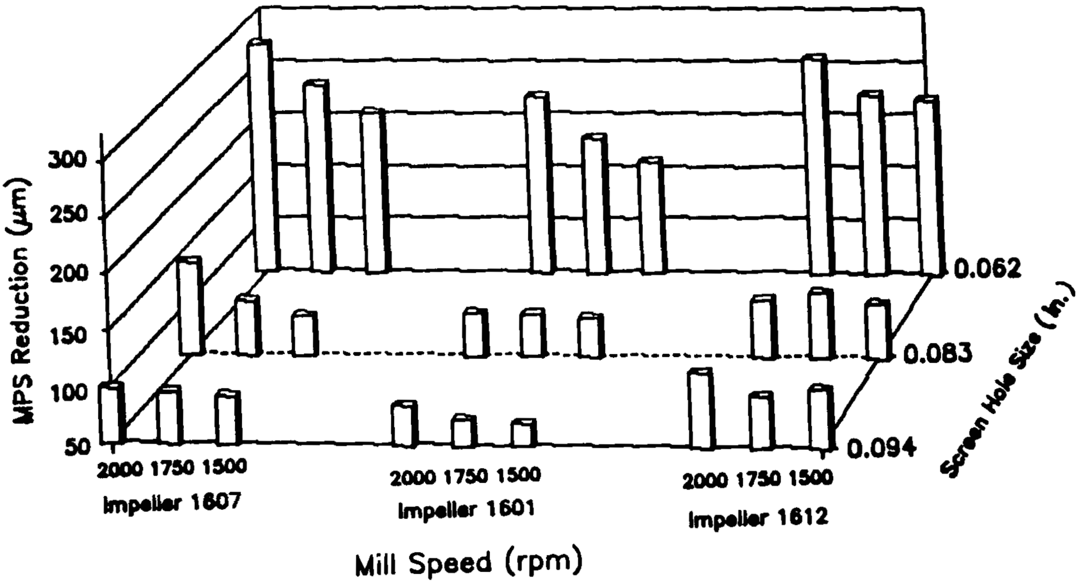

Figure 2. Reduction in mean particle size caused by milling. Each point is the average of nine measurements.

combination of mill variables. The results of the milling tests for the reduction in mean particle size are graphically illustrated in Figure 2. The effect of impeller-screen clearance is not illustrated since it had the least overall significance.

From Figure 2, it can be seen that the screen hole size of 0.062 inch produced the greatest reduction in mean particle size. The smallest screen hole size corresponded more closely to the actual mesh size of the material being milled. Material cannot escape the milling chamber until it can pass through the holes in the screen. Therefore, the screen hole size of 0.062 inch restricted a much larger percentage of the granules and required them to be reduced in size before they passed out of the mill.

Impellers 1607 and 1612 both produced significantly greater reductions in mean particle size than impeller 1601. Impellers 1607 and 1612 possessed sidearms with flat faces and sharp edges, while impeller 1601 did not. This provided evidence that these characteristics cause increased particle size reduction.

The reductions in mean particle size for the two smallest clearances were not significantly different. The particle size reduction due to the largest clearance was significantly less than both of the smaller clearances. The thinnest washer, created a gap between the impeller and the screen that was larger than all but the largest particles in the 16/30 mesh sample. It appears then, that particle size reduction is greatest when the impeller-screen clearance is equal to or less than the particle size of the material being milled. This provides evidence that interaction between the impeller and the screen is an important mechanism of milling action.

In addition, the reduction in mean particle size became greater as mill speed was increased.

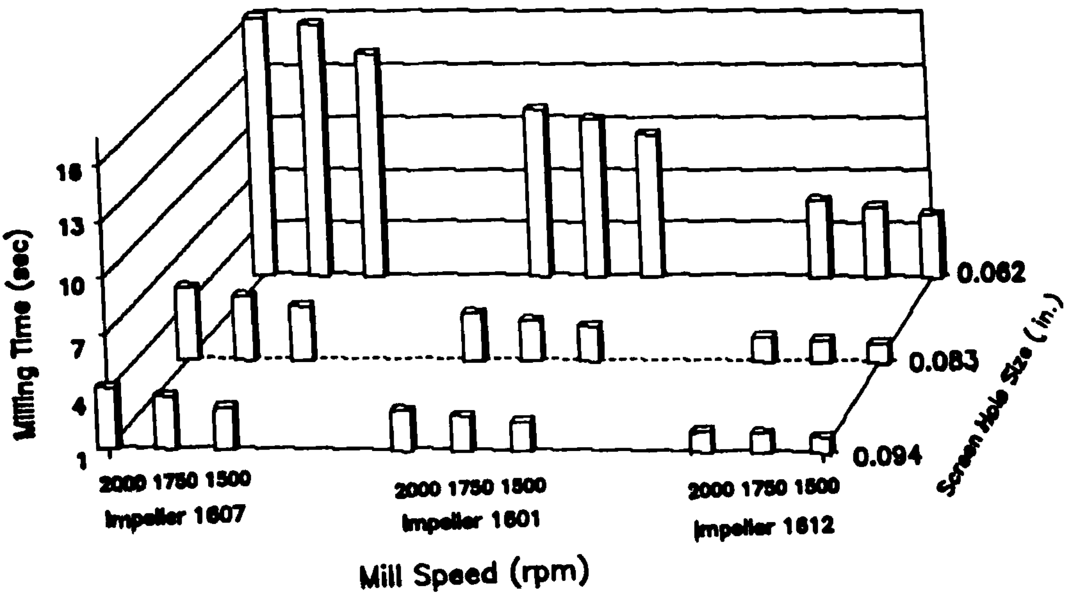

Figure 3. Time required to mill 250 grams of aspirin granulation. Each point is the average of nine measurements.

Time to Mill a Fixed Sample Size of Granulation

To establish the improvement in mill output rate brought about by the various combinations of mill variables, the time required to mill 250 grams of granulation was recorded. The results of the milling tests are graphically represented in Figure 3.

The results obtained from the milling tests clearly show the effects of screen hole size, impeller type, and mill speed on the time to mill the samples.

The smallest screen hole size, 0.062 inch, produced the largest milling time values. This has been explained based on the ability of the smaller

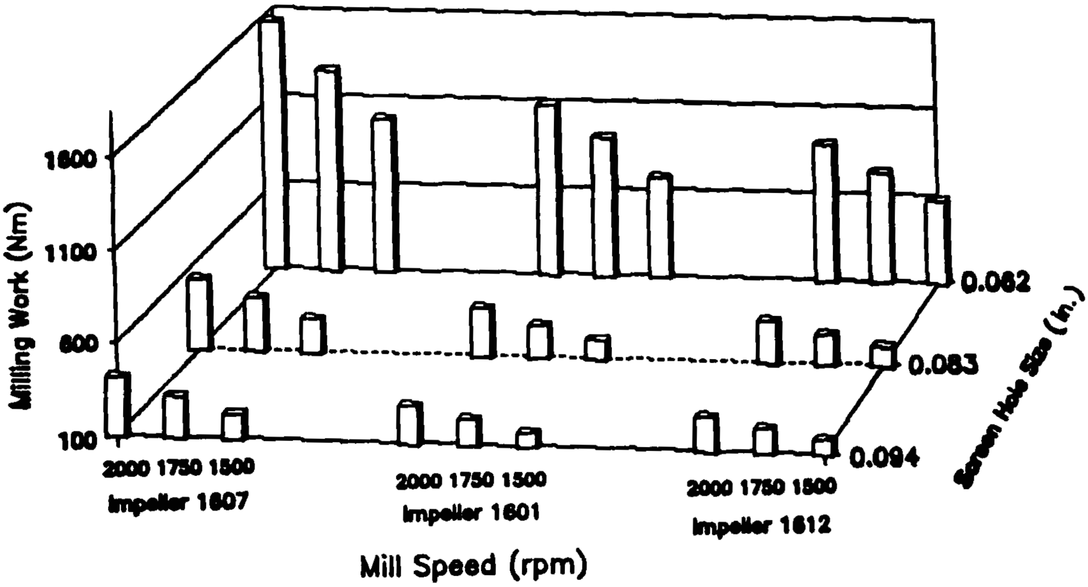

Figure 4. Work required to mill 250 grams of aspirin granulation. Each point is the average of nine measurements.

holes to restrict a much larger percentage of the granulation.

The results also indicate the effect of impeller type on milling time. Impeller 1607, with no outward directed faces, produced the longest milling times. Material impacting with the flat face of this impeller was not directed entirely toward the screen where it could exit. Impellers 1601 and 1612, which did possess outward directed faces, produced shorter milling times. Here, material impacting with the impeller was directed toward the screen. The fact that impeller 1612 produced shorter milling times than impeller 1601 may be explained by the increased amount of particle size reduction achieved with impeller 1612. Larger particles were reduced in size faster and allowed to escape the milling chamber sooner with impeller 1612 than with impeller 1601.

In general, increasing mill speed caused increased milling time. These results could be due to decreased impeller efficiency. At higher speeds, particles colliding with the impellers could be deflected toward the interior of the milling chamber as well as toward the screen. At slower mill speeds, however, the material would not be deflected toward the center of the milling chamber.

Work to Mill a Fixed Sample Size of Granulation

The amount of work which was used to compare the different combinations of impeller type, impeller-screen clearance, mill speed, and screen hole size was the total work required to mill 250 grams of granulation. The effect of the mill variables on the work of milling is graphically represented in Figure 4.

The 0.062 inch screen hole size produced the largest work of milling values, since more work was required to reduce the granules to a particle size small enough to pass through the holes.

Impeller 1607 produced significantly higher work of milling values than the other two impellers. In virtually all cases, impeller 1601 produced significantly higher work of milling values than impeller 1612. The high work of milling values of impeller 1607 are explained by the relative inability of that impeller to move material out of the milling chamber. Material remained in the milling chamber for a longer time and underwent numerous collisions with the impeller. Much more energy was consumed moving material around the milling chamber than toward the screen. The fact that impeller 1601 produced higher work of milling values than impeller 1612 is more difficult to explain since impeller 1612 actually produced more particle size reduction. The sharp outer edge of impeller 1612 may have allowed it to quickly shear the material while its outward directed face then directed the material rapidly out of the milling chamber. On the other hand, the curvature of impeller 1601 merely caused the granules to be dragged between the impeller and the screen causing higher resistance and, therefore, higher work values.

In general, the largest clearance produced significantly smaller work of milling values than the two smaller clearances. This again provided evidence that interaction between the impeller and the screen is an important mechanism of milling action.

Increasing mill speed caused concomitant increases in milling work. This is explained by the fact that the work of milling, as calculated, is directly related to mill speed.

Milling Performance Indices

Milling Work Index

The milling work index values produced by each combination of impeller type, screen hole size, and mill speed are shown in Figure 5.

Impeller 1612 produced milling work index values that were much higher than impeller 1601 or 1607. This is due to the fact that impeller 1612 produced a high degree of particle size reduction without the use of a great amount of mill work. Although impellers 1601 and 1607 had distinctly different mechanisms of action, each produced M_W values that were significantly lower than impeller 1612. Impeller 1601 used an amount of mill work somewhat higher than impeller 1612, but did not produce a high degree of particle size reduction. Impeller 1607 produced a high degree of particle size reduction but used a very large amount of mill energy. Thus, the design of impeller 1612, being a combination of impellers 1601 and 1607, provided the highest levels of milling performance according to the milling work index.

The screens with hole sizes of 0.094 inch and 0.083 inch did not produce significantly different

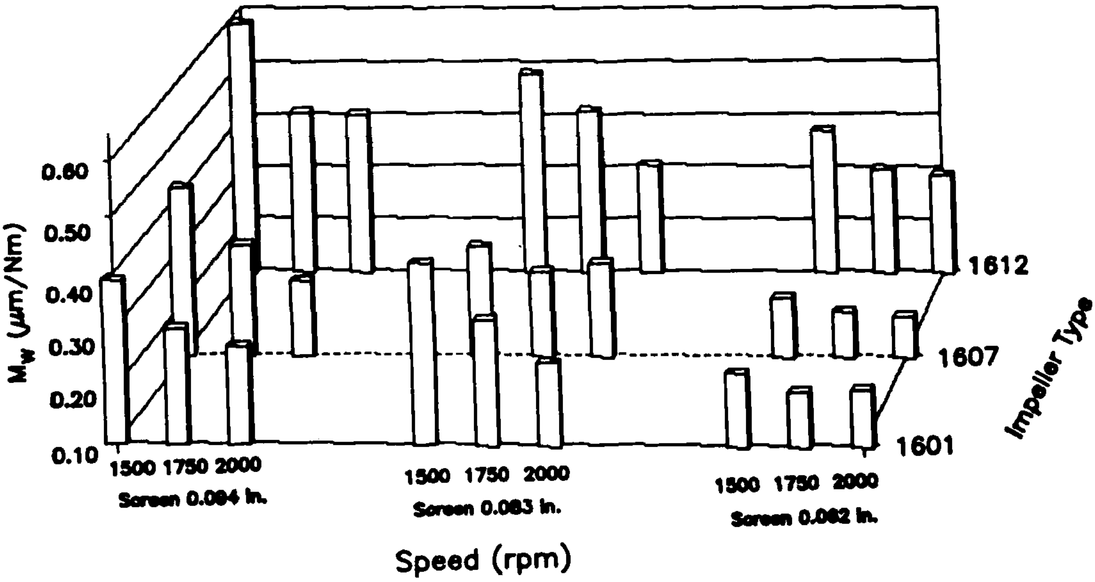

Figure 5. Milling Work Index (M_W) values obtained from milling 250 grams of aspirin granulation. Each point is the average of nine measurements.

milling work index values. However, the 0.062 inch screen hole size produced significantly lower M_W values. It was seen earlier that the smallest screen hole size produced much larger values of particle size reduction and milling work. By severely restricting the passage of material out of the milling chamber, the screen with the smallest holes ensured that the granules underwent much more contact with the impeller. While this caused an increased amount of particle size reduction, it also increased the amount of work required to mill the granulation. In many cases, the reduction in particle size may be the primary consideration leading to the choice of the smaller screen hole size. However, in situations where severe milling conditions or heat accumulation could cause increased degradation or a polymorphic change, the use of a larger screen hole size may be justified.

The milling work index values produced by the the lowest mill speed, 1500 rpm, were significantly greater than those produced by the higher speeds. The speeds of 1750 rpm and 2000 rpm did not produce M_W values that were significantly different. Thus, the lowest mill speed produced the highest levels of milling performance as denoted by the milling work index. These results provide evidence that the area between the impeller and the screen is the site of the most milling action. Higher mill speeds may cause deflection of material away from this area, leading to lower milling efficiency.

Milling Time Index

The milling time index values produced by each combination of impeller type, screen hole size, and impeller-screen clearance are shown in Figure 6. In this case, the effect of mill speed was not significant.

The screens with hole sizes of 0.094 inch and 0.083 inch did not produce significantly different

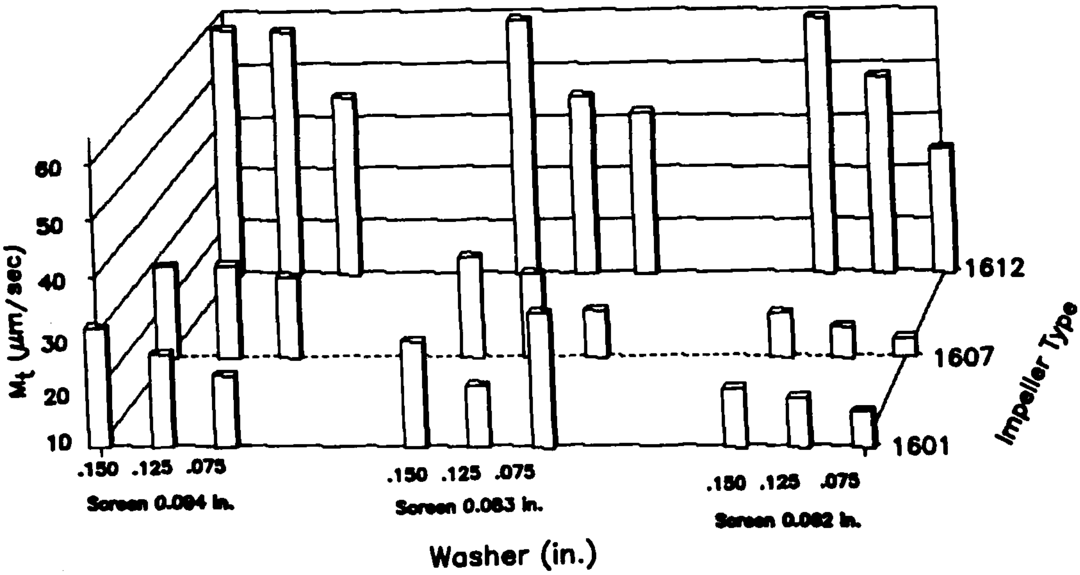

Figure 6. Milling Time Index (M_t) values obtained from milling 250 grams of aspirin granulation. Each point is the average of nine measurements.

milling time index values. However, the 0.062 inch screen hole size produced significantly lower M_t values. This situation is analogous to that seen with the milling work index. By severely restricting the passage of material out of the milling chamber, the screen with the smallest holes caused an increased amount of particle size reduction. However, this also increased the amount of time required to mill the granulation. The choice of a larger screen hole size may again be justified in situations where a prolonged milling time could cause heat accumulation leading to increased degradation or a polymorphic change.

Impellers 1601 and 1607 did not produce milling time index values that were significantly different. However, impeller 1612 produced milling time index values significantly greater than the other two impellers. The dramatic increase in milling performance caused by impeller 1612 can be explained in a manner analogous to that of the milling work index. Impeller 1612 produced a high degree of particle size reduction while at the same time using the least amount of milling time. Thus, by designing the desirable features of impellers 1601 and impeller 1607 into impeller 1612, overall milling performance, as denoted by the milling time index, was dramatically increased.

In general, decreasing impeller-screen clearances resulted in increased M_t values. As clearance decreased, an increased percentage of material was trapped between the impeller and the screen. More material was then milled with each pass of the impeller, leading to increased milling effeciency.

In conclusion, the instrumented mill was shown to be a valuable tool in determining the effect of mill variables on the milling of a granulation. Screen hole size had the greatest influence on milling time and work as well as particle size reduction. However, examining the overall milling process, as denoted by the milling performance indices, revealed the influence of the other mill variables. In that case, impeller design was shown to be an important factor as well.

In the milling of granules, particle size and distribution are the primary considerations. However, in cases where milling can have deleterious effects on material stability or behavior, the choice of milling conditions should also be considered.

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