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OBTAINING A SCALABLE AND REPRODUCIBLE MICRONIZATION PROCESS WITH HIGH YIELDS USING 5 GRAMS OF THE PRODUCT

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ABSTRACT

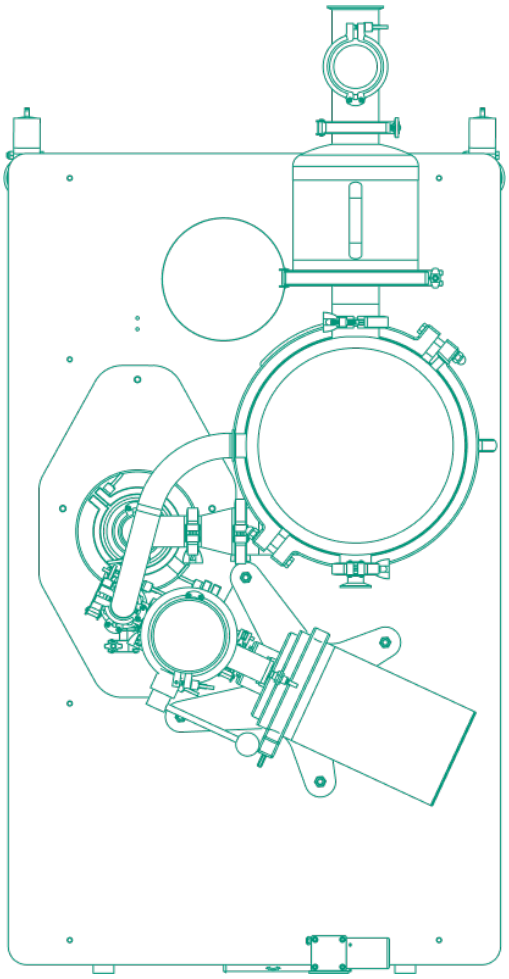
Pharmaceutical companies put valuable time and effort into their next big product. From beginning formulations, product creations, pre-clinical trials, clinical trials, etc... There is major spending and long hours of work that are behind the scenes, helping the product become a reality. With micronization being key to the pharmaceutical industry, along with milling machinery that performs the micronization process, it is very important to always find ways of making the process more streamlined and more efficient.

The big questions are:

- How can operators and formulators recover the most product at the end of micronization?
- What kind of machinery setups are needed to achieve a more efficient process?
- Will the process be able to be maintained and easily replicable, so that there is consistency?

In this whitepaper, we examine the yield values of the SSM44 mill in terms of powder output, along with observing the amounts of product that can be recovered for use versus the amount of starting product and how the process could possibly be scaled up for bigger and faster production.

Learn more about the verification of yield values of the SSM44 for process improvement and how it can help pharmaceutical companies make use of recovered product (produced at high values) during initial testing trials, before scaling up to commercial development.
See how Schedio can help you with maximizing your quantity of product by using smaller batch sizes (5g-10g) and making the most of it by recovering a high value of product after the micronization process.



Schedio Spiral jet mill SSM44

ONLY 5gr. TO SET A SCALABLE PROCESS

CONTENT

PROBLEMS AND CHALLENGES THAT FORMULATORS FACE

Getting the perfect machinery setup is ideal for any formulator or innovator company. It can make the entire micronization process seamless and produce a high quantity of usable product. For most formulators it can be difficult to produce a good amount of product during micronization because they are working on a smaller scale of machinery at the beginning phases, which means lower yield values and lower batches for trials. This can put the commercial phase of development at risk, and mass production process on pause because of the inability to reproduce the process at a larger scale.

Sometimes you are only able to carry out feasibility trials due to the amount of usable product at the end, which means there is only enough for one testing trial and risk of not being able to re-create the same process for the product. Also, it is not easy on a smaller scale to recover high quantities of product because smaller machines use lower yield values.

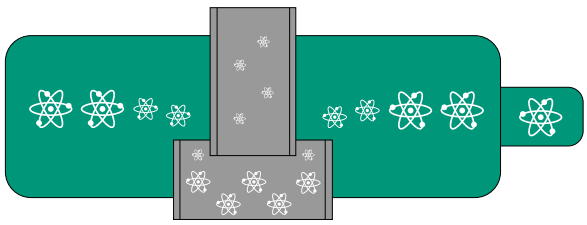
VERIFYING THE YIELD VALUES OF THE SSM44 MILL TO SEE THE OUTCOMES

As we know, Spiral Mills are devices widely used in the micronization process of powders, as they allow to obtain an excellent degree of particle size reduction and a restricted particle size distribution. They are devices without moving mechanical elements, which makes them robust and reliable devices.

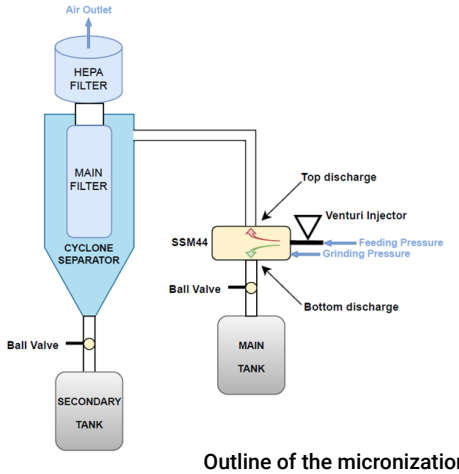
The powders are introduced into the micronization chamber where, once englobed by the swirling motion of the gas (air or nitrogen), they fragment due to the collision between themselves. The larger particles remain in the flow while the smaller particles are evacuated through an outlet in the center, called the static classifier; or a rotating device called dynamic classifier which evacuates a small fraction of particles at a time.

The SSM44 is a spiral mill with a 44mm diameter micronization chamber. It is equipped with a screw feeder to convey the powder into the injector, a venturi injector that feeds the powder tangentially to the chamber and has a double outlet (bottom-discharge configuration), a lower one directed to a primary collection tank, and an upper one that leads to a cartridge filter and a secondary tank. The SSM44 is able to process small batches of powder between 10 g/h and 600 g/h and was used in testing to verify the yield values of collected powder during the micronization process.

The main parameter for micronization is the specific energy, which is the amount of energy provided by gas and distributed on the particles inside the chamber. Energy given by gas is a result of the pressure in use, dimensioning and number of grinding nozzles, while the amount of particles inside the chamber depends on the feed rate, determined by the feeder. These two sub-parameters (gas pressure and feedrate) are key in order to reproduce or scale up a process. The geometry of the nozzles shall be replicable and scalable, and this depends on each manufacturer, but what is also important is that the feeder is there, so that you can reproduce the same constant amount of particles inside the chamber.
With most small-scale jet mills used for early development, the feeder is not there, and the feeding is done manually, which means that the test is not reproducible, nor scalable. Usually when a feeder is there, it means that the machine is also slightly larger, and therefore requires a higher minimum quantity of product to be handled, in order to properly use the feeder and obtain a reproducible / scalable process.



Top/Bottom Outlet



Outline of the micronization process

The focus of the test was to see how the SSM44 could maximize the quantity of micronized powder collected under the mill and minimize the quantity of powder dragged by the fluid towards the filtration system (because specific applications require that the product must never come in contact with fabrics or materials that usually compose cartridge filters). The test also included finding aspects that can be optimized in order to maximize the quantity of powder collected in the main tank, along with high yield values that allow formulators to scale the production to a bigger size and improve their process.

During the trials we were able to test with only 5 grams of product, obtaining a good yield, along with using a feeder, with a constant feeding. It ensured that the process was reproducible and scalable. The trials were performed by adjusting the process parameters, while examining 3 substances (powders):

- Bicarbonate
- Lactose
- Talc

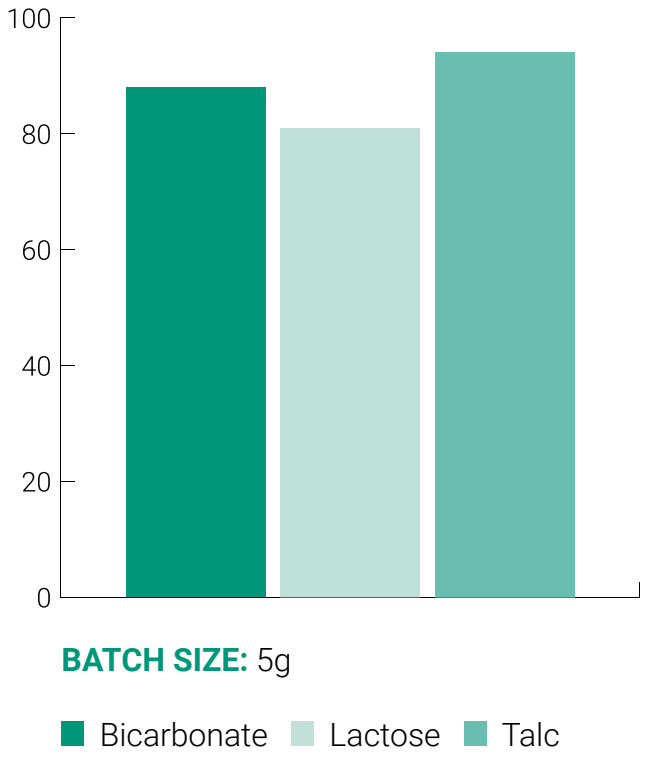
The parameters were set by:

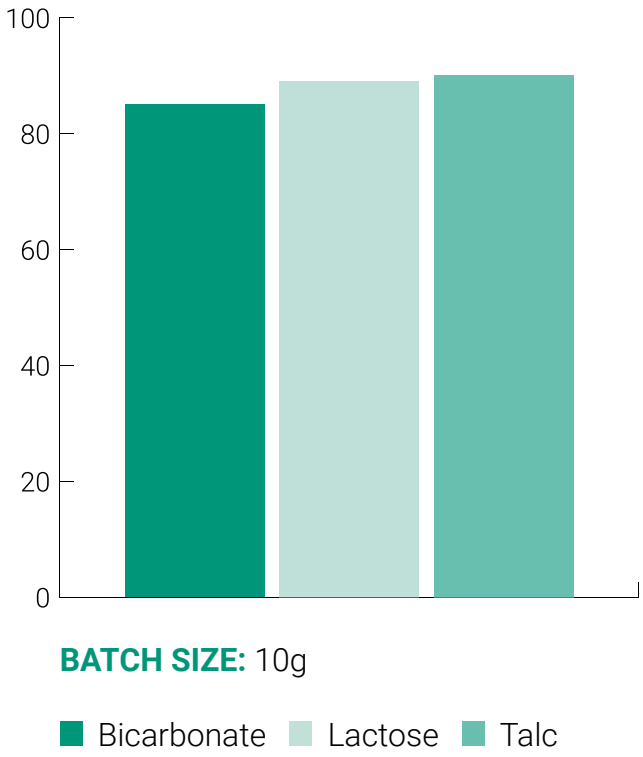
Quantity of powder processed	5g - 10g
Feeding rate	300g/h
Feeding Pressure	8bar
Grinding Pressure	from 6.5bar to 7.5bar

For each substance (Bicarbonate, Lactose, Talc), multiple runs were carried out to obtain the results as the operative parameters varied, resulting in average yield values of 85% from batch testing in accordance with the process parameters (Grinding Pressure, Feeding Pressure and Feeding Rate). The results obtained with lactose and talc, can be considered equivalent to a 90% global yield value, while trials done with bicarbonate resulted in a lower yield value at 10% less because of the bulk proprieties of the powder:

- Hardness
- Structure
- Geometry of the particles
- External factors such as humidity and exposure to ambient air

YIELD VALUES: 5g.and 10g.





IN CONCLUSION

The yield values of the SSM44 have been evaluated at 90% (talc, lactose and bicarbonate) with both 5g and 10g batches. It has shown that by increasing the mass of the batch, the yield value on the same plant should increase as well.

Results obtained:

GP	FP	FR
[bar]	[bar]	[g/h]
7.5	8	300
7	8	300
6.5	8	300

Bicarbonate		
In [g]	Out [g]	%
10,06	8,295	82,46
10,025	8,71	86,88
10,008	8,55	85,43

avg. % 84,92

Lactose		
In [g]	Out [g]	%
10,079	9,08	90,09
10,062	8,96	89,05
10,067	8,82	87,59

avg. % 88,91

Talc		
In [g]	Out [g]	%
10,09	9,034	89,53
10,084	9,202	91,25
10,05	9,036	89,91

avg. % 90,23

GP	FP	FR
[bar]	[bar]	[g/h]
7.5	8	300
7	8	300
6.5	8	300

Bicarbonate		
In [g]	Out [g]	%
5,098	4,413	86,56
5,106	4,672	91,5
5,104	4,323	86,7

avg. % 87,59

Lactose		
In [g]	Out [g]	%
5,114	4,241	82,93
5,122	4,323	84,4
5,115	3,888	76

avg. % 81,11

Talc		
In [g]	Out [g]	%
5,128	4,729	92,22
5,116	4,674	91,36
5,1	4,933	96,72

avg. % 93,44

The system has a great level of yield, by upscaling the system it is expected to obtain great results on a larger scale… making the production process easy to reproduce.

Schedio has done work to have a machine that is as compact as possible to help formulators and innovator companies get back a decent amount of product from trials, along with being able to reproduce product easier and on a larger scale. It has been confirmed and verified that the system has an overall yield value of 90% at the usual process parameters of the SSM44 plant. We are able to appoint and suggest points of optimization that can increase the yield value up to 5%. Let us help you make the most out of smaller batch sizes (5g-10g) by recovering most of the useable product, which can help the reproduction of the process move to a bigger scale for commercial development, if needed.

Are you ready to maximize your quantity of product during micronization, saving you cost and time on your production and clinical trials? We can help you obtain higher yield values on a small scale, so that you are able to reproduce on a bigger scale with a more, efficient process.

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