

Basic Principles of Dry Granulation and Roller Compaction Technology

This white paper explains the basics of the dry granulation process in pharmaceutical manufacturing, including a detailed understanding of the roller compactor.

Granulation is a process in which powder particles are made to adhere to each other, resulting in larger, multiparticle entities, so called granules. If such a process is performed without adding liquids, this is called dry granulation.

In dry granulation, the powder blend is compacted by applying a force onto the powder, which in general causes a considerable size enlargement. The compacts thus obtained are called briquettes, flakes or ribbons.

In order to obtain the desired granules, the compaction process is followed by a milling step.

PROCESS BASICS

Principally there are two methods to obtain the compacts when using dry granulation: slugging and roller compaction.

Slugging

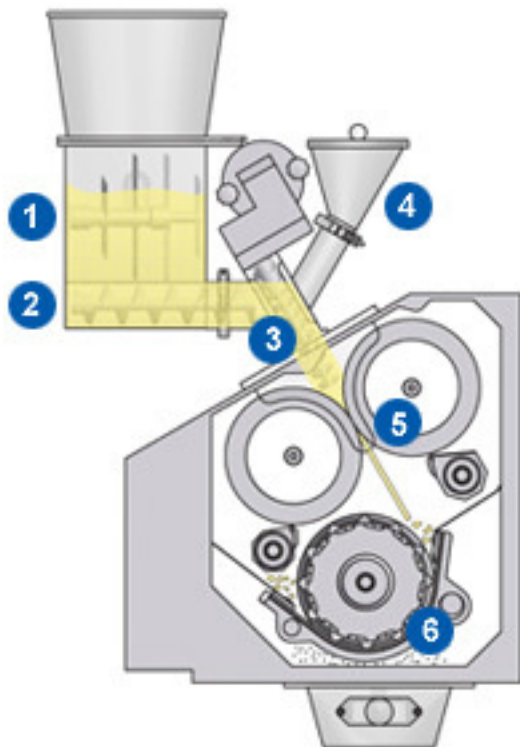
If a tablet press is used for the compaction

process, the term slugging is used. But since particles with a small particle size do not flow well into the die of a tablet press, the results are weight differences from one tablet (slug) to another. This in turn causes large fluctuations in the forces applied onto the individual slugs, with translates in variations of the slug's mechanical strength. Therefore, the properties of these granulates obtained by milling the slugs cannot be controlled well either. This is one of the main reasons why slugging is hardly used any more as a dry granulation method.

Roller Compaction

A roller compactor generally consists of three major units:

1. A feeding system, which conveys the powder to the compaction area between the rolls
2. A compaction unit, where powder is compacted between two counter rotating rolls to a ribbon by applying a force
3. A size reduction unit, for milling the ribbons to the desired particle size.



Roller Compaction

- 1 Inlet funnel with agitator
- 2 Feed auger
- 3 Tamp auger
- 4 Small quantity inlet funnel
- 5 Press rollers with ribbon
- 6 Rotor with desired granules

PRODUCT QUALITY ASPECTS

Process Parameters: Force and Gap

The powder is compacted between two rolls by applying a force, which is the most important parameter in the dry granulation process. The applied force is expressed in kN/cm, being the force per cm roll width. Occasionally the press force is also indicated in bar. This, however, merely represents the pressure within the hydraulic system, and is in fact not an appropriate measuring unit for the force applied onto the powder.

At a given force, depending on the amount of powder conveyed to the rolls, the powder will be compacted to a predefined ribbon thickness.

A precise process control is essential to obtain equal granules properties from a homogenous ribbon. (For more on that topic see the PAT section on the next page.)

Variable and Fixed Gap Roller Compactors

Roller compactors can be divided into two categories: one is equipped with a fixed gap, the other one with a floating gap. Both consist of the three major units as explained above but differ in the way in which the smallest distance (gap) between the rolls is realized.

When a fixed gap is installed, the amount of powder drawn in into the compaction area between the rolls is inconsistent, which results in different forces applied to

the powder bed. Like in slugging, this will cause large fluctuations in the ribbon and granulate properties.

With floating gap (e.g. GERTEIS®-Machines) the distance between the rolls change according to the amount of powder provided. The force applied to the powder remains constant. This ensures that property fluctuations in the granules are reduced to a minimum.

Milling

With our integrated models, the ribbons are being milled right after compaction using a screen with a given mesh size, thus limiting the upper particle size.

This milling process should be performed as gently as possible to avoid creating too many fines.

PAT (Process Analytical Technology)

The GERTEIS® roller compactors are able to control and measure all product quality relevant parameters (e.g. force, gap and roll speed) online in order to fulfill the requirements of the pharmaceutical industry for a well controlled and documented manufacturing process. All the parameters are calibrated and validated. Additionally, in order to cope with batch to batch variations, our machines are fitted with control systems to allow equal granule properties during manufacturing according to PAT.

APPLICATIONS

Improving Flow Ability

Dry granulation is used for increasing the bulk density of powders, whilst increasing the particle size, resulting in better flowing material, which is a prerequisite for manufacturing capsules and tablets on high speed production equipment.

Furthermore, bonding the particles of various substances together during the compaction

process reduces the tendency to segregation of powder particles of different substances. This results in an improvement of the homogeneity of the active ingredients (API) within the powder blend, causing an improvement of dose uniformity of such dosage forms.

Wet- & Dry Granulation

In contrast to wet granulation, dry granulation is a continuous process. This results in various economical advantages. Nowadays the throughput of common dry granulation systems can reach 400kg/h.

Dry granulation systems require comparatively fewer investments into buildings or equipment. Coupled with lower maintenance costs, this results in a much higher overall profit.

Thanks to countless innovations, nearly 100% of all dry powders can be processed on dry granulation systems.

Further Advantages of Dry Granulation:

- Minimal floor space
- Large throughput of material (highly efficient process)
- Continuous process
- Highly energy efficient; no heat for drying and no air conditioning required as for other granulation techniques
- Ultra-high containment options are available to avoid contamination of manufacturing areas and personnel by high-potent actives
- Low running costs

FOR MORE INFORMATION

Gerteis Maschinen + Processengineering AG

Stampfstrasse 85
8645 Jona Switzerland
Phone +41 55 222 55 22
Fax +41 55 222 55 23
Service Hotline +41 55 222 55 11
info@gerteis.com