Dry Agglomeration Technology

Using

BEPEX Roller Compaction Technology

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The objective of this paper is to present a detailed overview of the theory and practical applications for granulation of dry powders using BEPEX roller compaction technology.

Introduction

Approximately 75% of all pharmaceutical products produced today are sold in solid dosage form. Examples include: a capsule; tablet or powdered drinks. Material for these products can undergo many processing steps including (but not limited to): milling; blending; classification; drying; granulation and pressing. Granulation (or sometimes also referred to as agglomeration) is the art and science behind enlarging the average particle size. Granulation of material is usually required to enhance flow properties required for processing operations.

In addition to enhancing flow properties, there are other reasons why granulation is performed. Some of these reasons include:

Composition uniformity – Mixtures and blends of differing bulk densities and particle sizes have a tendency to segregate. Proper granulation techniques will yield similar bulk densities and offer excellent control over particle size.

Dust control - Very fine or micronized material has a tendency to become airborne. This can cause hazardous conditions for operators. The stricter operator exposure levels (OELs) results in an ever-increasing need for minimizing dusting.

Improvement of dispersion rates – Granular materials can absorb liquids more readily. This leads to faster dissolving and better dispersion.

Three methods of granulation (agglomeration) commonly performed include:

- Direct Compression
- Wet Granulation
- Dry Granulation

Bonding Mechanisms

There are two different bonding mechanisms which hold particles together on both the microscopic and macroscopic level:

Bonding with material bridges (also known as composite agglomeration / wet agglomeration) will include:

- Chemical bonds – reaction, sintering and partial melting
- Adsorption layers
- Liquid bridges – usage of binders

Bonding without material bridges (known as press agglomeration / dry granulation) will include:

- Molecular forces – van der Waals' forces
- Electrostatic forces
- Magnetic forces
- Valence forces

The strongest force observed is by far the van der Waal's force, the attraction force between molecules. The molecular attractive force is an inverse squared relationship to the distance. During compaction, the material is squeezed such that these forces bind all the material together to form a solid flake.

Key Charateristics

During testing and operation of this equipment, there are several key material characteristics to consider. These include (but are not limited to): bulk density; particle size distribution; angle of repose; particle shape; chemical composition and shear trials. These characteristics reveal a tremendous amount of information on the handling (or flow) characteristics of the material both before and after compaction.

Prior to testing, the operator must ensure the testing material is dry. Roller compactors cannot process a slurry or pasty material. This technology does work well with moisture sensitive products and those that are susceptible to heat. Most pharma-compaction processes do not see a temperature rise of more than 10°C from either the compactor or the mill. It is critical that the test engineer achieves the correct compaction force. If there is inadequate compaction force, the material will return to its original state in the granulator (post-compaction milling). If the pressure is too high, the product will be overpressed. Overpressing is observed when the material comes out discolored, extremely hot or severely cracked or plasticized. The proper press force will yield a well-compacted product that also mills easily with minimal fines generation.

Densification Theory

The basic theory of compaction states that material is denisfied and then formed into granules which achieve a higher bulk density. Material is densified on roller compaction equipment according to the following theory:

Assuming α equals densification factor then:

$$\alpha = V_{in} / V_{out}$$

where V_{in} is the volume of material fed into the machine and
V_{out} is the volume of material that exits the machine

Defining further the volume in and out:

$$\alpha = (fn * Geo_s * RPM_s) / (fn' * Geo_r * RPM_r)$$

where: fn and fn’ is a function or constant of the material
$Geo_{s\&r}$ are the geometry of the feed screw and rolls
and $RPM_{s\&r}$ is the rpm of the feed screw and the compaction rolls

This equation can be further simplified considering steady state processing, the functions (fn and fn’) and the geometry’s are constants. This will result in the following:

$$\alpha = C * RPM_s / RPM_r$$

This result shows that the densification of the material is a direct function of the speed of the feed screw versus the speed of the rolls.

To summarize the above relationship, if the product is to be made more dense, either the feed screw speed can be increased or the rolls speed can be decreased. Conversely, if the product is overpressed, the feed screw speed can be decreased or the roll speed can be increased.

Figure 1

Mechanics of Design

Figure 1 shows an illustration of the Bepex Pharmapaktor. There are two counter rotating rolls, which are fixed in position. The force between the rolls is directly measured by a strain gauge. A feed screw feeds material into the nip area (the compaction area between the rolls). This feed screw has a constant pitch, but a tapered outside diameter. The function of this design is to pre-compress, de-aerate the material and consistently feed the compaction rolls. By varying the speed of this feed screw, the amount of material fed into the compactor can be varied (V_{in}). The speed of the feed screw is driven by an inverter duty motor.

The rolls are fixed in the bearing housings so they cannot float. The rolls are precisely driven by a counter rotating gearbox which is in turn driven by an inverter duty motor (V_{out}). A clutch mechanism enables the rolls to be quickly removed for cleaning.

Compaction Head

The objective of compaction is to compress all the material fed into the machine. To help eliminate uncompacted fines from passing through the compaction head, cheek plates are used to seal the gap between both rolls. Additionally, the rolls are machined in a concave fashion, mechanically the gap is almost totally closed to prevent fines from leaking out. The tolerance between the roll sides and the cheek plates must be very tight, less than 0.8 mm. This minimal spacing is crucial since seals are not used in this region. Seals or gaskets have a tendency to wear and therefore become introduced into the final product. (See Fig 2).

Figure 2

Equipment Control

The success of any piece of equipment depends on the control involved for making a consistent product. The most important parameter to control during compaction is the press force between the rolls. The press force is directly measured by an electronic strain gauge. This strain gauge sends a signal to a controller interfaced with a PLC. A desired press force is programmed into the controller. During processing, the roll speed is kept constant. If the signal from the strain gauge indicates a low press force, the controller will send a signal to the VFD driving the feed screw motor. The feed screw motor will then increase in speed, resulting in a higher compaction force back to the original set point. The opposite scenario holds true when the press force goes over a certain pre-set limit. This type of control is only the basics of typical systems produced today. Many control panels have recipes for different batches and data logging abilities to examine results.

Granulation Equipment

More often than expected, the trickiest part of granulation is the milling of compacted flakes. Milling (granulation) of these flakes should be done with a low energy type of mill. Either a bar and rotor type of mill or a conical screen mill works best for these applications. The rotor to screen spacing and the type of screen used has a big impact on the type, size and percentage of fines in the final granulated product. For some difficult to process materials, recirculation loops are used. This system utilizes a single deck screener under the granulator to separate unwanted fines from the final product. These fines are then re-circulated back to the feed hopper and processed in proportion with the virgin feed material. Processes with this type of loop can yield an extremely tight particle size distribution of finished product.

Benefits of dry granulation

The overall cost of process equipment is about ¼ to ⅓ that of conventional wet agglomeration equipment. In addition, the overall processing time is significantly faster. Compactors typically used in the pharmaceutical industry can produce from 25kg/hr to 1000 kg/hr of finished product. On certain material, the shelf life can also be extended. This can be attributed to the total absence of moisture during processing. Even the best fluid bed dryers may leave 0.1% moisture in the product, which can affect shelf life. Automated operation is another benefit of this equipment. Many systems have been built and validated where PLC's can completely start, run and shut down the equipment when finished processing eliminating operator involvement and additional costs.

For more information, please contact Hosokawa Micron Powder Systems.

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