GRANU TOOLS™

ALL WE DO IS
POWDER FLOW
CHARACTERIZATION

OPTIMIZED POWDER CHARACTERIZATION METHODS
FOR PHARMACEUTICAL APPLICATIONS

Powders are widely used in pharmaceutical applications as excipient or active ingredient in formulations. Consequently, many production processes are dealing with powders: tableting, wet and dry granulation, blending, caps filling, etc. Therefore, any progress in the understanding of powders flowing behaviours can have huge consequences for pharmaceutical industries. Indeed, a powder with inappropriate flowing properties can cause serious complications in production lines (clogging, agglomeration, segregation, etc.) [1].

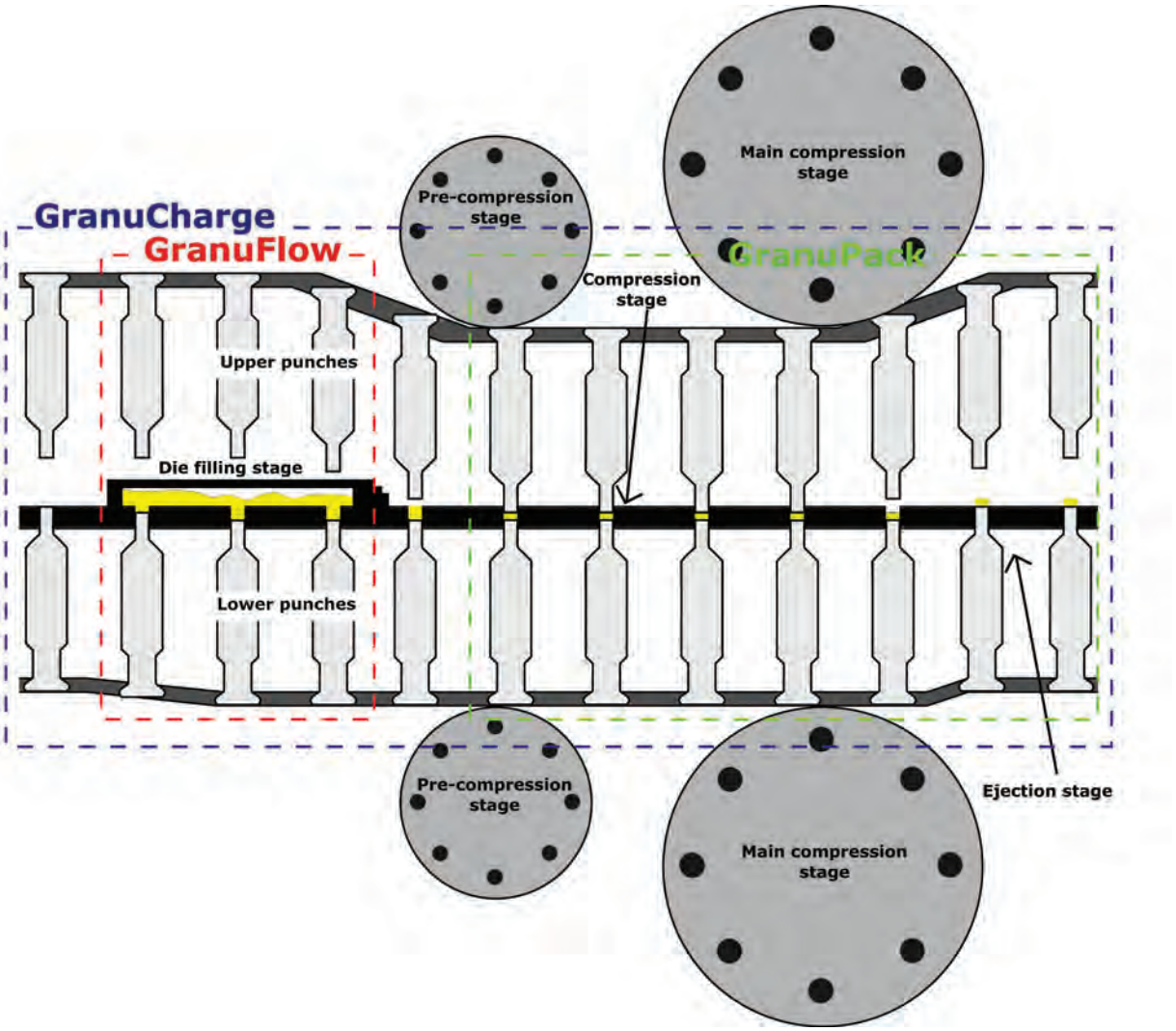
APPLICATIONS

TABLETTING PROCESS OPTIMIZATION

In pharmaceutical industries, it is well-known that the variation in composition and the quality of tablets are determined by material properties and process conditions.

Tablets are manufactured by compressing dry powders or granules in a die. This process consists in three primary stages: die filling, compaction, and ejection. Powders flowability and compressibility during die filling process controls the tablet composition, the tablet properties as well as the homogeneity. Therefore, the study of die filling process parameters has a significant role in controlling tablet manufacturing industry [2].

TO OPTIMIZE TABLETING PROCESS, GRANUTOOLS OFFERS A WORKFLOW OF TWO INSTRUMENTS: **GRANUFLOW** FOR DIE FILLING, AND **GRANUPACK** FOR POWDERS COMPRESSIBILITY.



PNEUMATIC VACUUM CONVEYING OPTIMIZATION

Powder transfer by pneumatic conveying is a common means of transport for a wide variety of pharmaceutical, and food materials. The use of either dense- or dilute-phase pneumatic transport can be applied to a wide variety of pharmaceutical operations including the loading of blenders, sifters, mills, capsule fillers, tablet presses, and even finished tablet and capsule handling without damage to the finished product.

Due to the friction between the grains and the system wall, the ability of the powder to create electrical charges is a critical parameter in this process because these charges induce clogging. Moreover, powder flowability is an important parameter.

WITH **GRANUDRUM** AND **GRANUCHARGE** INSTRUMENTS, GRANUTOOLS PROPOSES LEADING EDGE PHYSICAL CHARACTERIZATION TOOLS TO SOLVE PROBLEMS ENCOUNTERED DURING PNEUMATIC PROCESSES.

DRY POWDER INHALERS (DPI) OPTIMIZATION

Inhalers have been developed because of difficulties when using the conventional metered dose inhaler (MDI). Dry powder inhalers (DPI) in general are easier to use than the MDI and cause fewer irritant effects. Unlike the MDI few patients develop a poor inhalation technique with continued use of DPI.

The inspiratory flow necessary to achieve a therapeutic effect is critical with Dry Powder Inhalers (DPI). Moreover, this technology faces with various problems: powder ageing, agglomeration induced by electrostatic charges, blend homogeneity during capsule filling, ...

TO UNDERSTAND AND IMPROVE DPI TECHNOLOGY, GRANUTOOLS RECOMMEND THE USE OF THE **GRANUPACK** FOR THE FLOWABILITY, AND THE **GRANUCHARGE** FOR ELECTRICAL CHARGES BUILD UP DURING API ADMISSION.

GALENIC FORMULATION OPTIMIZATION

Active Pharmaceutics Ingredient (API) must be incorporated into a suitable form to be transported to the needed body parts properly. Therefore, the composition of the blend (excipient + API) and its flowability must be precisely characterized.

Indeed, knowing the flowing behaviour in quasi-static and dynamic conditions alows to be representative of every process parts.

MANY INDUSTRIES ARE ALREADY USING OUR COMBINATION OF TWO INSTRUMENTS **GRANUHEAP** (IMPROVED HEAP SHAPE ANALYSER) AND **GRANUDRUM** (RHEOMETER FOR POWDER) FOR A COMPLETE PROCESS CHARACTERIZATION.

[1] F. Boschini et al., 2015. **International Journal of Pharmaceutics** 494 312–320.

[2] Varun Kumar Ojha et al., 2017. **Neural Computing and Application.**

GRANUTOOLS WORKFLOW FOR POWDER CHARACTERIZATION

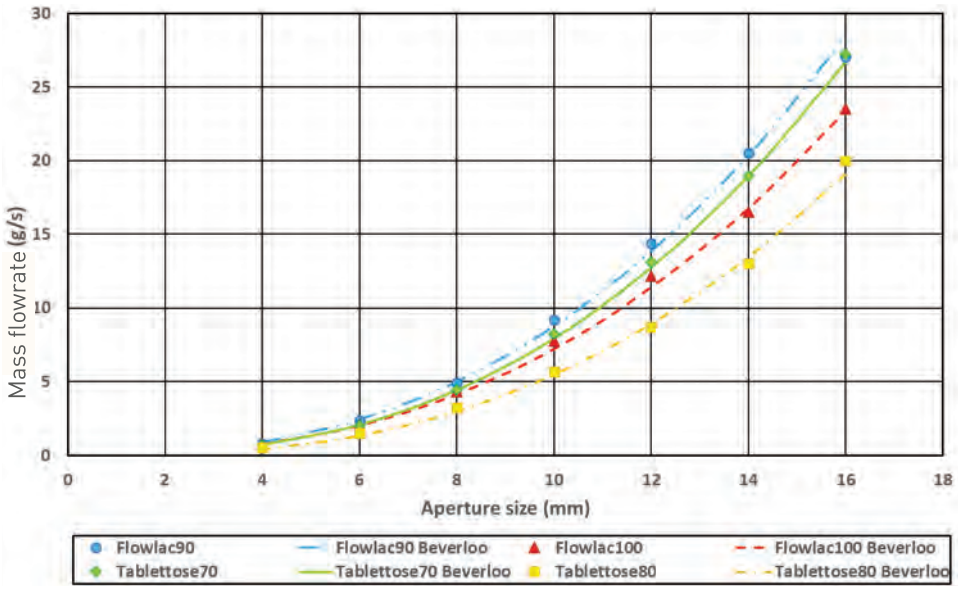
GRANUFLOW™

NEW IMPROVED LABORATORY SILO

GranuFlow is an improved laboratory silo compared to the "Flow Through An Orifice" method described in the Pharmacopeia (USP1174). GranuFlow is a straightforward powder flowability measurement device composed of a silo with different apertures associated with a dedicated electronic balance to measure the powder flowrate. This parameter is computed automatically from the slope of the mass temporal evolution measured with the balance. The aperture size is modified quickly and easily with an original rotating system. Thus, the flowability in a die filling configuration can be easily achieved with great accuracy (1%).

The following figure shows that flowability classification between different grades of lactose can be easily achieved.

MASS FLOWRATE
VERSUS APERTURE SIZE >

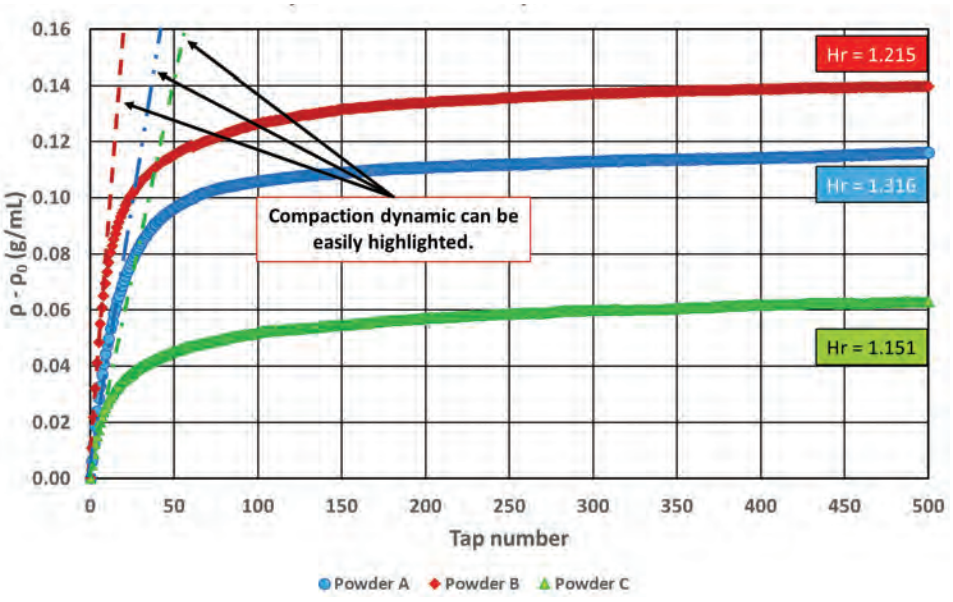


GRANUPACK™

HIGH RESOLUTION TAPPED DENSITY ANALYSER

In addition to the flowability, the powder packing fraction is the other key parameter for a tabletting process. Indeed, a high packing fraction reduces the porosity of the produced part and give information about powders compressibility. Therefore, a precise measurement of the range of packing fractions accessible by the powder is also necessary. Contrary to the classical manual tapped density measurement, GranuPack instrument measures a compaction curve (density plotted as a function of the tap number) very precisely (0.4%) [3]. The precision results from the measurement automation (any influence of the operator) and from the use of an initialization protocol. The bulk density, the optimal density, the compaction range and the compaction speed are extracted from this compaction curve. Moreover, the compaction curves of different samples can be compared to evidence differences regarding density, compressibility and flowability [4].

BULK DENSITY VARIATIONS VERSUS TAPS NUMBER - GRANUPACK >

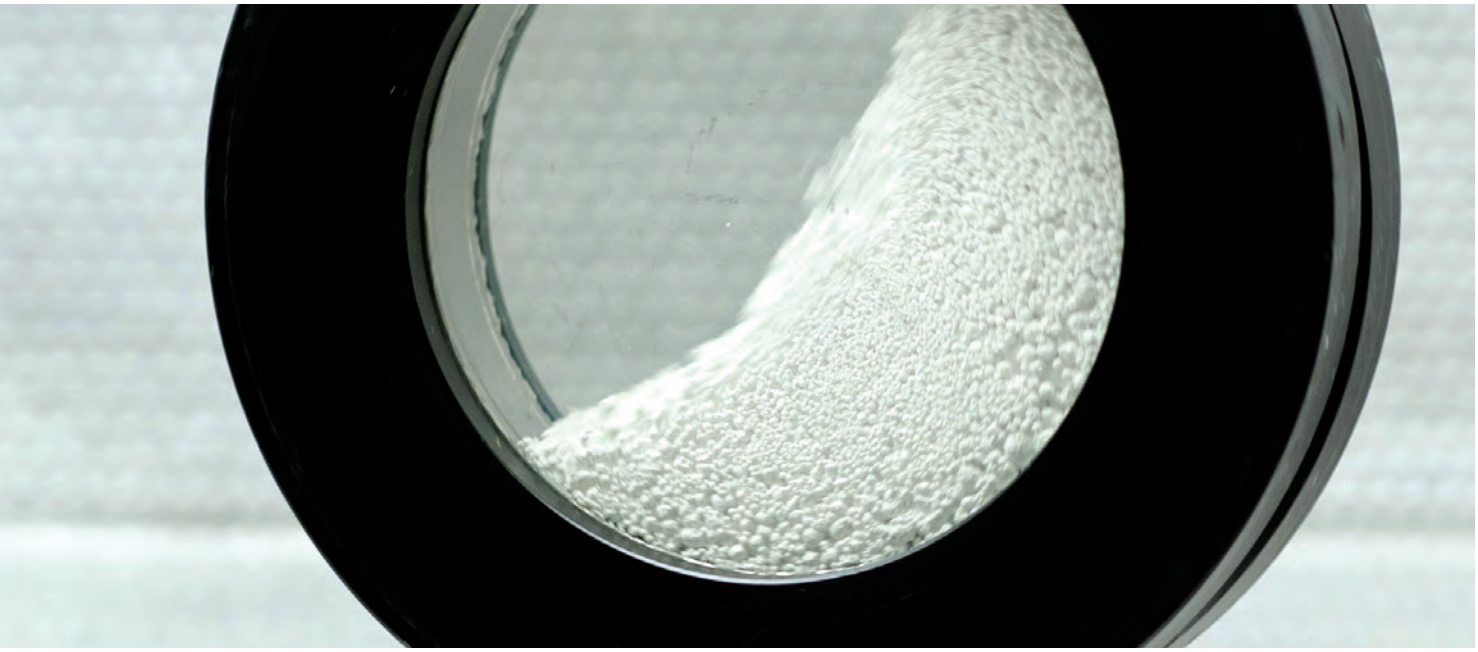


[3] Powder Technology 224, 19–27 (2012).

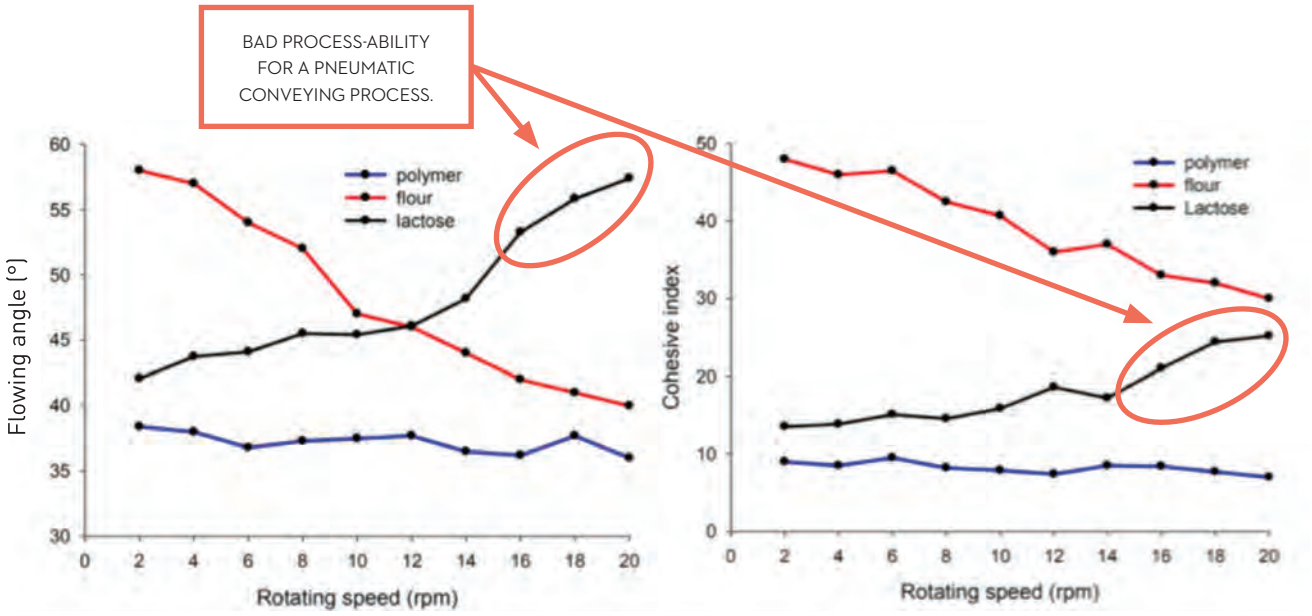
[4] Lumay et al., 2006. Applied Physics Letters 89.

GRANUDRUM™

NEW POWDER RHEOMETER



GranuDrum instrument is an automated powder flowability measurement method based on the rotating drum principle. A horizontal cylinder with transparent sidewalls is filled with the sample. The drum rotates around its axis at a fixed angular velocity. A CCD camera takes snapshots for each velocity. The air/powder interface is detected on each snapshot with an edge detection algorithm. Afterward, the average interface position and the fluctuations around this average position are computed. Then, for each rotating speed, the flowing angle α_f is computed from the average interface position and the dynamic cohesive index, σ_f, is measured from the interface fluctuations. In general, a low value of the flowing angle α_f corresponds to a good flowability. Thus, it is possible to compute the powder flowing behaviour at various velocities, and then, to predict the optimal process speed.

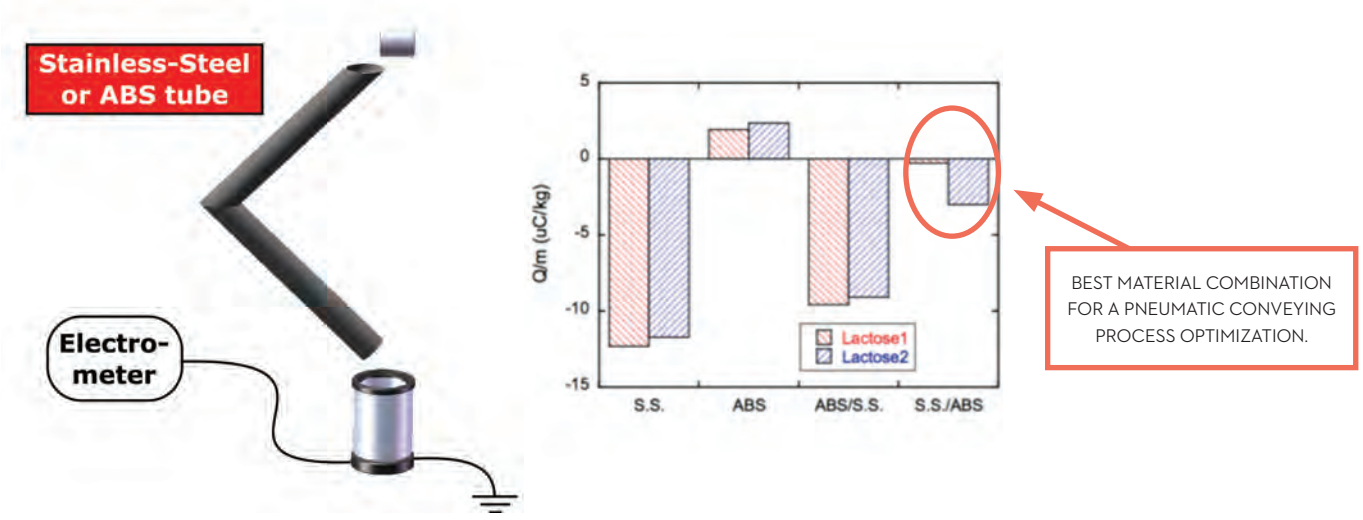


GRANUCHARGE™

TRIBOELECTRIC EFFECT ANALYSER

The presence of electrostatic charges inside a powder is known to influence drastically the material flowing properties. The triboelectric charges produced at the contacts between the grains and at the contacts between the grains and the container produces electrostatic forces. On the one hand, the triboelectric effect is useful for many applications, but on the other hand, the triboelectrification causes complications (powder sticking on pipes surface, agglomeration). Thus, to help industries to quantify this phenomenon GranuTools develops the GranuCharge instrument. It measures automatically and precisely the quantity of electrostatic charges created inside a powder during a flow in contact with a selected material.

This instrument allows highly accurate charge density measurements (0.5nC). Moreover, the results allow to classify the powders and to detect problematic samples before their introduction inside the pneumatic conveying device. Finally, the pipes material influence can be investigated, and the optimal one selected to limit electrical charge build up during the process.



GRANUHEAP™

IMPROVED HEAP SHAPE ANALYSER

GranuHeap instrument is an automated heap shape measurement method based on image processing and analysis. The powder heap is created by following a rigourous procedure. This step ensure the heap reproducibility and avoid user dependency. Once it is done, a controlled rotation of the support coupled to pictures analysis allows obtaining different heap projections. A custom algorithm treatment determines the heap angle with great accuracy (5%) and also the heap shape fluctuation linked to powder cohesive interparticle forces.

Therefore, the powders flowability classification can be easily achieved.

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