



ACHEMA
2018

WINNER OF THE INNOVATION AWARD
CATEGORY „PHARMACEUTICAL TECHNOLOGIES“

REPRINT

QUICKER AND MORE EFFICIENT DRY GRANULATE PRODUCTION

TwinPro - Glatt wins Achema Innovation Award for granulation batch process

Decisive facts for operators

- » Granulation is an important process in the manufacture of OSD products such as tablets. It ensures the flowability of the solids produced.
- » A completely new batch process has been developed to shorten overall process times and achieve higher process efficiency.
- » The TwinPro combines two separate stages of batch processing: high-shear granulation and fluidized bed drying.



The TwinPro combines granulation and fluidized bed drying batch processes in one compact machine.

Traditional wet granulation is the most common method. It is a very reliable method which can be used for almost all types and dosages of drugs. The process can produce almost any tablet shape and is suitable for any active ingredient. Additionally, it improves the flowability and compressibility of the powder mixture.

In the pharmaceutical industry, a traditional granulation line (Image. 4) refers to a sequence of processes: high-shear wet granulation with water or another binder, the addition of additional constituents, wet sieving and fluidized bed drying, further

Industry		Function	
Plant Eng.	□ □ □	Planner	□ □ □
Chemistry	□ □ □	Operator	□ □ □
Pharma	□ □ □	Purchaser	□ □ □
Supplier	□ □ □	Manager	□ □ □

lubrication and final compression.

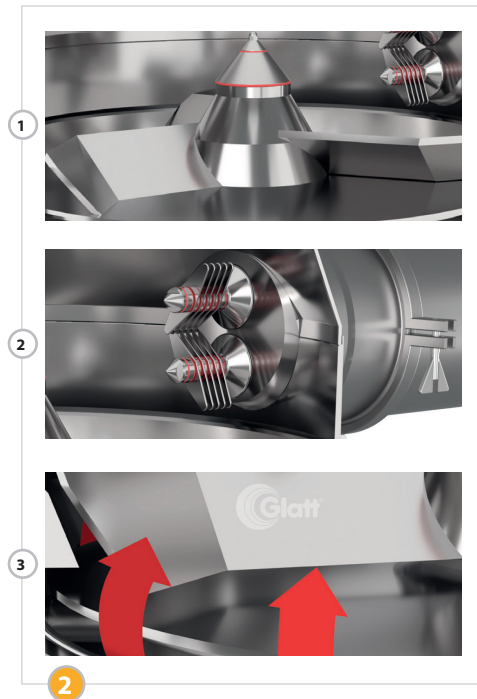
Common excipients are diluents, binders, disintegrants and lubricants; stabilizers and pigments may also be added. These include microcrystalline cellulose (MCC), lactose and starch. Until now, three systems have been required for this process sequence, which require large amounts of space in the production area and are often installed in two separate process rooms.

Innovative Glatt technology combines two batch processes

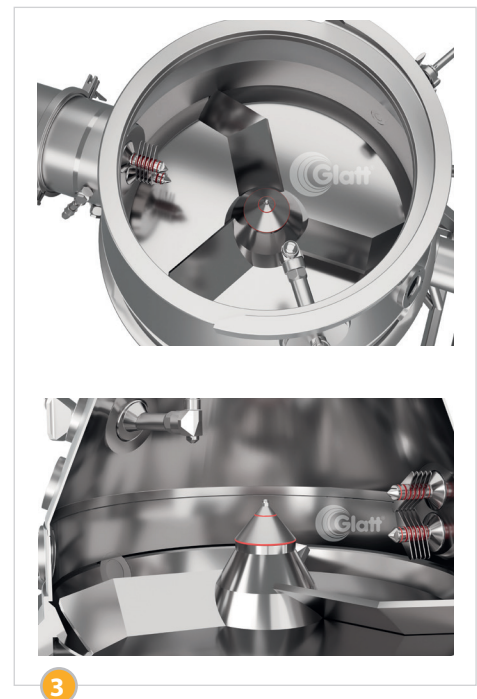
The new TwinPro batch process, the winner of the Achema Innovation Award in the Pharmaceutical Technology category, combines mixing and granulating with milling and drying. For this purpose, the process insert with lockable bottom plate is equipped with a rotor, a mill (a.k.a. 'chopper') and a spray nozzle. Both top spray and tangential spray nozzle configurations are available for the administering of binder fluid, allowing the implementation of the tried and tested high-shear granulation spray process. The geometry of the product bowl is based on the design used in the VG series high-shear granulator. This is also where the rotor is located. Additionally, twin mills are used for granulation, eliminating the need for wet sieving between granulation and drying.

For drying, the bottom plate is lowered, whereby the air for drying is directed into the product. The product is therefore dried

2: The new process uses a high-shear granulation Z-rotor (1) and a double-wall chopper (2) to produce dense granules. Subsequently, the base is lowered, and the drying air flows in through annular gaps (3).



3: The process has been designed to work with the same bowl geometries, rotational speeds and spray rates as used in classic high-shear granulation. Air quantity requirements for drying are also identical.



Christian Knopf is Project Manager of New Technologies & Product Design at Glatt Process Technology. „Our goal for the development of the TwinPro was to fuse high-shear granulation and subsequent drying processes together in just one machine.“

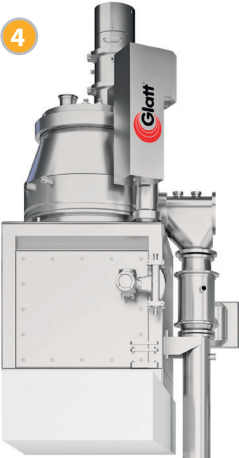
directly after granulation; product transfer between individual processes is superfluous, which in turn results in a significant saving of time. “This fusion of processes enables us to dispense with wet sieving and product transfer. This eliminates one whole step of the process,” explains Christian Knopf, Project Manager for New Technologies & Product Design. By reducing the number of separate machines required from three down to one, process time has been reduced by around 20% compared to a conventional batch granulation line. In addition, installation and building expenses are also reduced. Knopf continues: “by combining two existing processes, an entirely new batch process has been created. This is completely new technology which can replace a traditional granulation line.”

The new process has been made possible by several design tricks: The Z-rotor’s new Quantum Q Drive offers equally high torque at all speeds and has such a compact design that it does not impede the drying air coming in from below.

In addition, the double-wall mill has been implemented, which, in combination with the Z-rotor, completely eliminates the need for wet sieving. The two counter-rotating mills create uniform granules. Knopf adds: “Having two mills in a single machine increases output and ensures reproducible product quality.”

An important aspect for pharmacists is the transferability of processes from previously used technologies. According to Christian Knopf: „Changes in geometry can lead to different product properties. Therefore, an important development goal was to maintain proven batch sizes and product bowl geometries, the typical process tool revolution rates, identical spray rates and spray systems. This allows processes to be transferred from any technology previously used.”

As with the high-shear granulator of the VG Pro series, the wet granulate is produced with the help of a nozzle used in combination with an agitator, the so-called Z-rotor. The mills are tuned to the rotor so that a granulate with uniform particle distribution is formed. When the granulation



4: The classic batch granulation line consists of a granulator, a wet sieve and a fluidized



process is completed, the bottom plate is lowered and two annular gaps open, allowing the drying air to flow into the equipment. Axel Friese, Head of Marketing at Glatt GmbH explains: „the interaction between the outer and central annular gaps make it possible to let in the same amount of air as a conventional fluidized bed dryer

equipped with a fine mesh screen. “The air distribution is in fact so good that the drying time corresponds to the drying time required for a classic fluidized bed process. Additionally, an air seal prevents any product from falling into the annular gaps.

A further advantage is the hermetic sealing of the construction, which enables total containment up to OEB 6.

As less surfaces come into contact with the product, cleaning is made easier. The system can also be extended to

include fully automatic and validatable cleaning. Christian Knopf mentions: „CIP processes in particular are becoming increasingly popular for containment, as the cleaning process is fully automatic and reproducible and the machine does not have to be opened at any point.”

Like the manufacturer’s fluidized bed dryers, the TwinPro unit is resistant to pressure shocks of up to 12 bar when closed and therefore offers reliable protection against dust explosions and when processing solvents (hybrid mixtures). “As granulation and drying are now one continuous process, the ergonomic design allows greater freedom in terms of setting up; the layout is much easier to plan,” states

Christian Knopf, naming a further feature of the new system.

Summary: The process offers an effective alternative to the traditional batch granulation line. The new process can be tested alongside other batch and continuous processing technology in Glatt’s technical department.

The technology: Better product conditioning and a new base concept

By combining high shear granulation and drying in a single process, significant savings are possible:

1. Reduced capital costs by purchasing a complete process system.
2. Savings on infrastructure, building maintenance, steelwork and utility supply costs for preexisting and new process sites.
3. As product transfer is no longer necessary, the process becomes 20% faster.

The combination of with a newly-developed mill, the blades of which can be varied in type, shape and distance to each other, replaces the otherwise mandatory wet sieving. The double-wall design of the mill means that energy input is optimized and the product is specifically conditioned. Another new feature is the drying concept: the sophisticated construction of two annular gaps which are variable in size and placed above a lowerable bottom plate, enables a controlled, efficient and gentle drying process. All driving elements are integrated into the process housing and the new process insert can also be easily integrated into existing fluidized bed systems. The processor’s design and execution simplify applications with containment requirements up to OEB 6. By integrating a so-called multiport, flexible integration of various process applications and sensors (PATs) is made possible.



About the author
Axel Friese is the Head of Marketing at Glatt