



Twin-screw granulation: continuously improve your drug development process

Batch to continuous...an industry evolution

The majority of oral drugs today come in the form of tablets and capsules. The pharmaceutical industry is advancing the way it shapes granules of powder into these oral dosage forms.

Traditional batch granulation methods

Traditionally drugs are granulated in small, medium or large batches. While a familiar method, batch processing has challenges that can cause product quality to fluctuate and increase costs:

- High risk of batch-to-batch variation due to many manual process steps
- Labor-intensive disassembly and cleaning of batch equipment (long downtimes)
- Storage and transportation between process steps increases time and cost of batch process
- Slow, expensive product development as equipment is inflexible for different size batches

Modern continuous granulation methods

Many pharmaceutical manufacturers are moving toward continuous manufacturing because twin-screw extruders (for wet or melt granulation) can help overcome the challenges of batch processing.

Efficiency & reliability

A twin-screw extruder is a very efficient high shear mixer that operates continuously. When used for granulation, carefully chosen process parameters generate granules with tailored sizes and properties. Once the process is in a steady-state, no human intervention is needed, and online monitoring ensures proper product quality.

Ability to choose your scale

Twin-screw extruders come in different sizes to accommodate requirements for granulation from R&D to commercial scale. They help save expensive starting material in early development and can run longer hours to deliver increased production amounts as stages progress. Transfer to large-scale production is fast and easy with Thermo Scientific™ twin-screw extruders which are designed for inherent scalability.

Flexibility & cost savings

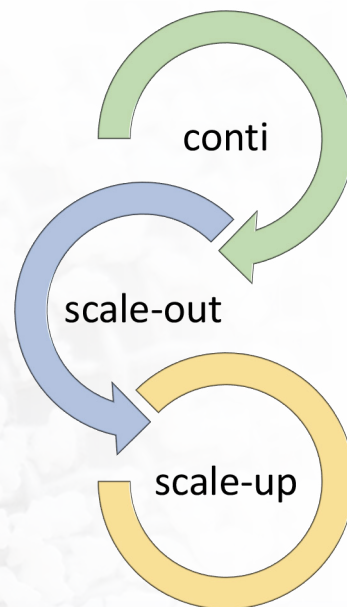
Twin-screw extruders have a flexible screw and barrel setup. Different screw elements can be applied to build a screw that provides exactly the right granulation for a given formulation. The ability to alter parameters while the instrument is running can save up to 80% of time and material during R&D. Batch sizes are also flexible as they can be set by individual run times.

Step into continuous manufacturing

Step into continuous manufacturing at your own pace. Convert all at once, with part of your process, or one step at a time starting with an extruder for granulation development. More process modules can be added to extend continuous processes to dosing, drying, tableting...everything until your continuous line is complete.

There are different ways to increase production in **continuous manufacturing**:

1. **Scale-out** by using the same instrumentation for development and production. Simply let it run longer if more product is needed. Or create copycat systems to be used in other locations or in variable manufacturing.
2. **Scale-up** by establishing the process on larger systems for consistent, high volume and high speed production. Thermo Scientific systems are designed to provide fast, easy scale up in production.



Twin-screw granulation provides:

- ▶ Ultimate process flexibility
- ▶ Higher production yield
- ▶ Faster process development
- ▶ Consistent, high-quality final product

TSG instrument solutions

One solution...different sizes

Maximum throughput in continuous granulation is determined by extruder size (11, 16 or 24 mm), but the instrument solution also needs to match the process. And process needs can differ greatly! Some processes can run economically from R&D to manufacturing with just an 11 mm extruder, while other processes need larger scale instruments right from the start.

Our experts can help you select the ideal size instrument for your drug process, from R&D to pilot-scale and large-scale manufacturing. We have the experience, the full product line, and our instruments are truly scalable from one size to the next.

See our full product line below. We can accommodate your needs from 11 mm to 24 mm, and for full or partial integration. For example, our 24 mm extruder can be used as a stand-alone instrument or seamlessly integrated into a continuous process line.



The Pharma 16 Extruder fully integrated into a continuous granulation process line.



Pharma Twin-Screw Extruders	Pharma 11 Extruder	Pharma 16 Extruder	Pharma 24 Extruder	Pharma 24 TSG
Typical max throughput TSG*	2.5 kg/h	15 kg/h	70 kg/h	70 kg/h
Convertible to HME operation	Yes	Yes	Yes	No
Dimensions (LxWxH)	820x4480x410mm	1750x610x1220mm	1900x800x1300mm	2000x320x550mm
max. Torque	12 Nm (6 Nm per shaft)	36 Nm (18 Nm per shaft)	105 Nm (52,5 Nm per shaft)	36 Nm (18 Nm per shaft)
ATEX desgin	–	–	–	On request

*Depending on formulaltion

Thermo Scientific extruder systems feature:

- Compliance with GMP standards including access to full validation (e.g., FAT, SAT, IQ/OQ)
- Parallel co-rotating screws for optimal mixing
- Split barrel design for easy operation and cleaning
- Convertibility from TSG to HME operation (except the dedicated Pharma 24 TSG)
- Batch report and audit trail functionality (with the Pharma 16 and Pharma 24 instruments)

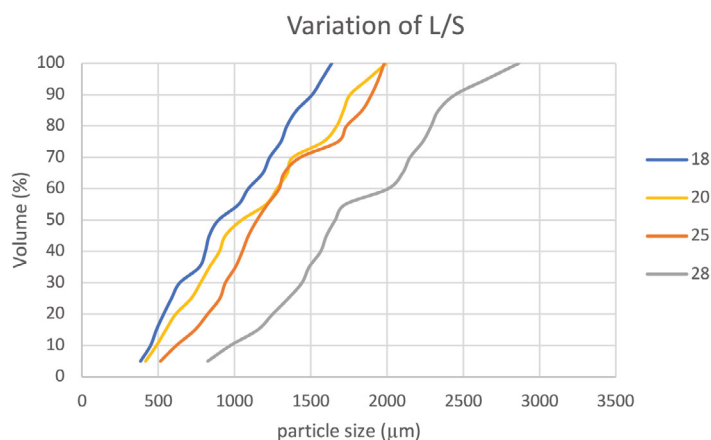
Application solutions: know-how makes the difference

Having the right system is only half the equation; knowing how to implement a continuous manufacturing process turns an investment into a success.

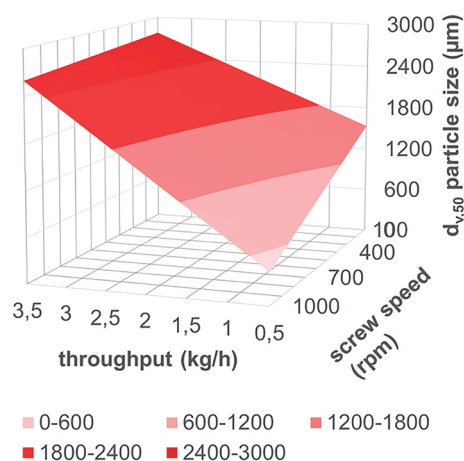
Understanding how changing the liquid-to-solid ratio impacts granule sizes is important. Another critical factor is understanding the interdependency that exists between particle size and extruder throughput and screw speed.

Our pharmaceutical granulation systems are backed by solid applications support and industry experts to help you identify key parameters, determine their interdependencies and meet scale-up challenges head-on.

Tap into this knowledge to support your transition to continuous manufacturing. We can help you make sure your investment in continuous granulation becomes a success.



Understanding the influence of the liquid-to-solid ratio on granule size.



Examining the interdependence of particle size, throughput and screw speed.

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