

Hot-Melt Extrusion Technology

Producing amorphous solid dispersions with lower manufacturing costs



Amorphous solid dispersions (ASDs) have enabled the successful formulation and advancement of many low aqueous solubility compounds by providing enhanced oral bioavailability from the modified drug form. While there are several platform technologies and manufacturing techniques to produce ASDs, hot-melt extrusion (HME) is a leading approach based on mature process understanding, small process footprint, continuous operation and readily scalable. These attributes allow for more of a plug-and-play unit operation, resulting in relatively lower manufacturing costs and making it a more appealing commercial process train.

Proven technology

HME is a technique for manufacturing ASDs in which the drug substance is melted or dissolved within a dispersion carrier and mixed to produce and stabilize the amorphous form of the drug substance. Functional excipients, such as surfactants, are often added to further aid in processability or improve the dissolution performance of the formulation upon administration. The melt is extruded through a shape-forming orifice and, upon rapid cooling, remains a solid, single-phase, glassy amorphous matrix that is shelf-stable.

Post-extrusion processing equipment can be adapted to manage the extruded shape, making it amendable to downstream

processing into a dosage form. In general, these materials are milled to reduce the particle size to be incorporated into a traditional oral solid dosage form such as a tablet or capsule, while maintaining the desired release profile for the drug.

Extensive experience

By combining Lonza's depth of solubilization technologies with our fundamental understanding of pharmacokinetics, we can rapidly help identify, prototype and optimize an ASD formulation that improves the bioavailability of a low aqueous solubility drug substance. Formulation selection is based on our proven *in vivo* predictive dissolution performance testing and physical state stability modeling, then coupled to the HME process to assess manufacturability and throughput.

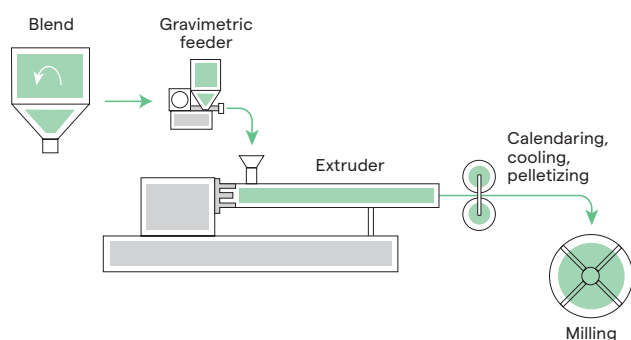
Lonza has more than a decade of experience in formulation and process development using twin-screw extruders, and has been involved in multiple process transfers and scale-ups — including an active commercial process that utilizes a 50 mm extruder. And our experience with ASDs can be leveraged in further formulating solid dosage forms for oral delivery, whether the project goals are for immediate- or extended-release forms.

Well-defined process

Properties of the drug, polymer and dispersion formulation are used to vet the process space for the appropriate scale of the project.

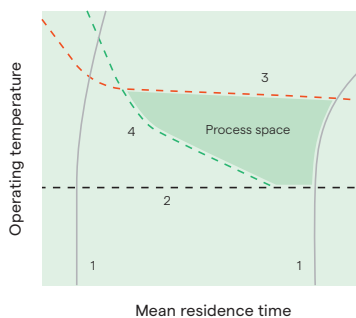
1. Operating limits defined by material handling properties for a given equipment scale, configuration and operating limits
2. The minimum operating temperature defined by the viscosity of the formulation and torque limits for the given equipment
3. The maximum operating temperature defined by the kinetic thermal stability of the drug, polymer or dispersion
4. Process interface to achieve a single-phase amorphous dispersion defined by the thermodynamic miscibility of the formulation combined with the degree of mixing that can be achieved for a given equipment scale and configuration operated at specific parameters

Typical hot-melt extrusion process train



Advanced equipment

We utilize a range of co-rotating, fully intermeshing, twin-screw extruders, feeders and post-processing equipment. Extruders exclusively for development work include both 18 mm and 27 mm Leistritz units. We have additional 27 mm Leistritz extruders exclusively used for cGMP manufacturing. Multiple loss-in-weight powder feeders and liquid injection pumps are available for inputs to the extruders; downstream equipment includes chilled rolls for cooling and initial size reduction and a variety of mills for final particle size reduction.



Leistritz extruder details

Equipment	18 mm	27 mm
Batch size	> 500 grams	> 1.5 kilograms
Throughputs	0.3 to 6 kg/hr	1 to 20 kg/hr



18 mm Leistritz extruder



27 mm Leistritz extruder

[Learn more](#) about how Lonza's hot-melt extrusion technology can address your bioavailability challenges.

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