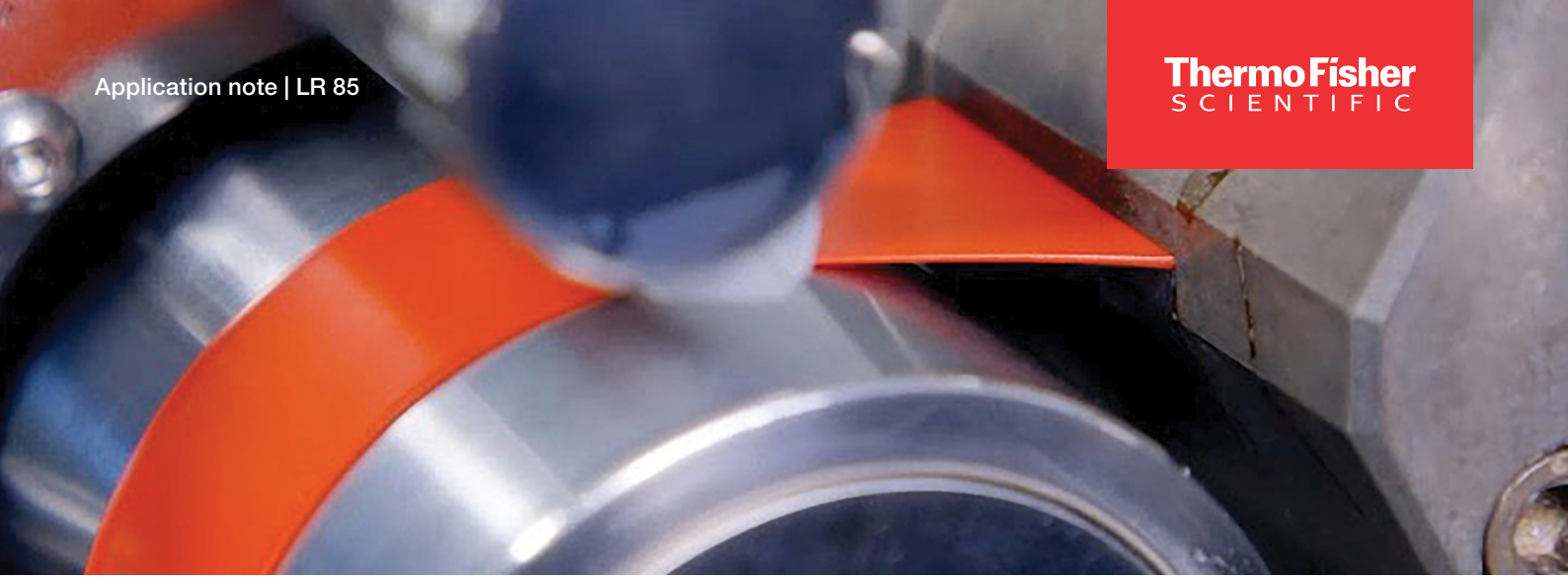

Hot-melt extrusion of orally disintegrating films

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Executive summary

Orally disintegrating films (ODFs) are an appealing dosage form because they allow safe, easy, and exact dose administration of an active pharmaceutical ingredient (API). Additional benefits of ODF forms include improved bio-availability of the drug and avoidance of the first-pass effect.

There are several possible manufacturing techniques for ODFs. Of those, hot-melt extrusion is recommended as a continuous, well-reproducible process that operates without adding solvents.

With Thermo Scientific pharmaceutical extruders and downstream equipment, high-quality ODFs can be produced on a lab scale or at a production scale.

Manufacturing methods for ODF

Typical manufacturing methods for ODFs include solvent casting and hot-melt extrusion (HME).[1] Solvent casting is a very common method for first studies and excipient screening. It is well-suited for thermolabile APIs but requires the handling of a solvent and can create problems during scale-up. HME offers a better alternative. In comparison to solvent casting, HME is a solvent-free, environmentally friendly technology. It is highly reproducible and shows better content uniformity with fewer processing steps and decreased production costs.[2]

Furthermore, API and excipients are mixed on a molecular level with HME, resulting in a more uniform dispersion of the API in the ODF, which increases the bioavailability of the drug. Scale-up in HME has been well established,[4] and it can be easily done with Thermo Scientific extruders. With a suitable range of excipients, HME is the method of choice for innovative ODF formulation.[2]

Hot-melt extrusion

With a long history in plastics and food processing, HME is a well-known and established manufacturing technique with growing popularity in the pharmaceutical industry. Pharmaceutical formulations for HME include combinations of API, polymers, and mostly plasticizers or other excipients. Here's how HME works. The polymer is melted in a twin-screw extruder, and all ingredients are mixed and kneaded; thus, intense compounding takes place. The die, which is placed at the end of the twin-screw extruder, defines the shape of the extrudate. The melt is squeezed through the die hole. Downstream equipment, such as a conveyor, pelletizer, or take-off system and cutters, provides further continuous processing. Using HME granules, tablets with a modified drug release profile can be produced as well as transdermal, transmucosal or subcutaneous drug delivery systems.[3]

Figure 1: Benchtop system including a Pharma 11 Twin-Screw Extruder for production of ODFs.

For the production of ODFs, a sheet die is used to define the width and thickness of the film. As most pharmaceutical polymers are quite brittle, the choice of plasticizing excipients is crucial. The extruded film should be flexible and stretchable. The extruded film is pulled at a constant speed using a take-off and wind-up system to achieve a homogenous thickness. A typical benchtop system (see Figure 1) consists of a gravimetric twin-screw feeder that feeds the pre-blended material into a Thermo Scientific™ Pharma 11 Twin-Screw Extruder. The extruded film is constantly pulled by the sheet take-off. In the end, the film is wound up on a roll (see Figure 2). With this system, thin films can be produced at a constant thickness of 100 µm. The thickness of the film can be changed by adjusting the slit of the sheet die as well as the pulling speed and throughput.

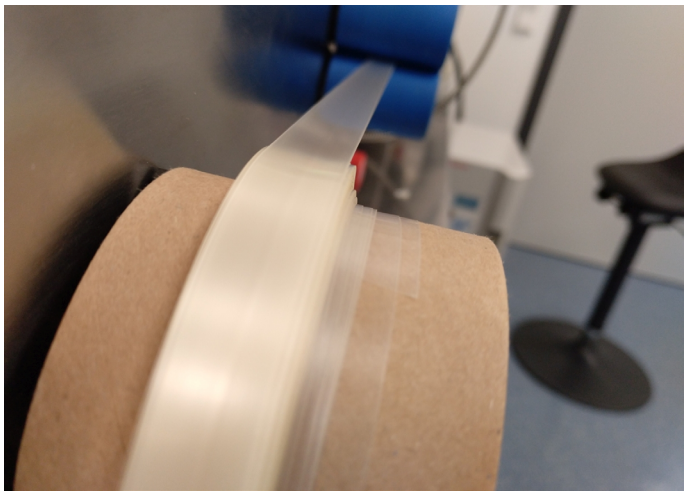

Figure 2: ODF being wound up on a roll.

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