Hot melt extrusion as a sustainable alternative to spray drying for amorphous solid dispersions

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Background & objectives

- Hot melt extrusion (HME) and spray drying (SD) represent two established manufacturing technologies for enhancing drug bioavailability.
- While both technologies can generate amorphous systems, their impact on downstream processability and manufacturing efficiency can differ substantially.
- The objective of this study was to directly compare HME and SD for the manufacture of celecoxib-based ASDs with respect to
  - Product quality
  - Dissolution performance
  - Yield
  - Processing time
  - Specific energy consumption.

Materials & methods

Table 1. Formulations

#	Celecoxib	EUDRAGIT® L100-55	HPC SSL
1	10%	45%	45%
2	20%	40%	40%
3	30%	35%	35%

HME

Powder blends were processed using a Thermo Scientific™ Pharma 11 twin-screw extruder at 150 °C, 300 rpm, and 500 g/h. Extruded strands were air-cooled, pelletized, and subsequently milled using a hammer mill equipped with a 250 µm sieve.

SD

The formulations were dissolved in ethanol at 5% solid content and processed using a PROCEPT™ Spray Dryer Lab at an inlet air temperature of 65 °C.

Characterization

- X-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC)
- Particle size distribution (PSD)
- Dissolution testing for 3 h in pH 6.8 buffer
- Process yield and processing time
- Specific energy consumption normalized to product output (kWh/kg)

Results

Both technologies produced amorphous solid dispersions

XRPD and DSC analysis confirmed successful amorphization of the investigated formulations following both manufacturing routes.

HME generated larger particles with favorable downstream properties

Following milling, HME produced a monomodal particle size distribution with a D_{90} of approximately 360 µm. In contrast, spray drying generated substantially finer material, with >80% of particles below 50 µm.
The larger particle size obtained by HME is expected to facilitate downstream processing through improved powder flow, reduced dust formation, and improved mixing behavior. Milling after HME also provides additional flexibility to tailor particle size to subsequent processing requirements.

HME reduced specific energy consumption by ~39-fold

The largest difference between the two technologies was observed in their specific energy consumption.

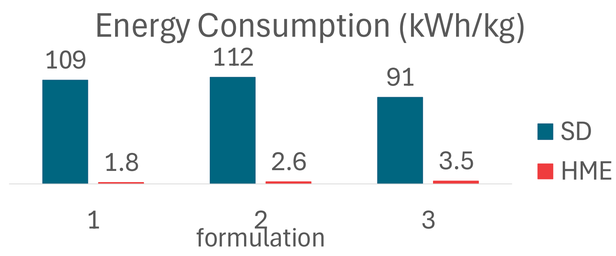

Figure 1. Specific energy consumption of HME and SD.
Specific energy consumption normalized to product output was substantially lower for HME than for SD across all three formulations.

HME enabled shorter processing times at comparable yields

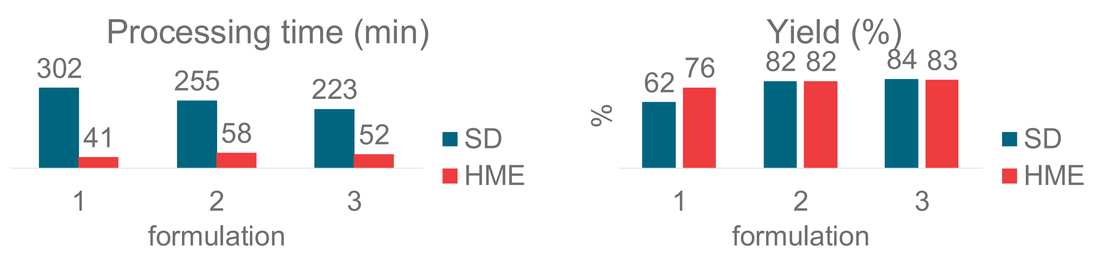

Figure 2. Processing times and yields.
While HME processing required 41–58 min, SD processing required 223–302 min under the investigated laboratory-scale conditions.

HME improved dissolution performance

HME-produced ASDs showed faster initial drug release and higher maximum drug release compared with the corresponding spray-dried formulations. The HME formulations also maintained elevated dissolved drug concentrations for longer periods, indicating improved precipitation inhibition.

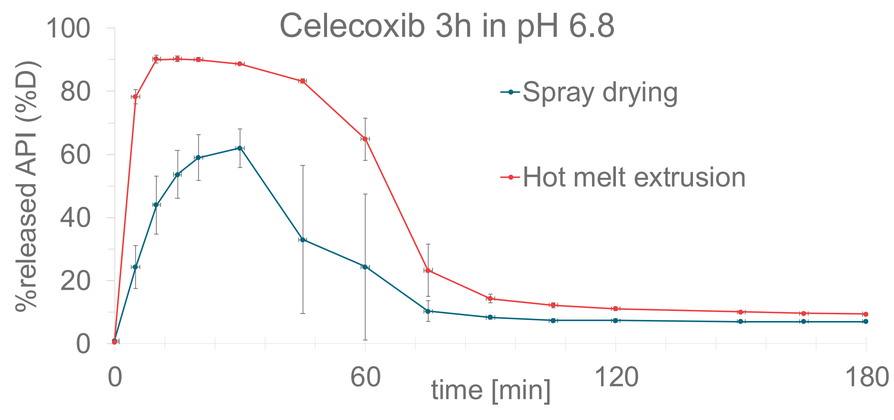

Figure 3. Representative dissolution performance of celecoxib ASDs (formulation 1). Drug release during dissolution testing in pH 6.8 buffer.

Conclusions

Both HME and SD successfully produced amorphous celecoxib-based solid dispersions. However, under the investigated laboratory-scale conditions, HME provided several distinct advantages:

- ~39x Lower specific energy consumption
- Substantially shorter processing times
- Larger particles favorable for downstream processing
- Faster dissolution and higher maximum drug release
- Continuous and solvent-free manufacturing

Both processes were investigated at laboratory scale and were not fully optimized. Further scale-up studies are therefore required to evaluate the magnitude of these differences under commercial manufacturing conditions.

Take-home message

When thermal stability permits extrusion, HME represents a highly promising alternative to spray drying for ASD manufacturing, combining favorable product performance with substantially improved process and energy efficiency.

References

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