



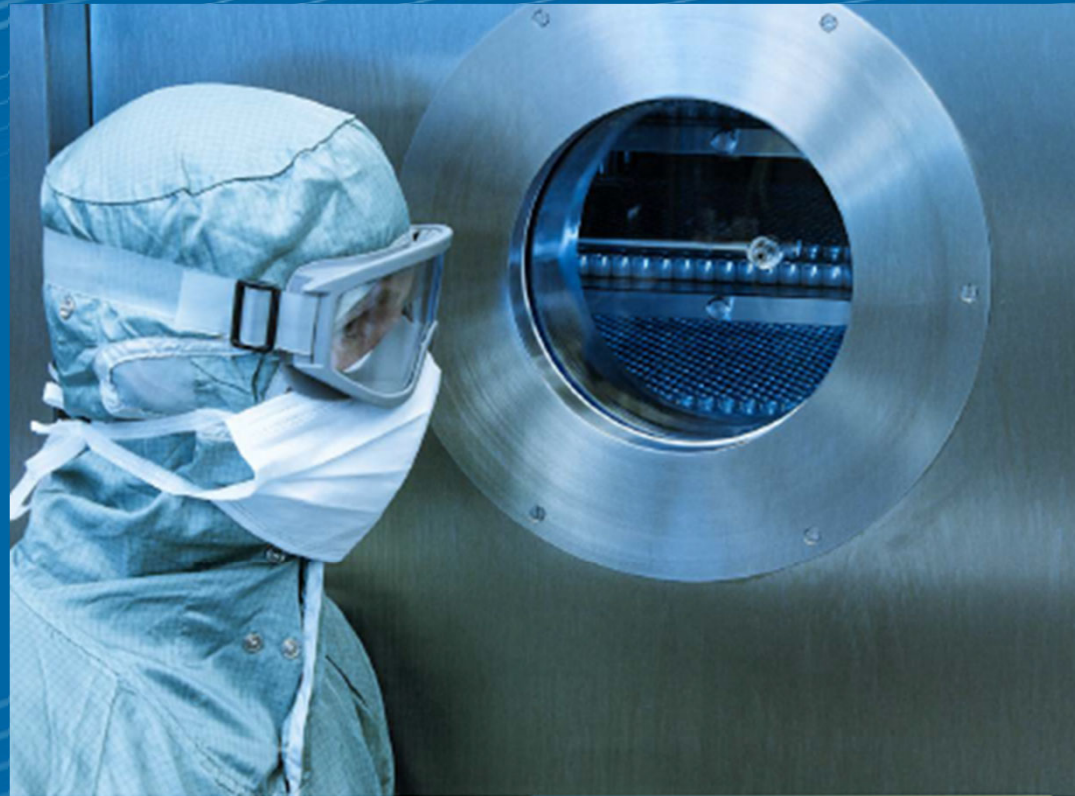
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Theory 10

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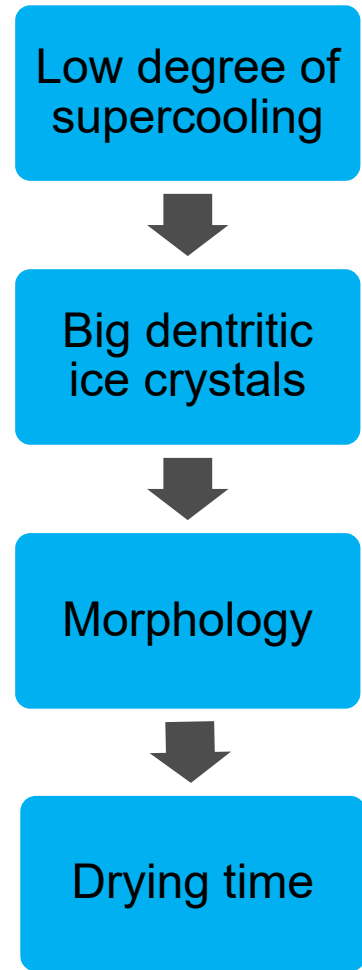
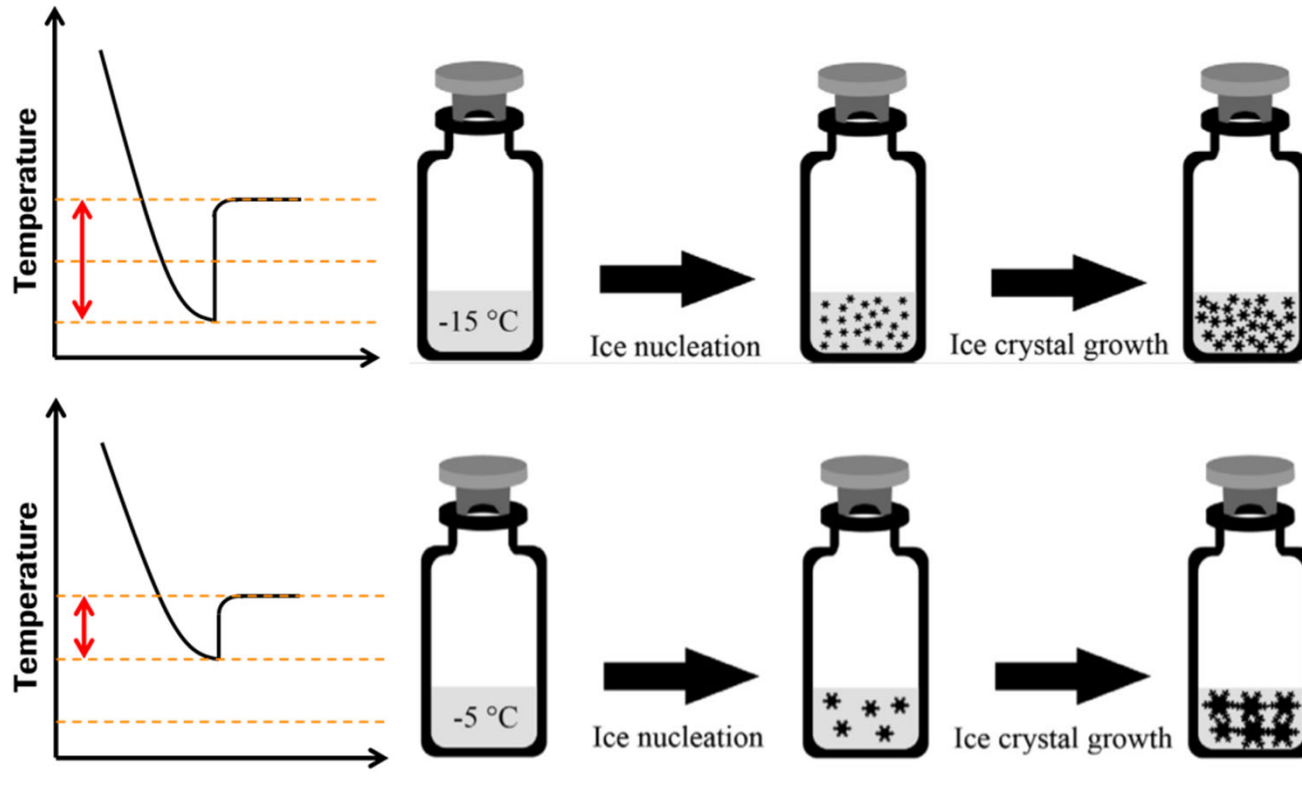


2019 PDA EUROPE TRAINING

Freeze Drying in Practice



Controlled nucleation



- Increases inter-/intra-batch- and vial-to-vial homogeneity
- Shorter primary drying
- Better stability (?)

Review: Geidobler R, Winter G.
Eur J Pharm Biopharm. 2013
Oct;85(2):214-22



Monitoring

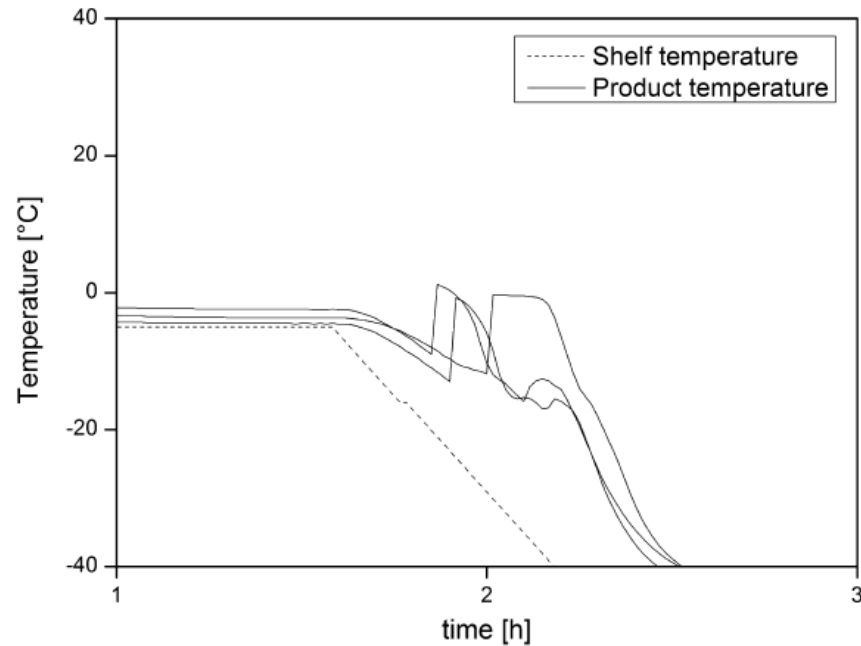


Fig. 1. Typical thermocouple readings for shelf ramp freezing.

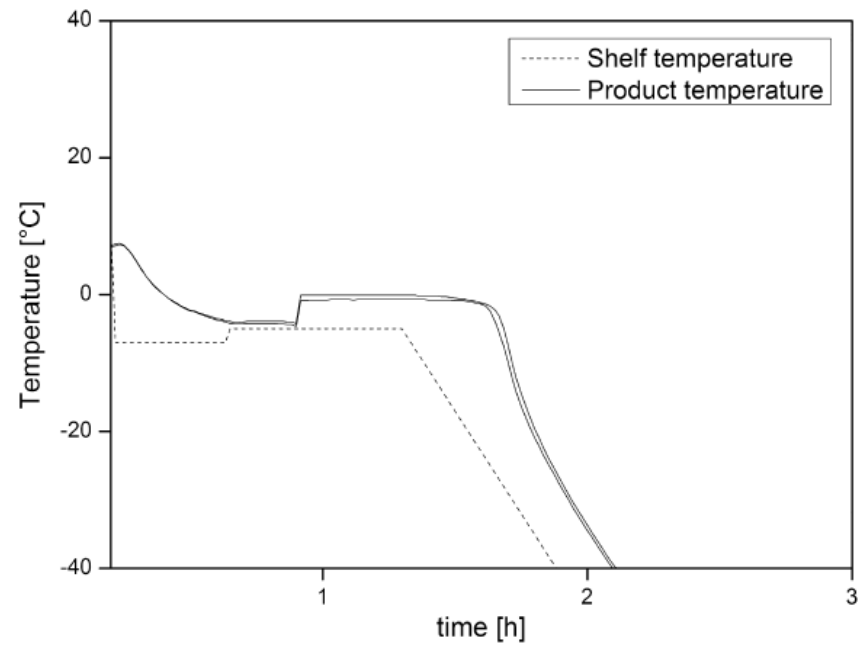


Fig. 3. Thermocouple readings for controlled nucleation at approximately -5°C followed by 20 min of isothermal hold (unpublished data by the authors).



Methods for controlled nucleation

**Vacuum induced
surface freezing
(Kramer et al.,
SynchroFreeze)**

Ice fog technique

**Alternatives:
annealing**

**Rapid
depressurization
(ControLyo/
LyoCon)**

**Ultrasound
induced freezing**

***Review: Geidobler
R, Winter G.
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