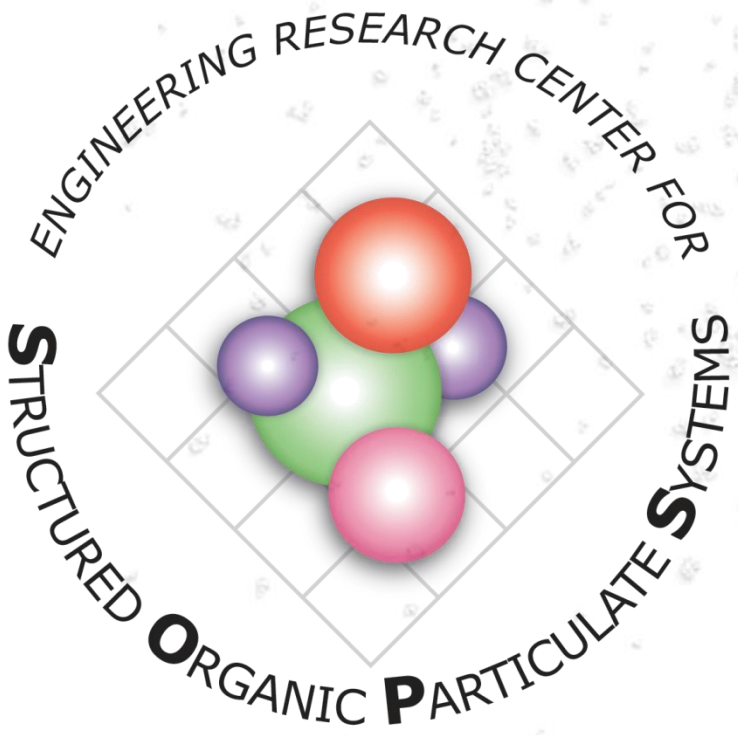
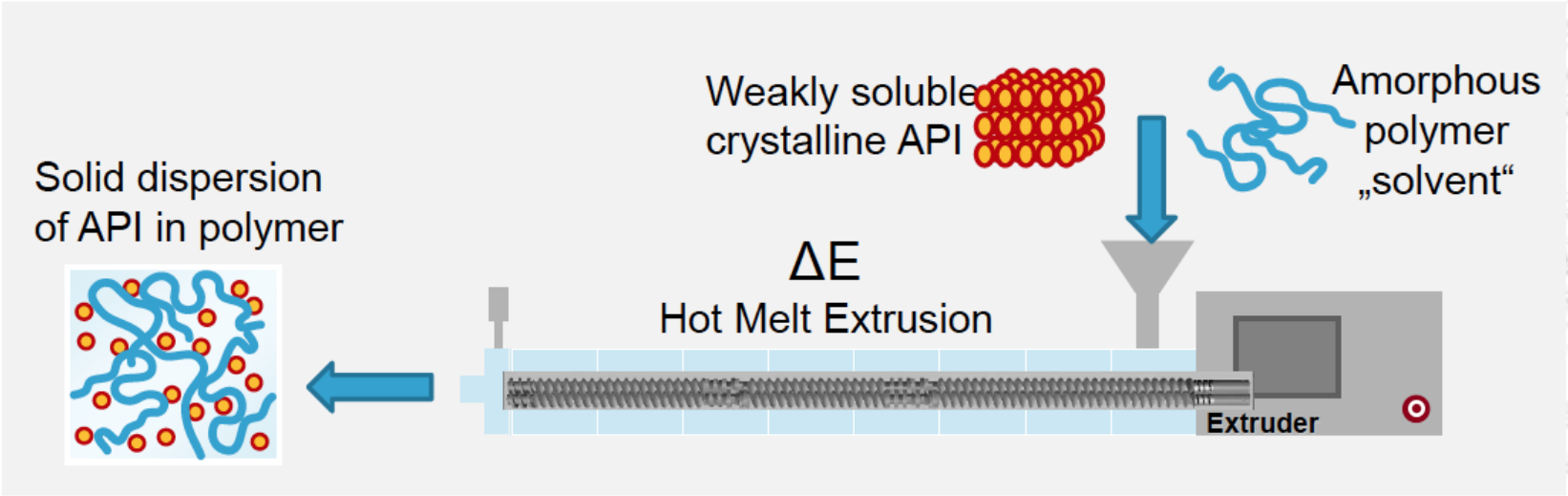
Hot melt extrusion: model development, validation and analysis



March 3, 2017

Presenter: Rohit Ramachandran

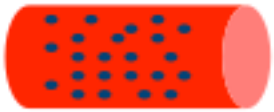
Introduction: Hot melt extruded amorphous solid dispersions



- A poorly soluble drug and an amorphous polymer are transferred into a solid dispersion by introducing thermal and mechanical energy

Crystalline Dispersion

DSC: Drug m.p. and polymer Tg
PXRD: Crystalline bands superimposed on amorphous halo



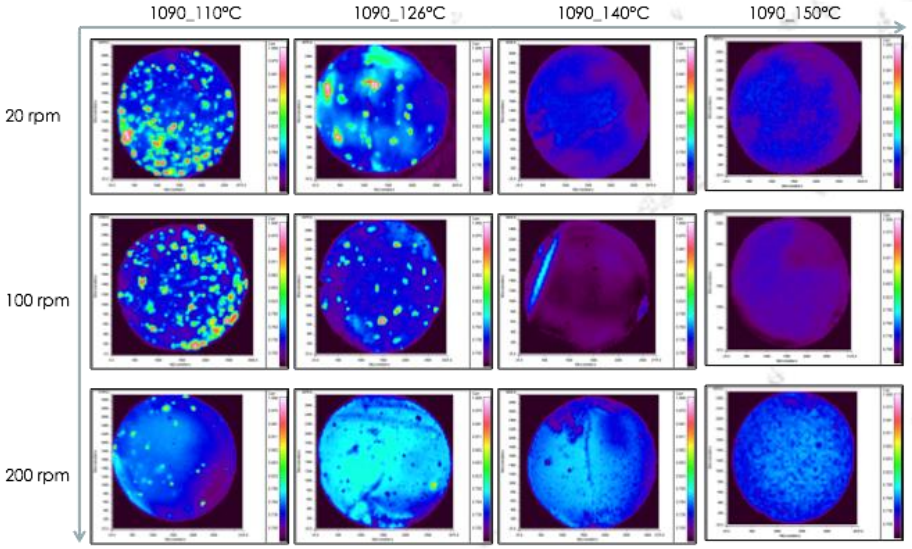
Amorphous Dispersion

DSC: Drug Tg & polymer Tg
PXRD: Amorphous Halo

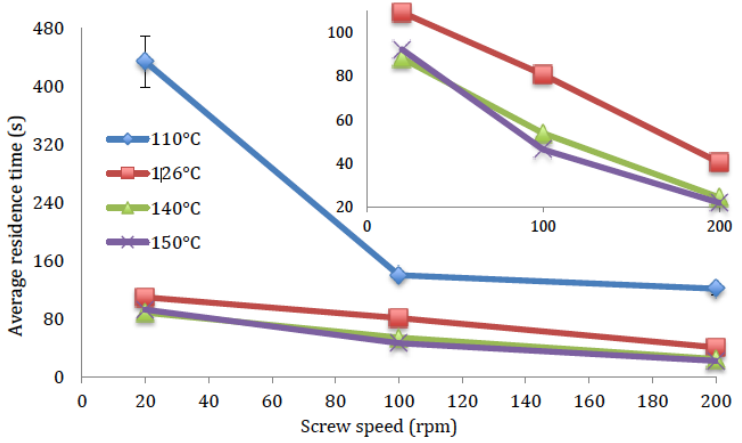
Glass solution

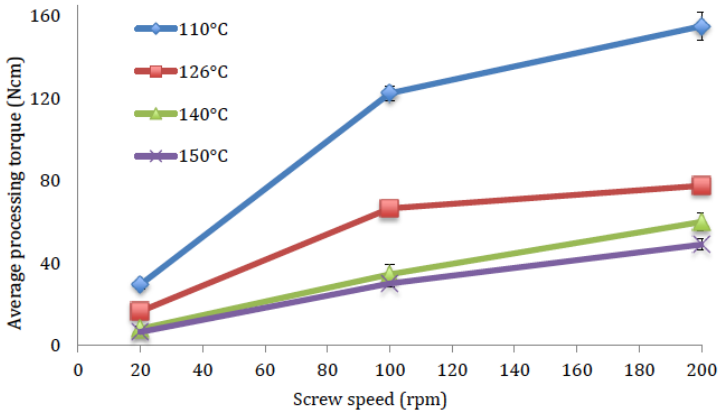
DSC: Single Tg
PXRD: Amorphous Halo

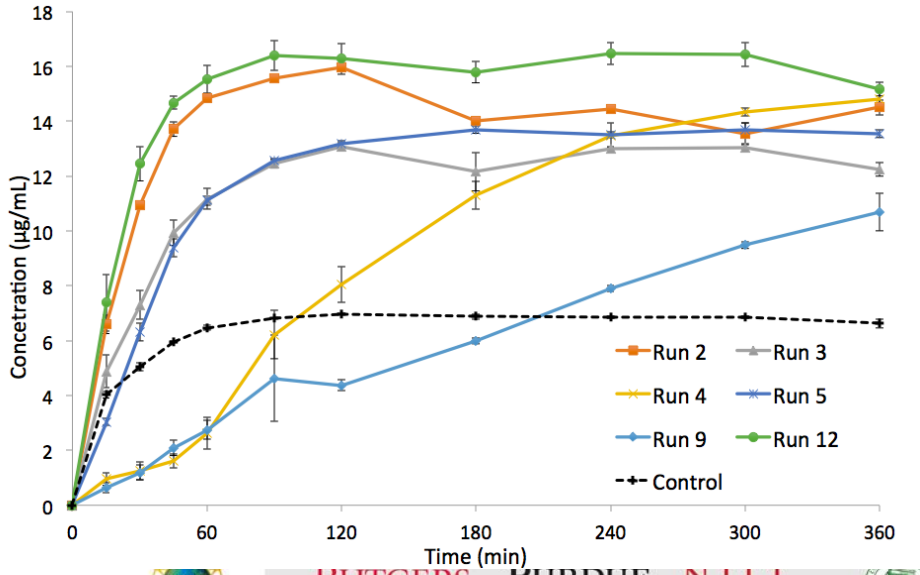
Literature studies: Identifying phases: crystalline/amorphous



Raman mapping showing correlation to crystalline FD as a function of extrusion temperature and screw speed. Recorded at 20x magnification on the cross section of an extrudate with 5 seconds by 4 fi exposure to Raman laser light (785nm) and 0.05mm spacing between each sampling point.







NSF Engineering Research Center for Structured Organic Particulate Systems (C-SOPS)

ThermoScientific Pharma 11 Twin Screw Extruder

Monocoque design; fan less without air ventilation

Touch screen control with password protection

Small footprint bench top design with integrated electronics

Segmented screw design

Removable and exchangeable product contact parts

ThermoScientific Pharma 11 Twin Screw Extruder

- Contains two parallel co-rotating 11mm screws housed in the extruder barrel.
- Can operate between throughput range of 20 g/hr to 2.5 kg/hr.
- Processing length: L/D ratio 40:1.
- Can be operated as stand alone equipment, and easily scalable.

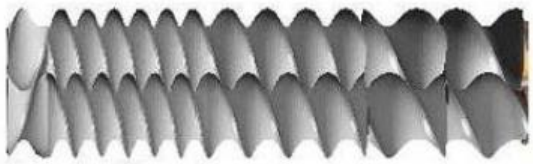
- Converts easily from hot melt extrusion (HME) to twin screw granulation (TSG) applications.
- Modular design allows flexibility with screw configuration and temperature control.

MODULAR SCREW AND BARREL ELEMENTS

Screws are assembled on high torque splined shafts

Flanged barrels, electrically heated and liquid cooled

Conveying Elements



Mixing Elements

Extrusion zone

Overall Aim: Predictive understanding of the effect of CPPs and formulation properties on extrudate CQAs and tablet dissolution.

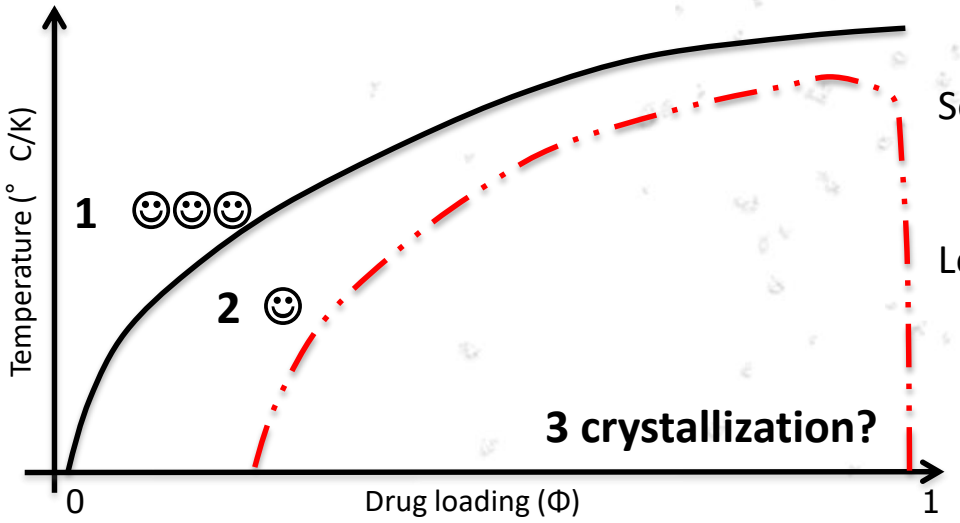
Year 1 Aim: Predictive understanding of the effect of drug loading, RPM, flowrate on mixing, temperature, shear and pressure profiles

Relevant process parameters

- Material throughput
- Screw configuration
- Temperature of barrel sections
- Screw rotational speed
- Material retention time (RTD
- Pressure drop across die

Year 1: proposed work

- Selection of drug and polymer in consultation with industrial partners: maximize design space of regions 1+2.



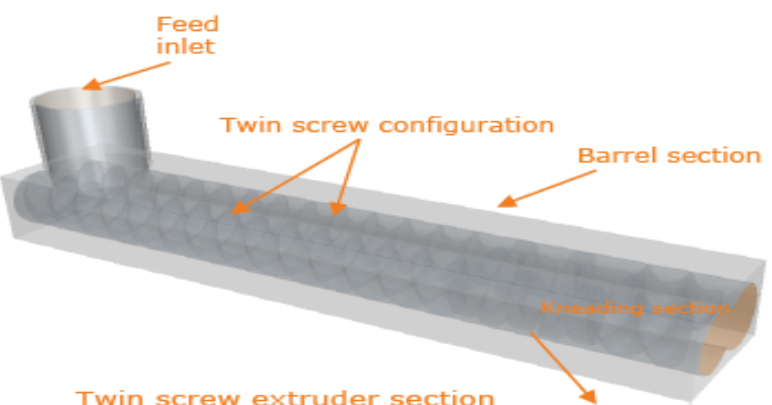
Solubility

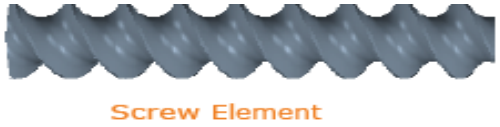
Solid line: Liquid-Solid curve

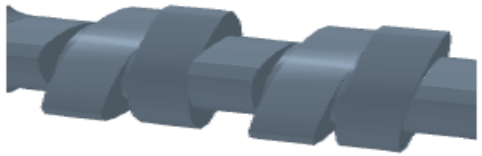
Miscibility metastable

Long dash dot: Spinodal curve

- Selection of screw configuration in consultation with ThermoFisher
- Initialization of extruder geometry in CAD/Star CCM+







Year 1: Proposed work

- Vary flowrate, RPM and drug loading
- In-line sensing of phases (Raman, NIR)
- RTD studies: experimental and model
- CFD studies to understand the effect of inputs on temp, pressure and shear profiles
- Effect of inputs on material viscosity: rheometer studies
- Torque and temperature in process measurements
- Develop predictive RTD and statistical models that can predict key outputs as a function of inputs

Collaborative arrangements

- Modeling expertise from Rutgers, Purdue
- Formulation expertise from Rutgers, Purdue, NJIT
- Sensing and analytical expertise from UPRM, Rutgers
- External collaborators from Uni. Of Limerick, Queens Uni.
- Industrial partners
- ThermoFisher

Acknowledgments

Background material from the group of Prof. G. Andrews, Dr. Y. Tan from QUB, UK.