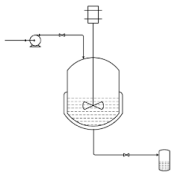
Experimental Exploration of an Industrial Pharmaceutical Crystallization Process

L. María Riquelme, Rune Lorits, Marta González, Giuliano Dragone, Solange I. Mussatto

Helix Lab

Introduction

Problem: optimize the precipitation capacity through experiments and mechanistic modelling



$$t_{current} > t_{new}$$

$$PSD_{current} \leq PSD_{new}$$

PSD: particle size distribution
t: process time

Background: precipitation is the limiting step and the antisolvent addition is time-consuming

Variables:

Antisolvent (AS) profiles

Temperature profiles

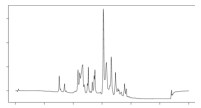
Methods

Solubility & induction time

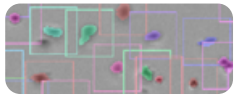
Antisolvent (AS) rate

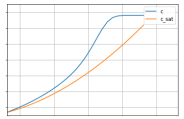
Process mimicking

API concentration



Particle size distribution

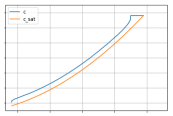




gPROMS

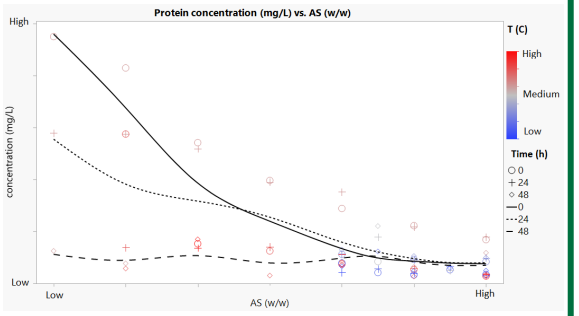
Precipitation model parameter estimation

Optimized precipitation batch

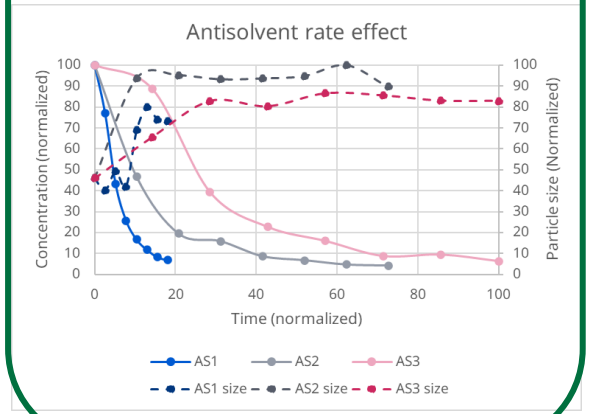


Results

API solubilities at different AS compositions and temperatures



Constant AS rate experiments to estimate precipitation kinetics
AS1-fast, AS2-medium, AS3-slow



Perspectives

Discussion: Nucleation point at low antisolvent concentrations and high temperatures

Temperature has little impact on solubility compared to antisolvent

Future work: Ensure agreement between lab scale and production scale results - by comparing with FBRM data from production

Perform additional experiments to improve the model accuracy

Helix lab fellowship:

- Networking opportunities
- Close collaboration with the industry