Mechanistic Understanding of Spray Drying
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Purpose
Spray drying is a growing technology in the pharmaceutical industry with several enabling applications in modern drug delivery. Its understanding is still vastly empirical, mainly in what relates to the particle formation step. Consequently, the design spaces are typically defined through costly experiments and their statistical interpretation. The purpose of this study is to examine the fundamental principles of particle formation during spray drying and establish a methodology to control the final particle properties. The methodology encompasses a mechanistic atomization model to predict droplet size and guidelines based on the drying kinetics to control the morphology of the particles.

Methods
Droplet size measurements (phase Doppler interferometer, PDI) were used to calibrate the atomization model. The atomization model predictions of droplet size were compared with the particle size (laser diffraction, LD) of 164 batches of spray drying at commercial scales. Simplified theoretical models were used to define the general trends of how the process parameters are related with evaporation and diffusion rate. Experimental investigations of the different paths of particle formation were performed to establish a methodology to control the particles morphology (SEM).

Results
The spray dried particles showed a particle size within the range of [5-150] microns – (figure 1) and with different morphologies - (figure 2). The atomization model was able to describe the variation in the particle size (R2=0.86) and the particle/droplet ratio observed was 0.3.

Conclusion
The present work describes how process parameters can be used to exert a rational control over particle morphology and size. The atomization model proved to be useful to control the particle size since droplet and particle sizes were highly correlated. Regarding the particle morphology, the theoretical description of the particle formation process, as presented herein, managed to relate qualitatively the evaporation rate, drying time and particle shell flexibility with the final particle morphology. The usefulness of this approach lies in its potential to provide a quick and pragmatic overview of general trends for a particular particle design problem. It allows the production of tailor made particles with defined properties in order to fulfill the requirements of a specific product application.

Figure 1 – Calibration of the atomization model and particle size predictions

Figure 2 – Experimental design of the most important parameters influencing the drying kinetics and their impact on the particle morphology: a) spherical b) inflated c) abraded d) broken particles