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Poster Session

Wet Granulation Investigated in Real-Time Using Synchrotron-Based Dynamic Microtomography (375)

Tue, October 25 | Exhibition Hall A | Poster

Part of:
Poster Session (Tuesday)

Info

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Abstract Text:
Wet granulation, the most widespread method of pharmaceutical granulation, is an area of interest in pharmaceutical research with attention towards the evolving granule porosity. Although the granule's changing external structures have been studied extensively, it is much more difficult to study the changing internal structures. The granule is opaque so direct observations cannot be made, and the granulation process is on the order seconds which requires ultrafast data acquisition. The synchrotron-based dynamic microtomography (μCT) technique can provide non-destructive and sub-second data acquisition. This technique was used to investigate wet granulation and revealed new insights by analyzing the evolving microstructures.

Lactose monohydrate (LMH) was used as a representative pharmaceutical powder. Dry powders were loaded into a container and placed onto a rotation stage which operated at a constant speed of 360 deg/sec. A 2.5 μL droplet of deionized water was released from 1.5 cm above the rotating powder bed and a single granule formed. Dynamic-μCT

was used to scan the changing internal structures of the granule *in-situ* for 20 sec at a rate of one CT every 0.5 sec.

CT is a three-dimensional (3D) technique and 3D renders of the granule microstructure quantified individual pores, networks of pores, and total pores evolving in real-time. The mean pore volume from t = 8 to 20 sec increased from 2.8 to 6.8 mm^3. The total number of pores fluctuated, but the total volume consistently increased, suggesting that individual pores consolidated into networks over time. Lastly, granule porosity increased from 1.9 to 8.8 % over the observed time period.

This study quantified the changing granule porosity in real-time. This is a key accomplishment towards understanding the factors that influence granule porosity which in turn, influences pharmaceutical performance. However, the literature has reported the porosity for dry granules of similar pharmaceutical materials to be around 12-15%. This discrepancy could be because 20 sec of scanning did not fully capture the evolving pores until the end. One way of extending the scanning time would be to use a smaller field-of-view (FOV). Since the data size of each image can be calculated from the FOV, it limits the total number of images that can be saved in one scan which in turn, limits the total scan time. Successful dynamic CT scans require careful consideration of how imaging parameters i.e., FOV, exposure time, rotation speed, and memory among others, work in tandem and restrict each other.

Dynamic-μCT is a powerful technique for investigating changing microstructures and the success in investigating a single material can lead towards more complex pharmaceutical formulations. By considering all parameters, experimental and imaging, robust dynamic-μCT procedures can be designed for more complex wet granulation studies. The demonstrations of this study were for wet granulation, but the approach can also be used in similarly fast occurring phenomenon in chemical engineering research. Recent literature has shown enthusiasm in studying the dynamics of colloidal systems, degrading material, and food sciences.

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