Title: 'Application of Nanofocused X-ray tomography and Image Processing for the Quantitative Analysis of Pharmaceutical Particulate Solid Products'

Abstract:

The quantitative evaluation of particle properties connected to their structure and morphology is a common objective during process development and product optimisation of particulate solid systems. This aims to improve material-handling in the manufacturing process or to influence their final performance. However, often solid state analysis techniques are limited to bulk information or to the characterisation of individual particles. X-ray tomography can be utilised to visualise and assess the 3D structure of a wide range of solid products.[1-3] This study demonstrates the use of a commercial nanofocused x-ray tomography system and subsequent image-processing and - analysis strategies for the quantitative non-destructive analysis applicable to pharmaceutical particulate solid products.

The application of nanofocused x-ray tomography to assess the multi-dimensional structural properties of particulate pharmaceutical solid systems was demonstrated on commercially available Ibuprofen capsule product containing a population of formulated pellets for sustained release. Special emphasis was the extraction of quantitative structural descriptors that allow a non-destructive descriptor-based statistical evaluation of the pellet population in each capsule. High-resolution image acquisition, image-processing and analysis enable in-depth investigation of each individual pellet. One important step during the image processing is the successful implementation of a 3D volume segmentation algorithm for connected volume elements. The volume separation of each pellet allows the subsequent extraction of structural descriptors related to pellet properties such as porosity, size/shape, surface area, and solid phase uniformity.[4] The full structural characterisation of each pellet enabled a conclusive descriptor-based statistical evaluation of the pellet population. Identification of population outliers can be linked to a number of broken pellets within the final dosage. The structure of the pellet population and the amount of broken pellets can have a significant impact on material disintegration and therefore, on the overall drug release performance. Their quantification can be used as part of a non-destructive final product quality assessment.

The implementation of robust strategies for the extraction of quantitative information on critical quality attributes related to structural properties of particulate systems can help the acceleration of process and product development for formulations of novel drug candidates. X-ray tomography in combination with advanced image-processing and –analysis techniques can be applied to a wide range of solid particulate systems for the quantitative characterisation of particle properties. The non-destructive nature of this method allows a further correlation of the structural properties to the product's final performance within the manufacturing process or after administration to the patient.

References:

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