Popularized summary in
comparing different methods of measuring particle size for pharmaceutical excipients

In pharmaceutical science, the particle size and particle size distribution (PSD) of drug substance and other ingredients play a critical role in the quality or safety of the final product. For example, they would affect how the drug dissolves in the human body, and stability of the drug. However, there are no exact and uniform standards among different particle-sizing analytical methods in practice. In order to give comparisons for several different ways to measure particle size, such as laser diffraction analysis, dynamic image analysis, and microscopic analysis were used and PSD for selected ingredients, and the applicable materials, benefits, and drawbacks of each approach were studied in the diploma work.

To acquire characteristics of particle size in laser diffraction, irregular particles are always assumed to be spheres with the same volume as the particle. Based on the principle of laser diffraction, the Malvern wet method and the Malvern dry method with excellent precision are compared:

For Malvern wet:

There are three modes to calculate the results, such as General Purpose mode (gp mode), Single mode(sm mode) and Multiple Narrow modes (mn mode). Gp mode and sm mode are more suitable for pure ingredients that can give one main peak, whereas mn modes are prefered for mixed ingredients due to that it can distinguish the peaks of their original ingredients better. Fraunhofer and Mie theory are the common theories in light scattering, which cannot get any bias in the paper because the data is not enough to select a better theory.

Furthermore, powders of different particle sizes have their applicable conditions in wet analysis. It is hard to measure larger particles in the wet method because too large particles cannot be suspended well in the dispersant. For blended powders, the optimal ratio of original ingredients is supposed to be considered before blending. The fraction of measured fines would be overestimated due to a non-linear relationship between the additional fines and the measured fine particles. When more fine particles need to be released from the blended powders, high intensity of sonication and surfactant like Span20 would be considered to improve its dispersivity. But it should be noted that sonication has a chance to destroy or fracture the particle when it has internal cracks in different orientations on its surface.

For Malvern dry:

The dry method is not suitable for measuring very fine particles due to the loss of powders, because very fine particles cannot be delivered to the detector; the jet pressure should be in a suitable range to avoid particles sticking to each other. Compared with Malvern wet, it takes less time to conduct malvern dry with a simple operation and cleaning process, and there is no waste of dispersant, which is more environmentally friendly.

The Qicpic method is to determine particle size using the real shape of particles by testing a number of fast-moving particles. It is found that the Qicpic results for particles that are closer to spherical are more consistent with the results from the Malvern methods.

From analysis of 2D and 3D images of ingredients by Qicpic and microscope technique (SEM), it is clear that SEM has more adjustable magnification and can detect the surface morphology better but is more expensive than the Qicpic images. Among ingredients, it can be observed that most cellets (microcrystalline cellulose pellets) particles are rounded, the shape of sodium bicarbonate is ovoid with some spikes on the surface, the particle of cellulose microcrystalline is fibrous with some pellet formation and lactose carrier is tomahawk-shape.

According to the above results, the correlation and accuracy of different particle-sizing methods could be basically determined, and pharmaceutical materials are able to be measured based on the recommendations.