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OPTIMIZING FLOW AND SEGREGATION PROPERTIES OF LACTOSE/MICROCRYSTALLINE CELLULOSE MIXTURE FOR TABLET COMPRESSION

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Lactose monohydrate/microcrystalline cellulose mixtures represent widely used formulation base for direct tablet compression. Both the lactose and celluloses are available in many grades, allowing for optimizing the flow and segregation properties of the formulation. The flow and segregation behavior may become even more complex, if other components of the mixture exhibit time-sensitive flow characteristics. The present study deals with optimizing the flow and segregation properties of levocetirizine hydrochloride formulation, where the delay between homogenization and tablet compression was found to affect the tablet content uniformity.

In addition to API, the base formulation comprised spray dried lactose monohydrate, milled lactose monohydrate 200 mesh, Avicel PH 101 microcrystalline cellulose, and minor excipients. Several alternative mixtures were prepared using the same total composition, but different grades of lactose and microcrystalline cellulose. These mixtures were then tested for the segregation behavior in an in-house segregation device and the flow properties using a powder rheometer Freeman FT4.

The segregation tests showed the grade of lactose is essential for mixture in-flow segregation. While SD lactose mixtures increased the API content in a direction countercurrent to flow, the milled lactose mixtures segregated API concurrently. Mixtures using both lactose grades showed combined effect, resulting in the least segregation due to the two segregation processes competing with each other. However, the segregation was extremely sensitive to ageing of the mixture. It was also found that each type of lactose causes a different flow regime of the mixture in process vessels.

In order to improve the content uniformity of the tablets, it was found the volumetric flow regime of transport to tablet press is required as well as the aggregate formation should be prevented. This objective was achieved by minimizing the delay between mixing and compression, but the more robust way was found in dry-granulating the API premix.