Exploring scale-up of roller compaction

Pfizer

The aim of this project is to develop methods for scaling up roller compaction process from lab scale to pilot scale, to determine the effect of processing parameters of roller compactors at both lab scale (instrumented roller compactor at University of Birmingham, micro-pactor at Pfizer) and pilot scale (mini-pactor from Gerteis) on the attributes of dry-granulated formulations, including the key properties of ribbons, characteristics of post-milling granules, and to explore the powder behaviour during roller compaction using numerical computations.

Although direct compression is the most effective and favorable manufacturing process for the production of oral dosage forms, such as tablets, most fine pharmaceutical formulations unfortunately cannot be processed using direct compression, mainly due to the poor flowability and processing properties of these formulations. To improve the flowability and processing properties, granulation has to be introduced prior to tableting. There are two types of granulation process: 1) wet granulation and 2) roller compaction (dry granulation). One of the distinctive advantages of roller compaction over wet granulation is that no moisture and negligible heat is involved in the process so that it can be used to process moisture, solvent or heat (drying) sensitive formulations. Due to the complexity of processing conditions and versatility of formulations, the fundamental mechanisms of roller compaction are still not well understood, although there has been an increased interest in understanding the roller compaction process. In particular, scale-up from lab to pilot, and to commercial production scale is always complicated and problematic, as optimal process conditions and formulation determined in a lab scale are often different from that in pilot and in a production scale. The development of feasible methods for scaling up the roller compaction process is of commercial significance to both Pfizer and other pharmaceutical companies. Therefore, in collaboration with Pfizer, we aim to perform systematic investigation of roller compaction at both lab scale and pilot scale and to explore the feasible methods that can scale up the roller compaction from lab scale to pilot scale, based upon a better understanding of the roller compaction process at both scales.

Methodologies

Experimentally, two grades of standard Pfizer placebo Formulations will be chosen as model materials. These formulations will be tested at both lab scale, using instrumented roller compactor at Birmingham and micro-pactor at Pfizer, and pilot scale using mini-pactor from Gerteis. For consistence, the material batches and processing methods (other than given variables, where appropriate) should remain constant where possible. Focus will be placed upon roller compaction in this project, the subsequent milling and compression / tableting condition (to be agreed with Pfizer) will hence be fixed throughout the whole project. These formulations will be roller compacted using the three roller compactor mentioned above by systematically varying the processing parameters, i.e., roll speed, roll pressure, roll gap and raw materials feeding rate, where possible. The properties of produced ribbons including
porosity, tensile strength, Young’s modulus, will be determined using standard methods. The spatial distribution of the ribbon porosity (relative density) will also be determined using X-ray computed tomography and/or indentation testing. The produced ribbon will then be milled and post-milling granules will be collected. The raw formulations and post milling granules will be characterized in terms of density, flowability, size distributions, compressibility and compatibility using standard methods. The data will be analyzed and will be compared with Johanson theory and computational results where appropriate. Correlation between the processing parameters and the key attributes of ribbons and post-milling granules will be established, so will be the correlation between the process at different scales.

As a part of this project aiming to better understand the powder behaviour during roller compaction, the roller compaction will also be numerically analysed using Finite Element Methods (FEM). A commercial package ABAQUS will be used, in which the chosen formulations will be modeled as a continuum media with a material model defined as Drucker Prager-Cap. The processing conditions used in the analysis will be identical to those employed in the experiments mentioned above. The numerical analysis will be compared with experimental results, such as the relative density distribution of ribbons, the pressure profile, where possible. In addition, stress, strain evolution during the roller compaction will be investigated to examine how the formulation behaves during the roller compaction.