364f Segregation Potential in Pharmaceutical Powder Blends: from the Bench to Production

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The dynamics of particulate systems have challenged researchers for decades and although progress has been made, there is still much to be understood. Much current research seeks to predict blend and segregation behaviors based off inherent properties of the constituent blend materials such as size, shape, density, and particle-particle interactions. Model blends are often simplified to be binary and/or consist of particles in which the difference in properties is greatly exaggerated. However, most industrially-relevant particulate blends consist of several components, each with its own unique characteristics. With so many degrees of complexity, computational prediction becomes intractable. Instead, we examine the phenomenological behavior of industrially relevant blends. We test segregation behavior of different pharmaceutical powder blends in a three-dimensional (3D) gravity-driven apparatus. The bench-scale apparatus requires small (500g) pre-blended samples and is able to control angle of repose and free-fall height. Blend uniformity and segregation potential are assessed by carefully sampling the discharged powder bed. We have successfully utilized this apparatus to guide excipient selection during formulation development, and to explain uniformity issues observed in production. We were able to show a strong correlation between measured segregation potential on the bench-scale and blend uniformity in plant trials. A possible mechanism based on the competition between the outward rolling of the convective cascade and inertial motion of large particles (or granules) is presented. In summary, rolling segregation data in a small scale apparatus seems to be a relevant and promising tool for formulation and process development.