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MECHANICS OF PHARMACEUTICAL SOLIDS

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Abstract. Solid pharmaceutical dosages are multi-component heterogeneous systems manufactured to deliver Active Pharmaceutical Ingredients (API) to patients. In particular, oral solid dosages (OSD) such as tablets are utilized in more than 80% of pharmaceutical treatments. The main performance characteristic of OSD is the API release profile, which determines the rate at which the active becomes available. Since the key importance of these profiles, different strategies have been developed to adjust them to desired medical treatments, going from immediate release to controlled release, in which the active is released gradually and predictably over a 12-hour to 24-hour period. If these profiles are not properly tuned, ineffective or unsafe treatments arises due to under or over dosages. Strategies for controlling the release profiles involve both manufacturing and materials. For example, freeze drying is used to for fast release OSD while surface modification and micro-encapsulation is utilized for controlled release.

The assessment of the drug dissolution profiles is a complex problem involving a number of competing and interacting factors including penetration of the fluid into the OSD matrix, alteration of the matrix structure, API dissolution and subsequent diffusion into an external medium. Several of these mechanisms are mediated by the external medium chemical conditions such as ph and physical conditions such as fluid flow. In addition, these processes are dependent upon the internal structure of the solid, which is determined by the formation process conditions such as compaction pressure and speed in tablets. Increasing the predictability window for dissolution and disintegration of heterogeneous solids in complex environments such as those encountered for in-vivo conditions, requires mechanistic models that capture the dominant behaviors of each unit process, as well as simulation platforms that can incorporate and integrate these models and their interactions into coherent computational tools.

This presentation describes a modeling and simulation framework that concurrently consider the fluid penetration into the solid, the spatial variation of the solid properties due to the fluid uptake and the dissolution and diffusion of the active in a time-evolving matrix whose surface is concurrently eroded. Models for each of the unit process are on themselves current topic of discussion and investigation, which are depended upon material characteristics as well as processing and testing conditions, are also presented.