Optimum drug dissolution time in an intermediate compression associated with different competing water penetration mechanisms

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ABSTRACT

Tablets of different composition of microcrystalline cellulose/a-monohydrate lactose and fixed drug (Acetaminophen) concentration are compressed in a rotary tablet press replicator at different compaction forces. Tablets are formulated to act as immediate release (IR) drug delivery system. Performance of IR tablets is usually controlled by the dynamics of solvent penetration into the tablet through competing mechanisms: capillarity, diffusion, and swelling/diffusion sometimes called case 2 diffusion, inducing matrix swelling. We design a device to measure tablet deformation dynamics and mass of liquid uptake simultaneously when a tablet is put in contact with a liquid through its bottom surface. On the other hand, dissolution profiles are measured in a standard USP II apparatus. Dissolution profiles present a nonmonotonic behavior with compression: the active dissolves relatively slowly when tablets are compressed below a certain threshold. Above the threshold, the dissolution rate decreases as expected due to decrease in porosity. Swelling and water uptake rates present the same nonmonotonic behavior with compression than dissolution profiles, indicating a very good correlation between them. This implies that the methodology may be used not only as a research tool and for quality by design development of tablets, but also for fast assessments in quality control environment. We finally demonstrate that a different mechanism for water penetration in the tablet is in place for differently compressed tablets: interparticle pore capillarity and swelling assisted uptake, respectively. We decoupled the two mechanisms by comparing dynamics of water versus a nonswelling liquid uptake. We postulate that the different mechanism for water uptake is responsible for the nonmonotonic behavior and the optimum dissolution rate.