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Probing the early stages of tablet disintegration by stress relaxation measurement

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Abstract

Rapid tablet disintegration is a requirement for the efficient dissolution of the Active Pharmaceutical Ingredient (API) from immediate release tablets. From the mechanistic viewpoint, tablet disintegration begins by the wetting of the tablet surface and the ingress of dissolution medium into the tablet pore structure, followed by the loosening of inter-particle bonds. The present work introduces a new methodology for probing and quantifying the early stages of tablet disintegration by stress relaxation measurements using texture analysis (TA). The method is based on applying a pre-defined load on the tablet by means of a needle-shaped probe and measuring the tablet resistance in time after the addition of the dissolution medium. This measurement provides information about the extent and rate of stress relaxation within the tablet upon hydration. Using a tablet formulation containing ibuprofen as the API and lactose as excipient, the effect of the API content, compaction pressure, and pH of the dissolution medium on the stress relaxation rate was systematically investigated. It is shown that using a dissolution medium pre-saturated by the formulation components has only a minor effect on the tablet disintegration rate compared to a pure phosphate buffer, meaning that the surface dissolution of particles within the tablet is not the main pre-requisite of disintegration in this case. On the other hand, pH of the dissolution medium was found to have a very strong effect on the stress relaxation rate in the tablet after wetting, suggesting that van der Waals interactions rather than solid bridges are the predominant particle bonding mechanism in the investigated formulations.

Keywords: Disintegration; wetting; texture analysis; stress relaxation; ibuprofen; lactose.