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Predictive modelling of liquid ingress into disintegrating pharmaceutical tablets

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In pharmaceutical science, the disintegration process refers to the mechanical breakup of an intact tablet into small fragments to increase the surface area of the drug substance in contact with the dissolution medium [1]. Within the pharmaceutical industry, the disintegration time, which is the time required to disintegrate a tablet until no palpable residues remain, has been employed as one of the critical quality attributes to ensure the bioavailability and efficacy of end products. Despite its significance and extensive studies on the process, a universally accepted and practically employed model to quantitatively describe the disintegration process remains elusive due to the intricate physiochemical interplay of the process, coupled with complex formulations and manufacturing conditions.

At the microscale, determining the propagation of a capillary driven flow requires a solid understanding of the capillary structure including its deformation over time. However, it is practically impossible to capture the complexity in sufficient detail using established analytical methods for pharmaceutical tablets. We instead studied the propagation of the liquid front within the porous matrix, recognising the role of the advancing liquid as the initiator of all subsequent phenomena. Employing the terahertz pulsed imaging (TPI) technique coupled to an open immersion setup allowed us to precisely monitor the in-situ location of the liquid front whilst controlling the influence from the experimental setup on the liquid flow [2]. This approach successfully captured the liquid ingress profiles of complex formulation tablets and revealed two regimes of liquid propagation: 1) an initial rapid uptake regime and 2) a subsequent slower linear regime, which was rate-limiting in determining the disintegration time.

Our results suggest that the linearity in transport results from the synchronised propagation of the liquid front and the erosion at the interface in touch with the dissolution medium [3]. Consequently, we employed this mechanism to develop a predictive model for the disintegration process of pharmaceutical tablets where each regime was modelled as a time-evolving porous medium in terms of swelling and erosion and its terminal structure transitioning inward. Based on TPI measurements, the associated fitting parameters were extracted to quantify the mass transport behaviour of the two regimes and compared across different tablets. This methodology and modelling offers insights into the disintegration process of pharmaceutical tablets and shows potential applicability in understanding disintegration for a range of swelling and eroding porous media.

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