MECHANISMS OF TABLET DISINTEGRATION AND DRUG RELEASE – TOWARDS THE DEEPER UNDERSTANDING OF THE DISSOLUTION PROCESS

Zámostný P., Bittner R., Dufková K., Römerová S.

Department of Organic Technology, University of Chemistry and Technology Prague, Technická 5, 16628 Praha 6, Czech Republic

The dissolution performance of a solid dosage form is pre-determined by its disintegration process. While the *in vivo* disintegration is a complex sequence of steps resulting in tablet fragmentation, which occurs in human body after liquid penetration into the porous matrix of the tablet, the pharmacopoeial method for testing disintegration is very simple and it is not suitable for studying detailed disintegration kinetics. New techniques to measure fragmentation during disintegration could facilitate the better understanding of the process and establish the relationships between the tablet structure and the disintegration process kinetics. Methods based on monitoring water uptake are used for determining the disintegrating force of disintegrant and tablet mechanical properties in wet state. Imaging techniques (light microscopy, scanning probe microscopy, high-speed video imaging or real-time magnetic resonance imagining) are best suited for understanding the mechanisms of particle release. Techniques based on particle size distribution (PSD) can be utilized to provide information on particle population development. Those techniques involve light scattering, micro CT, or focused beam reflectance measurement and they provide data for mathematical modeling of the disintegration process.

This paper describes a technique of in vitro monitoring of fragment population generated from a tablet during the dissolution test using static light scattering and optical microscope combined approach. Mathematical model is suggested for processing the experimental data by regression analysis to obtain rate constant of critical processes involved in the disintegration. A case study is present to demonstrate the possible application of the method on comparing alternative formulations using two different marketed formulations of ibuprofen. On those formulations, the primary erosion of the tablet was successfully identified as the rate controlling parameter for the dissolution. The proposed technique can be used to streamline the formulation efforts on a developed dosage form and for troubleshooting the development of drug generics. Also, it can be used as a tool for studying the microstructure effects in compressed solid dosage forms on the dissolution kinetics.