T09. PAT solution to the drug release prediction

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Numerous studies are devoted to mathematical modeling of drug release. The term "release" encompasses several processes that contribute to the API transfer from the dosage form to the bathing solution. In our case, the drug release kinetics has a sigmoid form with pronounced induction period for moderate and final coating thickness. Such kind of models is rarely presented in the literature. Several attempts have been made to explain the S-shaped profiles but till now there is no generally recognized theory. For this purpose, we propose the autocatalytic kinetic model, which still has no obvious physical background.

Two types of experiments were studied. The first one is the dissolution test, which shows the API release from the pellet core. Nonlinear regression analysis with the successive Bayesian estimation of the regression parameters is applied for processing of the dissolution profiles.

The second type of experiment is the NIR spectra acquired in the course of coating process. As the thickness of the pellet shells and the drug process dissolution are tightly connected, the spectra can be used for prediction of the drug release profiles. NIR data set is considered in PLS analysis as the predictor matrix X. The response matrix Y consists of the kinetic constants values estimated at the dissolution curves' fitting.

We have showed that such combination of the hard kinetic model and the soft PLS regression provides a unique possibility for the on-line prediction of the drug release profiles in the course of the pellets' production.