Conference abstract PMS22

Computer-Aided Design of Pharmaceutical Tablet Formulations

J. A. KIMBER [1], S. G. KAZARIAN [1], F. ŠTĚPÁNEK [1,2]

[1] Department of Chemical Engineering, Imperial College London, London, United Kingdom
[2] Institue of Chemical Technology, Prague, Czech Republic

E-mails: james.kimber03@imperial.ac.uk (J. A. Kimber), Frantisek.Stepanek@vscht.cz (F. Štěpánek)

Sci Pharm. 2010; 78: 649 doi:10.3797/scipharm.cespt.8.PMS22

The formulation of solid oral dosage forms significantly determines the release rate of active pharmaceutical ingredients (APIs). The release characteristics of the API are controled by the excipients in the tablet and the tablet microstructure. Computational simulation of tablet dissolution enables tablet designs and formulations to be tested quickly without resorting to many experiments. Crucially, the model offers a method of mapping the available design space with respect to both tablet composition and tablet geometry enabling parametric sensitivity studies to be carried out. This also enables the inverse problem to be solved i. e. for a desired API release rate, the model calculates the tablet composition and/or tablet geometry which achieves this.

The presented model discretises tablets using a grid of volume elements (for non swelling polymers) or discrete element method (DEM) (for swelling polymers), enabling the tablet microstructure to be explicitly defined. Mass transfer between volume elements is carried out using Fick's law with per-component porosity dependent diffusion coefficients. A concentration boundary layer is situated around the tablet whose thickness is defined by the Sherwood number based on flow conditions. Material diffusing across the boundary is considered released and plotted over time to form component release curves.

Optimisation minimises the difference between the simulated API release curve and the target release curve using the mean squared error and the downhill simplex method. This method can be used to find pure component parameters from dissolution experiments or can be used to optimise tablet formulations by adjusting one or more parameters. In this work, the method was applied to optimise a tablet formulation such that it meets a specified API release time. The tablet formulation contained a disintegrant whose fraction was varied in order to change this time. Two release times were specified (fast and slow) and the resulting formulations were then tested with dissolution experiments to validate the simulation.

The model demonstrates that optimisation can be applied to tablet formulation, leading to better Quality by Design (QbD) and faster realisation of custom formulations.