Establishing a phase diagram of polyoxyethylene (40) stearate and ibuprofen

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Since newly developed active pharmaceutical ingredients (API) are often poorly water-soluble, it may be required to formulate them in a way that enables appropriate dissolution properties. One way to increase the dissolution rate is the development of eutectics. A frequently chosen excipient for this attempt is the water-soluble polymer polyethylene glycol. During recrystallization, melts of a eutectic composition of polyethylene glycol and API build a specific structure containing finely dispersed crystals of API and polyethylene glycol. Upon contact with water, the recrystallized melts (eutectics) release the API as micronized crystals with increased dissolution rate caused by a higher specific surface area than in the conventional drug powder [1]. In contrast, melts containing the API above the eutectic concentration recrystallize building segregates of API with a much larger particle size. Hence, in order to obtain micronized particles, it is essential to get knowledge of the eutectic point of the composition of API and excipient.

With the intention of later developing self-dispersible pellets by extrusion-spheronization, the water-soluble surfactant polyoxyethylene (40) stearate (Myrj™ S40) and the poorly water-soluble model substance ibuprofen were selected in the current study to form a eutectic. Myrj™ S40 not only forms a eutectic mixture with ibuprofen but also may improve its solubilization in water upon dissolution. Using recrystallized melts of mixtures of these two substances, a phase diagram was created by differential scanning calorimetry and polarization microscopy. Depending on the mass ratio of API and excipient, the recrystallized formulations exhibited a significant melting point depression. The eutectic point was found to be around 30 wt.% ibuprofen and around 39 °C. With regard to the impact of the formation of the eutectic on the behavior to be expected upon dissolution, the particle size of ibuprofen crystals released from the prepared formulations in contact with water was estimated by polarization microscopy. The aqueous dispersion of the eutectic composition exhibited ibuprofen crystals around 12 µm in length and 6 µm in width.

The combination of DSC and hot stage polarization microscopy proved to be a good approach to determine the eutectic composition of ibuprofen and Myrj™ S40. Beyond its importance concerning the dissolution behavior, knowledge about the eutectic behavior is also of great interest with regard to the processing of these compositions by extrusion-spheronization, since the processing of low melting substances such as Myrj™ S40 by extrusion-spheronization is very challenging due to their sensitivity to temperature [2].

[1] Law, D., Wang, W., Schmitt, E. A., Qiu, Y., Krill, S. L. and Fort, J. J. 2003. Properties of rapidly dissolving eutectic mixtures of poly(ethylene glycol) and fenofibrate: the eutectic microstructure. Journal of Pharmaceutical Sciences, 3, 505–515.

[2] Petrovick, G. F., Pein, M., Thommes, M. and Breitkreutz, J. 2015. Spheronization of solid lipid extrudates: A novel approach on controlling critical process parameters. European Journal of Pharmaceutics and Biopharmaceutics, 15–21.