Development of a video-microscopic method to compare the effect of a precipitation inhibitor

Christfort, J.F.; Plum, J.; Madsen, C.M.; Nielsen, Line Hagner; Müllertz, A.; Rades, T.

Publication date: 2016

Development of a video-microscopic method to compare the effect of a precipitation inhibitor

J. F. Christfort¹, J. Plum¹, C. M. Madsen¹, L. H. Nielsen², A. Mullertz¹,³, and T. Rades¹

¹Department of Pharmacy, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen Ø, Denmark
²Department of Micro- and Nanotechnology, Technical University of Denmark, Ørsted Plads, 2800 Kgs. Lyngby, Denmark
³Bioneer FARMA, University of Copenhagen, Universitetsparken 2, 2100 Copenhagen Ø, Denmark

PURPOSE

The aim of this study was to develop a video-microscopic method to evaluate the effect of a precipitation inhibitor (PI) on supersaturated solutions of the poorly soluble drug tadalafil using a novel small scale setup.

CONCLUSION

• Tadalafil shows a prolonged induction time and a reduced growth rate in presence of HPMC.
• To significantly prolong the induction time and decrease particle growth, 0.01 % w/v HPMC is needed.
• This is a promising tool for evaluating the effect of PI’s on induction time and crystallization rate of supersaturated systems of poorly soluble drugs.

RESULTS

Proof of Concept using the commercial software

Top: Induction time for tadalafil in presence of HPMC
Bottom: The area of one well defined particle per well as a function of time, with different HPMC conc., mean ± SD, n=3-24

METHOD

1. 30µL
   5mg/mL tadalafil
   in DMSO

2. 200µL
   FaSSIF

3. oCelloScope
   System™
   Top: Tadalafil in FaSSIF
   Bottom: Tadalafil in 0.5% HPMC in FaSSIF

ACKNOWLEDGEMENTS

Philips BioCell A/S is acknowledged for support and access to the equipment.

This study was conducted as part of the Oral Biopharmaceuticals Tools (ORBITO) project (http://www.orbitoproject.eu), funded by the Innovative Medicines Initiative (IMI) Joint Undertaking under Grant Agreement No. 115369.