Solid state solubility of miconazole in poly[(ethylene glycol)-g-(vinyl alcohol)] using hot melt extrusion

V.M. Litvinov,1 S. Guns,2 P. Adriaensens,3 B.J.R. Scholtens,4 M.P. Quaedflieg,4 R. Carleer,3 G. Van den Mooter2

1 DSM Resolve, 2 University of Leuven, Belgium, 3 Hasselt University, Belgium, 4 DSM Xplore, Netherlands

Introduction
Aim: study dispersion of miconazole in poly[(ethylene glycol)-g-(vinyl alcohol)] using hot melt extrusion (HME)

HME: no solvent, easy to scale up, energy efficient

Xplore® pharma micro-extruder

• Easy to clean, no cross contamination
• Easy to fill, also sticky and fluffy powders
• Very small extruder / sample volume
• Very high torque, ability to process just above \( T_g \)
• More with less

Materials
Poly[(ethyleneglycol)-g-(vinyl alchol)] (PEG-g-PVA)

2 semi-crystalline polymers
*PEG (\( T_g1 \& T_m1 \))
*PVA (\( T_g2 \& T_m2 \))

Miconazole

• Basic drug compound
• Antimycotic
• Low aqueous solubility
• \( T_g = \text{ca. } 2°C \)
• \( T_m = \text{ca. } 83°C \)

Results
Physical structures on ~5-10 nm scale

WAXS
DSC

• No crystalline miconazole in extrudates
• Majority of miconazole resides in PEG phase

Dissolution of miconazole on (sub)nanometer scale

\( ^{13} \text{C NMR} \)

Similar \( ^{13} \text{C} T_{1H} \) for all components proves dispersion on the molecular level

\( L \approx (6\text{Deff}\cdot T_{1p})^{0.5} \approx 1.6 \text{ nm} \)

• Miconazole forms amorphous clusters in PEG phase with estimated cluster size of \( \approx 1.6 \text{ nm} \)

Conclusions

• PEG-g-PVA is a suitable carrier for formulation of solid dispersions with hot melt extrusion
• Miconazole preferably resides in PEG and forms amorphous domains of \( \approx 1.6 \text{ nm} \) size
• Hot melt extrusion with the table top, twin screw micro extruder of DSM Xplore offers an efficient and effective screening method for preparing reproducible pharmaceutical formulations at very small scale (2-5 ml volume)

Submitted to Molecular Pharmaceutics