Characterization and stability of lipid extrudates

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Solid lipids are advantageous pharmaceutical excipients being low cost, natural and biodegradable products with physiological, non-toxic properties. They are commonly used as lipid matrices with a variety of different functions, that lead to: - sustained release of high soluble drugs, - enhancement of bioavailability of poor soluble drugs, - floating of dosage forms and - a decrease of the effect of drugs having gastric irritant properties. Many studies have reported the use of lipids for sustained release matrices. The major disadvantage when using lipids in pharmaceutical formulations is the instability of their physical properties during storage.

The solid lipid extrusion process is used to extrude lipids of different composition and melting properties at temperatures below their melting ranges[1]. Drugs can be incorporated in the extrudate in various proportions. The effect of extrusion temperature and pressure on the solid state of the lipids was analyzed using DSC. A shift of melting peaks to higher temperatures could be observed after extrusion. The possibility of processing lipids without melting and subsequent formation of low-melting, metastable polymorphs could be demonstrated[2].

Two lipids with similar melting ranges but of different composition, a heterogeneous glyceryl palmitostearate and a more homogeneous glyceryl trimyristate were extruded and then stored at 40°C. For the glyceryl trimyristate / theophylline mixture the matrix structure was highly dependent on the extrusion conditions. Increasing the extrusion temperature led to higher matrix porosity and faster drug release, due to special properties of glyceryl trimyristate, which solidifies in porous structures after melting. Only solid lipid extrusion is able to provide extrudates of low porosity. After 6 weeks of storage at 40°C drug loaded lipid matrices based on glyceryl trimyristate showed only slight changes in melting enthalpy and relatively stable drug release profiles.

[1] J. Breitkreutz, F. El-Saleh, C. Kiera, P. Kleinebudde & W. Widey. Pediatric drug formulations of sodium benzoate: II. Coated granules with a lipophilic binder. *Eur. J. Pharm. Biopharm.* 56 (2003) 255-260.

[2] C. Reitz & P. Kleinebudde. Stability studies on extruded matrices: Solid state of lipids and drug release. Proc. 5th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Geneva 27-30 March 2006.