Towards simplified oral lipid-based drug delivery using mono-/di-glycerides as single component excipients

Alexandra-Roxana Ilie[1,2], Brendan T. Griffin[2], Maria Vertzoni[3], Martin Kuentz[4], Filip Cuyckens[5], Koen Wuyts[5], Ruzica Kolakovic[1], René Holm[1,6]

Supporting information

The excipients used for the eight lipid-based drug delivery systems used in this study are listed in Table S 1.

Table S 1 Name and composition of lipid excipients used for lipid-based drug delivery systems.

Excipient type	Excipient name	Composition
Long chain triglycerides (LCT)	Sesame oil	Triglycerides of fatty acids: C20 (0.8%); C18:2 (40.4%); C18:1 (45.4%); C18 (4.3%) and C16 (9.1%) [35](Rowe et al., n.d.)
Long chain mono-, di-glycerides (LCM)	Maisine CC	Monoglycerides (MG): 32-52%, Diglycerides (DG) : 40-55%, Triglycerides (TG) 5-20% of fatty acids: C18:2 (>50%); C18:1 (10-35%); C18:0 (<6%); C16 (4-20%)*
Medium chain triglycerides (MCT)	Labrafac Lipophile WL 1349	Triglycerides of fatty acids: C6 (2%), C8 (50-80%); C10 (20-50%); C12 (<3%), C14 (1%)*
Medium chain mono-, di-glycerides (MCM)	Capmul MCM C8 EP/NF	Monoglycerides (MG): 45-75%, Diglycerides (DG) 20-50%, Triglycerides (TG): <10% of fatty acids: C6 (<1%) C8 (>90%), C10 (<10%), C12 (<1%)*
Surfactant (S)	Labrasol	Mixed polyoxyglycerides of fatty acids C6 (<2%); C8 (50-80%); C10 (20-50%); C12 (< 3%); C14 (<1%)*
*according to manufacturer certificate of analysis/technical data sheet		

Precipitation times and XRD patterns of precipitate observed after dilution and dispersion testing of LBDDS containing celecoxib and cinnarizine are shown inTable S 2, Figure S 1 and Figure S 2, respectively.

Table S 2 Time point when precipitation was observed for lipid-based drug delivery systems after dilution and dispersion in FaSSIF at 37 °C.

Time (h)	Celecoxib LBDDS	Cinnarizine LBDDS
0.25	LCM+MCT+S MCM+S MCM+LCT+S MCM+MCT+S	MCM+S MCM+LCT+S MCM+MCT+S
1 - 2	LCM+S LCM+LCT+S MCM	MCM
4 - 24	LCM (pp at 4H)	

Precipitate formed after dilution and dispersion of 85% saturated LBDDS was analysed with XRPD and diffractograms for celecoxib and cinnarizine are shown in Figure S 1 and

Figure S 2 respectively. Presence of low intensity peaks are a result of limited available solid material. Absence of enough precipitate material after dispersion of celecoxib LCM system is a consequence of lack of diffractogram in Figure S 1.

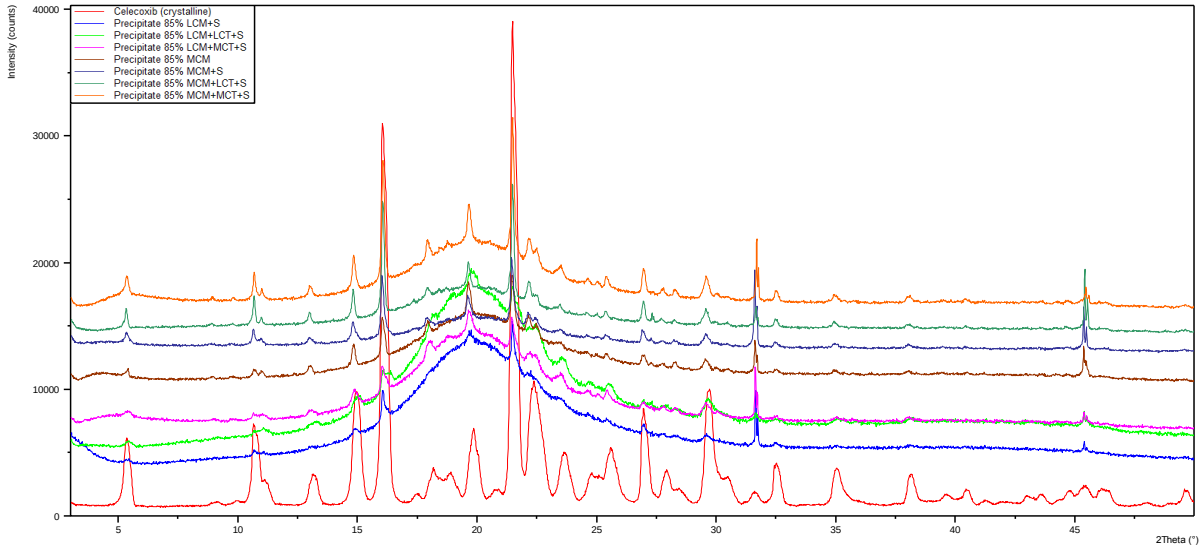

Figure S 1 Overlay of XRD diffractograms for precipitate observed after dilution and dispersion of celecoxib-loaded LBDDS in FaSSIF and crystalline celecoxib.

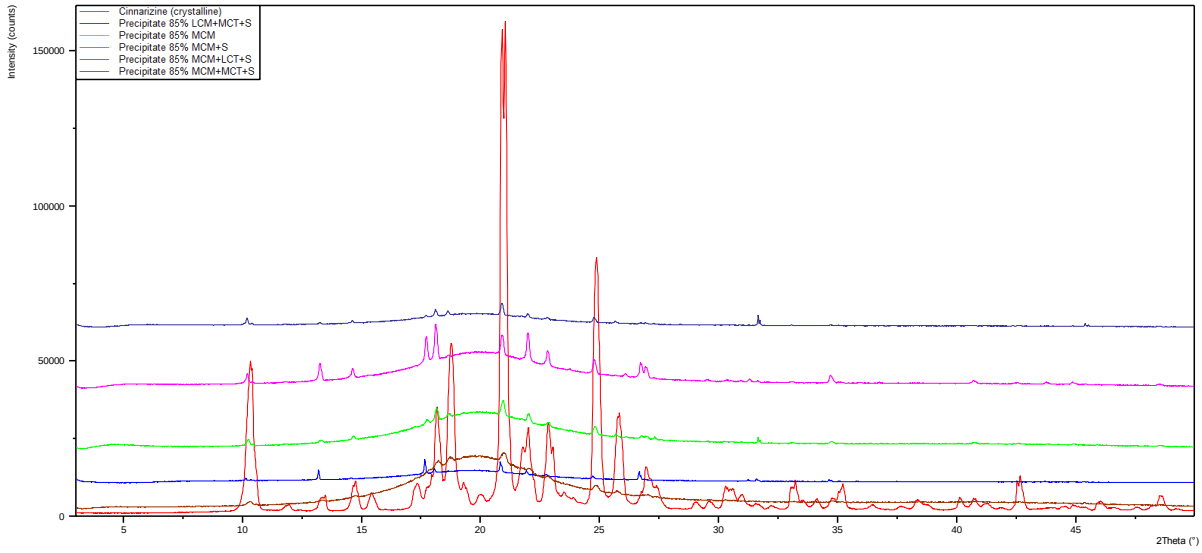

Figure S 2 Overlay of XRD diffractograms for precipitate observed after dilution and dispersion of cinnarizine-loaded LBDDS in FaSSIF and crystalline cinnarizine.

The area under the concentration-time curve of drug concentration in the aqueous phase of the dispersion medium after dispersion of LBDDS in FaSSIF is presented in Table S 3.

Table S 3 Area under the concentration-time curve after *in vitro* testing of LBDDS dispersion in FaSSIF and drug quantification in aqueous environment.

	Celecoxib	**Cinnarizine**	**JNJ-2A**
LCM	366.4 ± 20.1	882 ± 129	1203.3 ± 37.6
MCM	609 ± 331	83.8 ± 18.6	252.4 ± 38.9
LCM+S	943 ± 227	855 ± 111	3400 ± 379
MCM+S	101.0 ± 20.0	198.2 ± 33.0	1480 ± 134
LCM+LCT+S	1144.7 ± 60.4	947.2 ± 64.4	n.a.
MCM+MCT+S	1164 ± 209	1645 ± 230	1965 ± 292
LCM+MCT+S	1328.8 ± 32.3	1627 ± 103	n.a.
MCM+LCT+S	958.4 ± 94.7	745.1 ± 32.9	n.a.