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Supporting information

Exploring the impact of surfactant type and digestion: Highly digestible surfactants improve oral bioavailability of nilotinib

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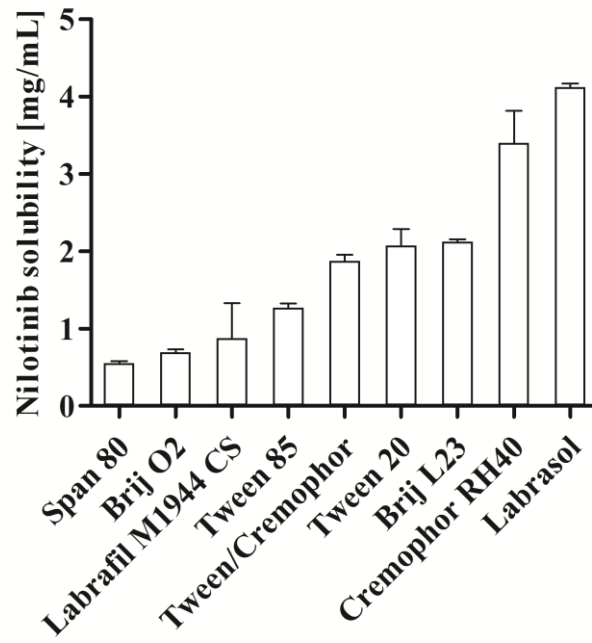


Figure S1. Solubility of nilotinib in the selected excipients at 37 °C. Tween/Cremophor is a mixture of Tween 85 and Cremophor RH40 (67:33 w/w). Solubility was measured up to 72 h (mean \pm SD, n = 3).

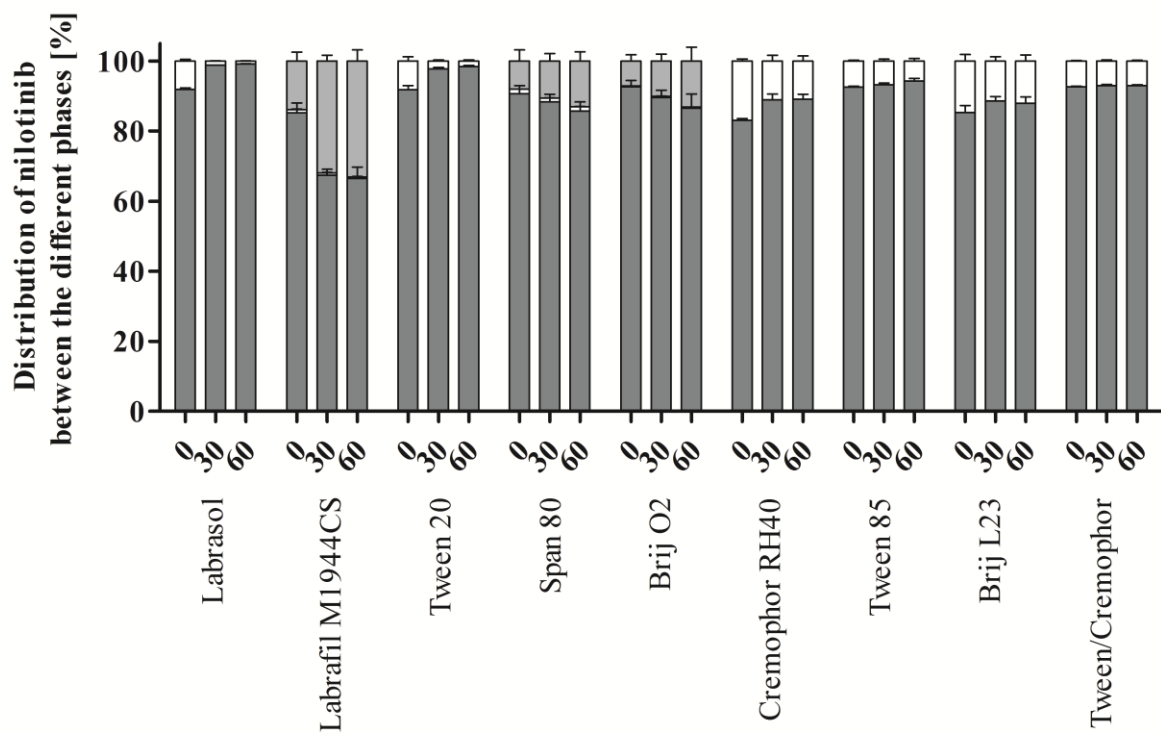


Figure S2. Distribution of nilotinib into the solid (dark grey bars), aqueous (white bars) and lipid phase (light grey bars) just before initiation of digestion (0) and after 30 and 60 min of digestion (mean \pm SD, n = 3). Tween/Cremophor is a mixture of Tween 85 and Cremophor RH40 (67:33 w/w).

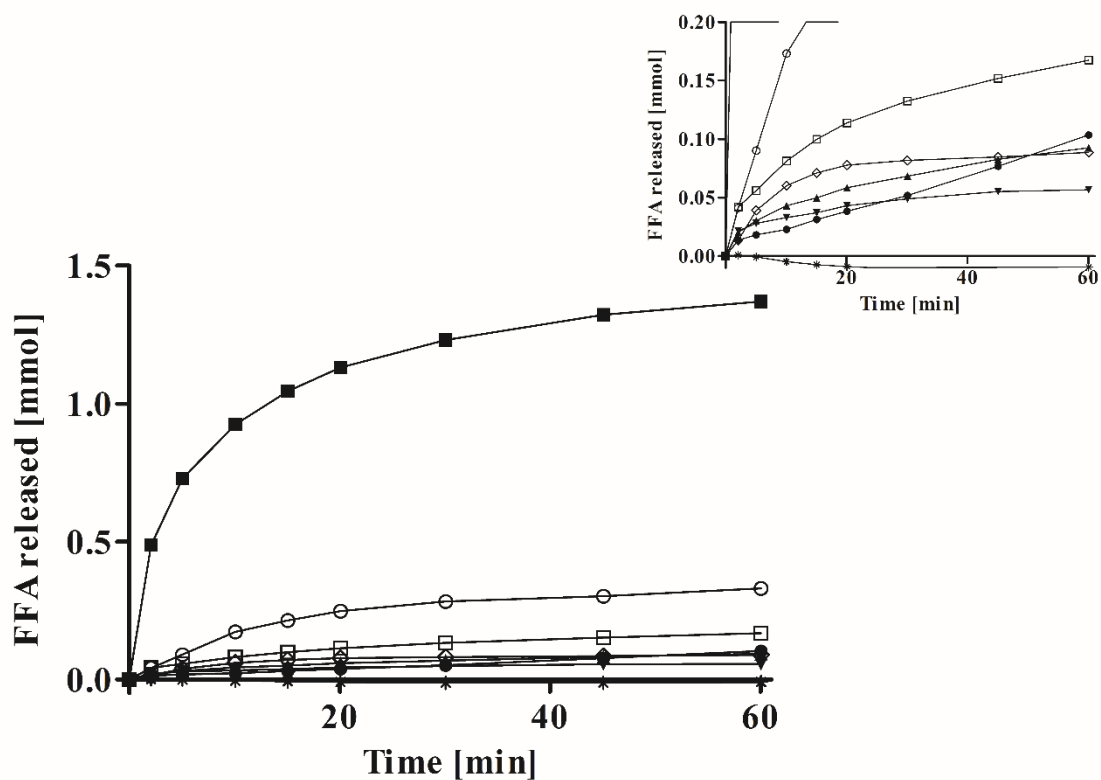


Figure S3. FFA released during 60 min of *in vitro* digestion at pH 6.5. The insert provides improved visibility on surfactants releasing less than 0.2 mmol FFAs. Cremophor RH40 (◇), Brij L23 (*), Tween 20 (○), Span 80 (▲), Labrasol (■), Labrafil M1944 CS (□), Tween 85 (●), Brij O2 (×), Tween 85/Cremophor RH40 mixture (67:33 w/w) (▼) (mean \pm SD, n = 3).

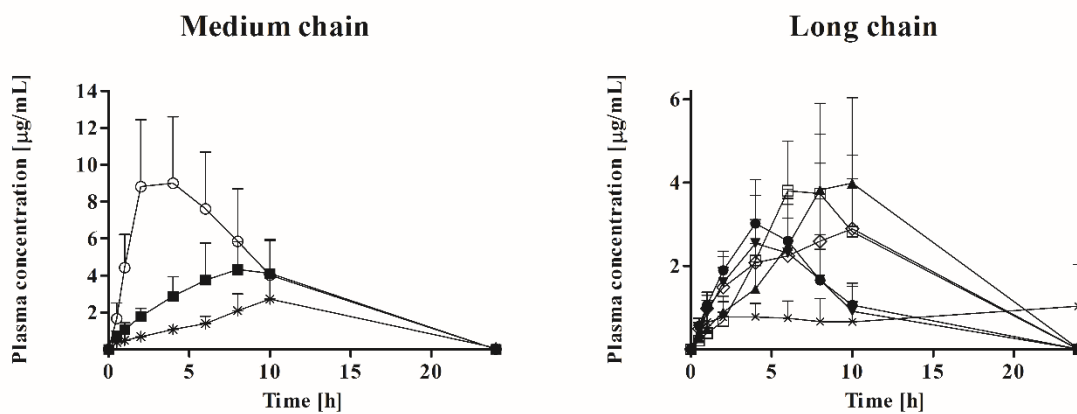


Figure S4. Plasma concentration profiles as a function of time for orally administered nilotinib surfactant suspensions dosed at 20 mg/kg and 2 mL surfactant/kg. (mean \pm SD, n = 5). Cremophor RH40 (\diamond), Brij L23 (*), Tween 20 (\circ), Span 80 (\blacktriangle), Labrasol (\blacksquare), Labrafil M1944 CS (\square), Tween 85 (\bullet), Brij O2 (\times), Tween 85/Cremophor RH40 mixture (67:33 w/w) (\blacktriangledown).

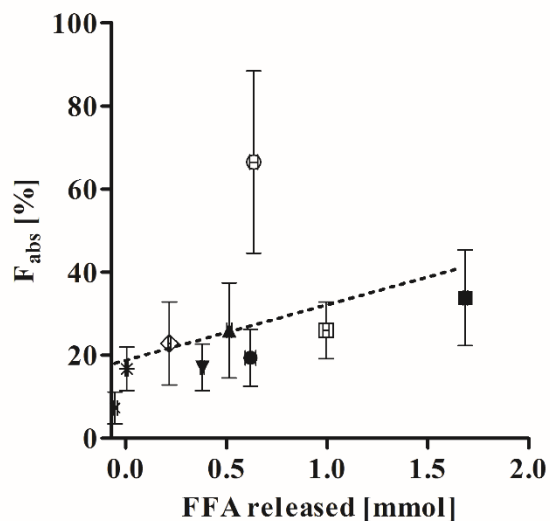


Figure S5. Relationship of absolute bioavailability (F_{abs}) and free fatty acids (FFA) released during *in vitro* digestion as a surrogate parameter for digestibility of the excipient. Cremophor RH40 (\diamond), Brij L23 (*), Tween 20 (\circ), Span 80 (\blacktriangle), Labrasol (\blacksquare), Labrafil M1944 CS (\square), Tween 85 (\bullet), Brij O2 (\times), Tween 85/Cremophor RH40 mixture (67:33 w/w) (\blacktriangledown) (mean \pm SD, F_{abs} n = 5, FFA released n = 3).