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Supporting information

In silico, in vitro and *in vivo* evaluation of precipitation inhibitors in supersaturated lipid-based formulations of venetoclax

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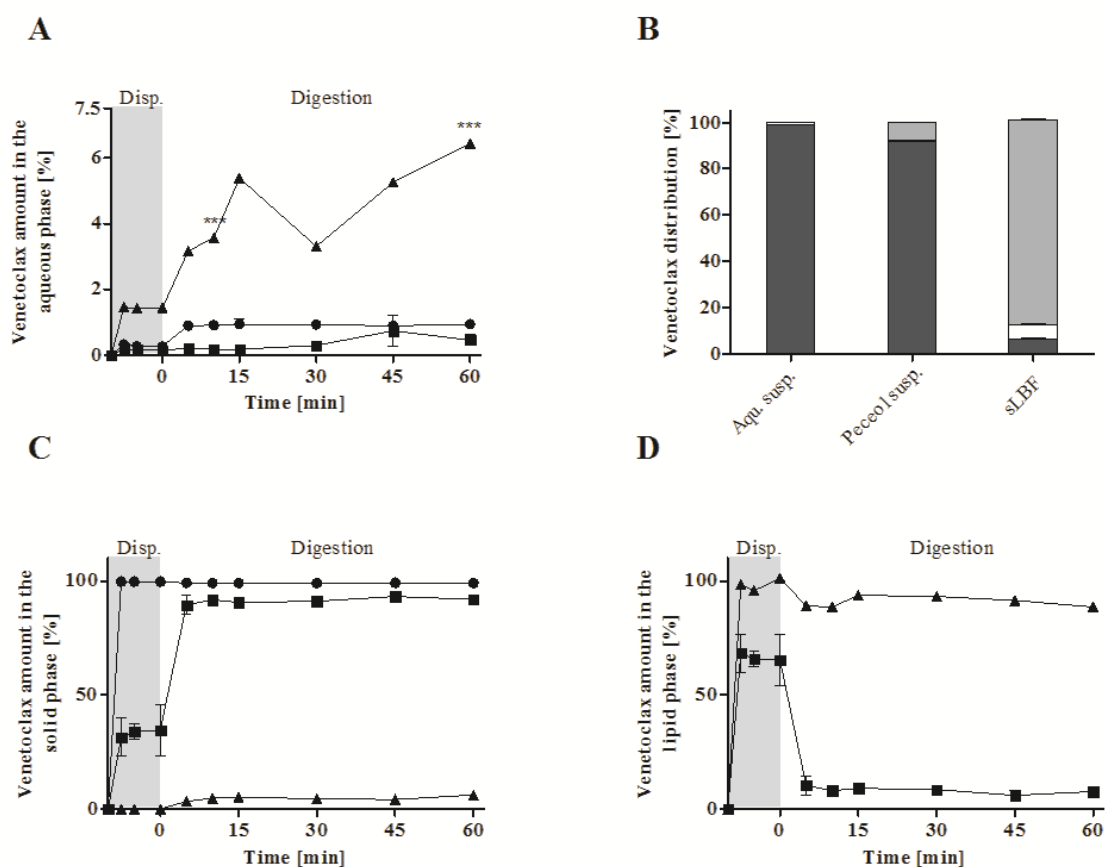


Figure S 1. *In vitro* lipolysis of venetoclax formulated as supersaturated Pecceol® solution (sLBF) (▲), as well as previously reported aqueous suspension (●), Pecceol® suspension (■).¹³ A: % of venetoclax in the aqueous phase, B: Distribution of venetoclax into the different phases after 60 min of lipolysis (black: solid phase, white: aqueous phase, grey: lipid phase), C: % of venetoclax in the solid phase, D: % of the venetoclax in the lipid phase. All experiments were run with n = 3 and results are shown as mean ± SD.

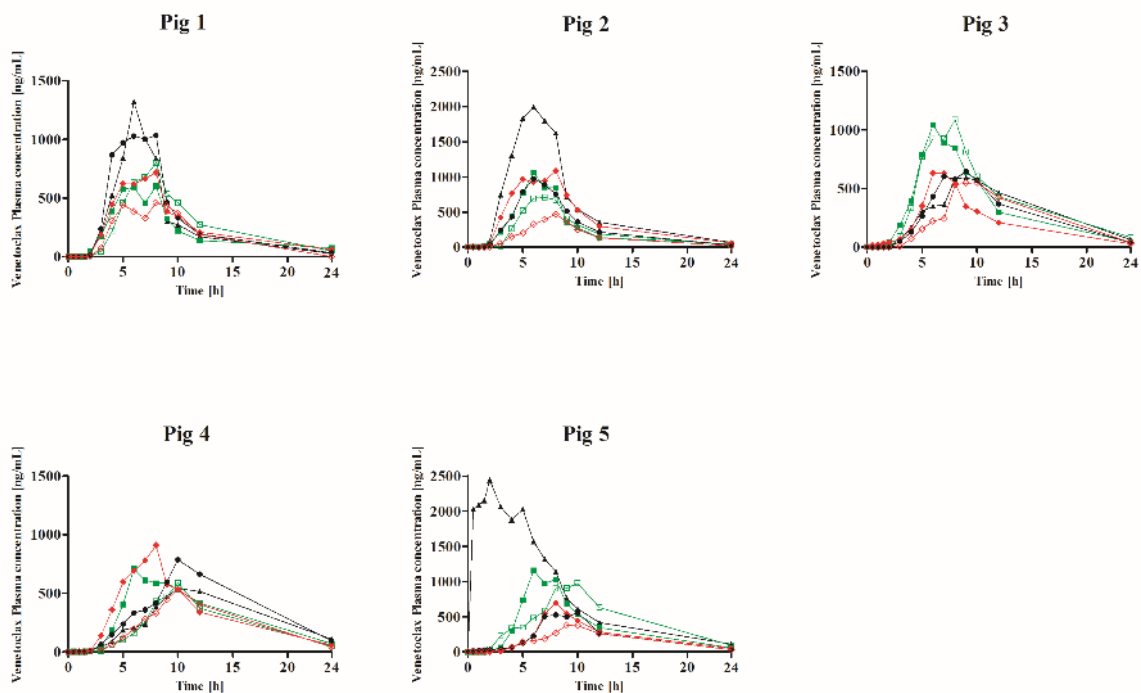


Figure S 2. Individual plasma concentration profile from 0 – 24 h of 100 mg venetoclax in landrace pigs for the tested formulations. sLBF-noPI (▲), sLBF-HPMC (■ - green), sLBF-HPMCAS (□ - green), sLBF-PVP (◆ - red), sLBF-PVP/VA (◇ - red), sLBF-Pluronic[®] F108 (●).

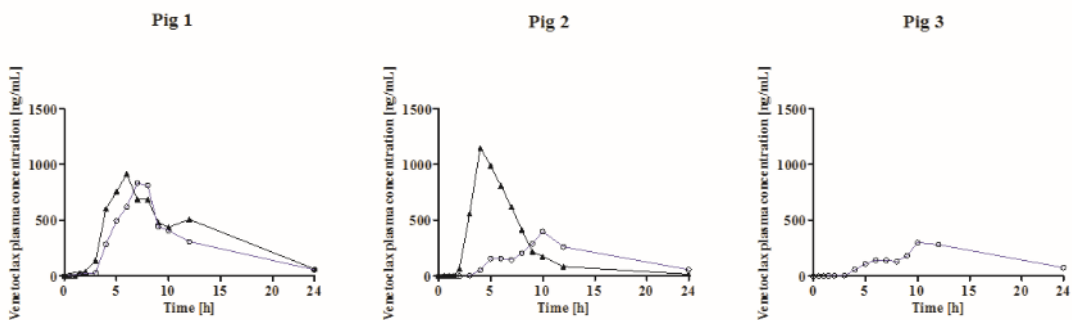


Figure S 3. Individual plasma concentration time profiles from 0 - 24 h of 100 mg venetoclax in landrace pigs for the tested formulations. sLBF-noPI (▲), sLBF-Eudragit[®] EPO (○ - blue). Due to an administration error, the sLBF-noPI of pig 3 was not obtained. sLBF-noPI has previously been reported.¹³



Figure S 4. PI test samples of sLBF-PI with HPMC, Eudragit[®] EPO and HPMCAS after 180 min in FaSSIF. Agglomeration of Eudragit[®] EPO can be observed.

Table S 1. Thermal properties of venetoclax. Melting point (T_m), Enthalpy of fusion (ΔH_{fus}), Entropy of fusion (ΔS_{fus}).

	T_m [°C]	ΔH_{fus} [kJ/mol]	$\Delta S_{fus} \times 10^{-2}$ [kJ/mol/K]
Venetoclax batch 1810004	139.1 ± 0.03	19.2 ± 0.03	4.7 ± 0.01

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