

Title	In silico, in vitro, and in vivo evaluation of precipitation inhibitors in supersaturated lipid-based formulations of venetoclax
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Publication date	2021-04-23
Original Citation	Koehl, N.J., Henze, L. J., Bennett-Lenane, H., Faisal, W., Price, D. J., Holm, R., Kuentz, M. and Griffin, B. T. (2021) 'In silico, in vitro, and in vivo evaluation of precipitation inhibitors in supersaturated lipid-based formulations of venetoclax', Molecular Pharmaceutics, 18(6), pp. 2174-2188. doi: 10.1021/acs.molpharmaceut.0c00645
Type of publication	Article (peer-reviewed)
Link to publisher's version	10.1021/acs.molpharmaceut.0c00645
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Download date	2025-06-28 11:01:50
Item downloaded from	https://hdl.handle.net/10468/12204



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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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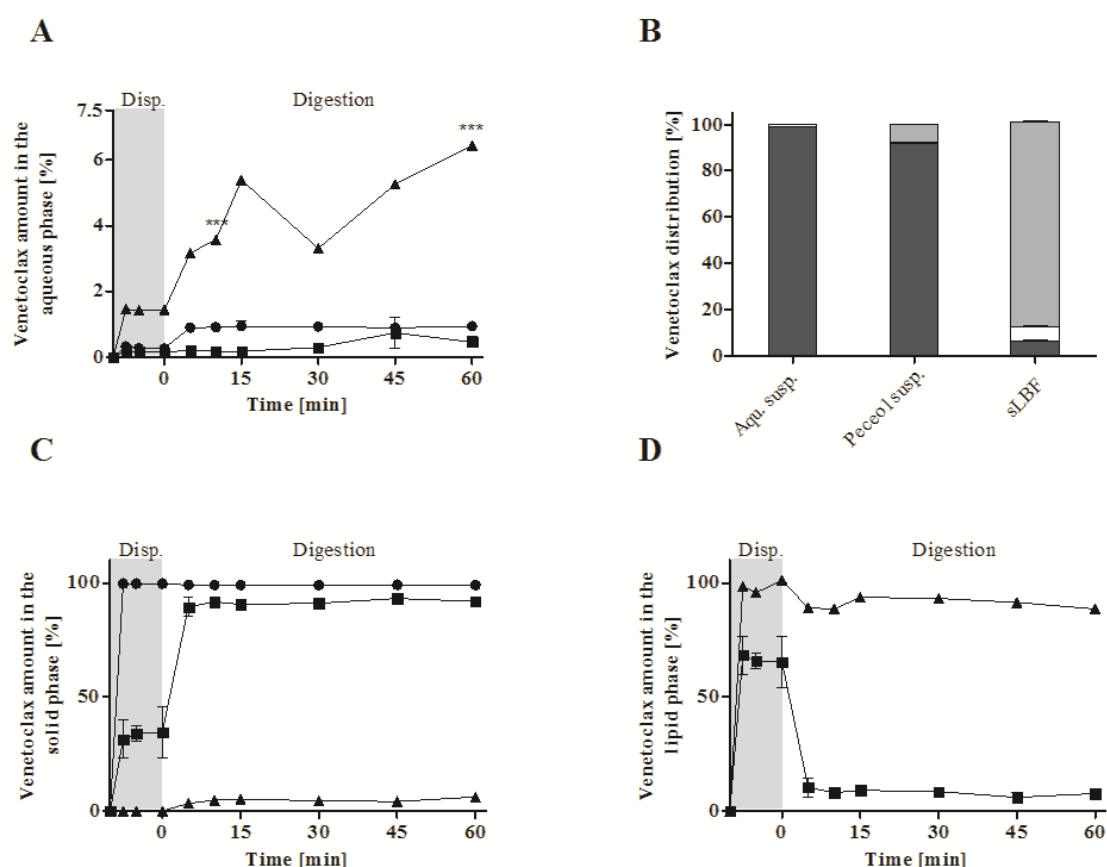


Figure S 1. *In vitro* lipolysis of venetoclax formulated as supersaturated Peceol® solution (sLBF) (▲), as well as previously reported aqueous suspension (●), Peceol® suspension (■).¹³ A: % of venetoclax in the aqueous phase, B: Distribution of venetoclax into the different phases after 60 min of lipolysis (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 \pm SD.

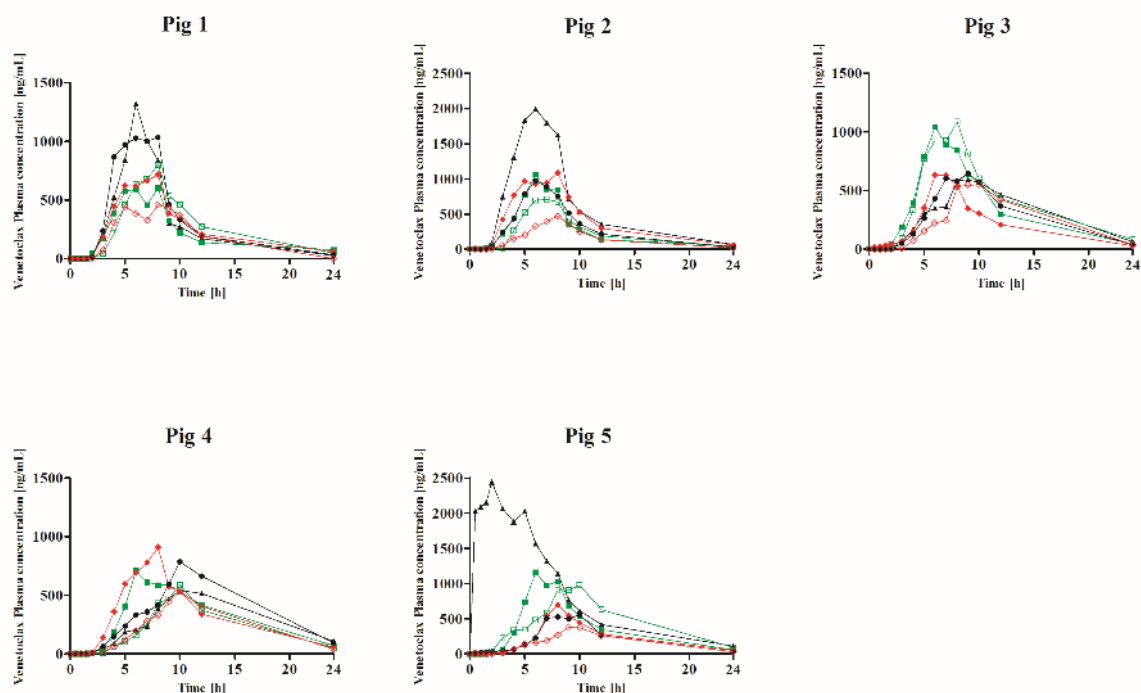


Figure S 2. Individual plasma concentration profile from 0 – 24 h of 100 mg venetoclax in landrace pigs for the tested formulations. sLBF-noPI (▲), sLBF-HPMC (■ - green), sLBF-HPMCAS (□ - green), sLBF-PVP (◆ - red), sLBF-PVP/VA (◇ - red), sLBF-Pluronic® F108 (●).

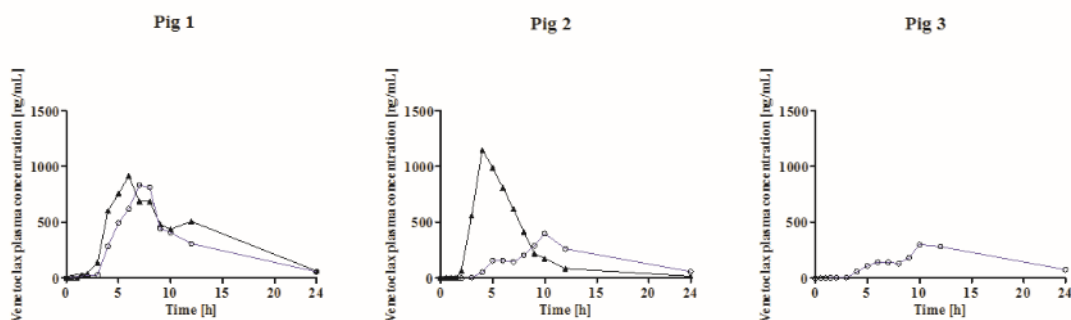


Figure S 3. Individual plasma concentration time profiles from 0 - 24 h of 100 mg venetoclax in landrace pigs for the tested formulations. sLBF-noPI (▲), sLBF-Eudragit® EPO (○ - blue). Due to an administration error, the sLBF-noPI of pig 3 was not obtained. sLBF-noPI has previously been reported.¹³

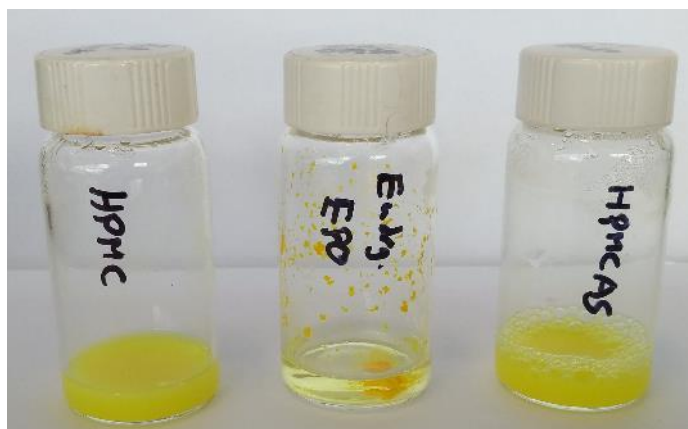


Figure S 4. PI test samples of sLBF-PI with HPMC, Eudragit® EPO and HPMCAS after 180 min in FaSSIF. Agglomeration of Eudragit® EPO can be observed.

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

ACKNOWLEDGEMENTS

N.J. Koehl, L.J. Henze, D.J. Price, B.T. Griffin, R. Holm and M. Kuentz are part of the PEARRL European Training network, which has received funding from the Horizon 2020 Marie Skłodowska-Curie Innovative Training Networks programme under grant agreement No. 674909.