Supplementary Information for:

A practical approach to modeling the impact of amorphous drug nanoparticles on the oral absorption of poorly soluble drugs

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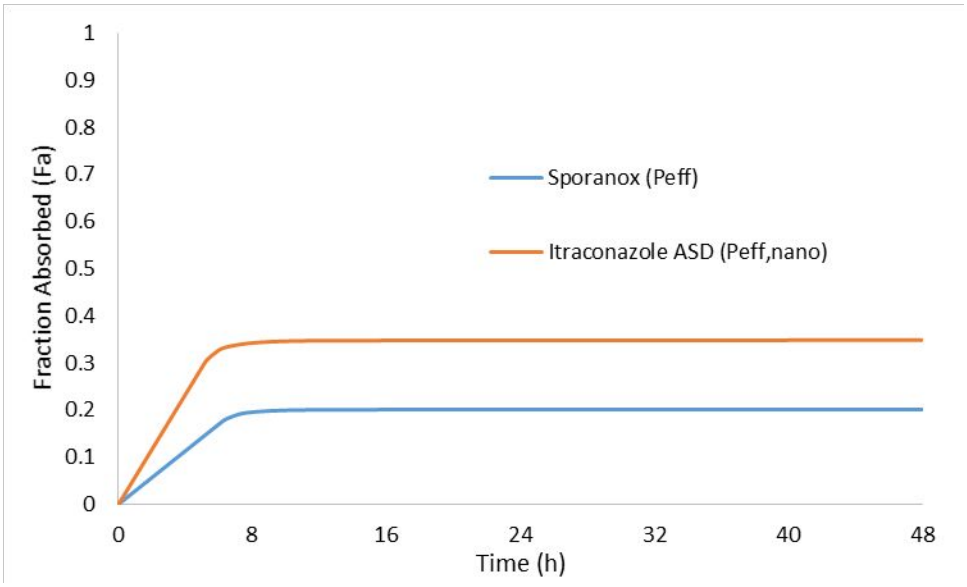

Figure S1. Simulated fraction dose absorbed vs. time for Sporanox (using P_{eff}) and itraconazole ASD (using $P_{eff,nano}$). Dose was 50 mg/kg to a 0.3 kg rat.

Table S1. Tabulated regional absorption simulations for Sporanox (using P_{eff}) and itraconazole ASD (using $P_{eff,nano}$).

Compartment	Sporanox, Peff	Itraconazole ASD, $Peff_{,nano}$
Stomach	0.0%	0.0%
Duodenum	4.2%	7.9%
Jejunum 1	11.8%	20.0%
Jejunum 2	4.0%	6.8%
Ileum 1	0.0%	0.1%
Ileum 2	0.0%	0.0%

Ileum 3	0.0%	0.0%
Caecum	0.0%	0.1%
Asc Colon	0.0%	0.1%
Total	20.1%	34.9%

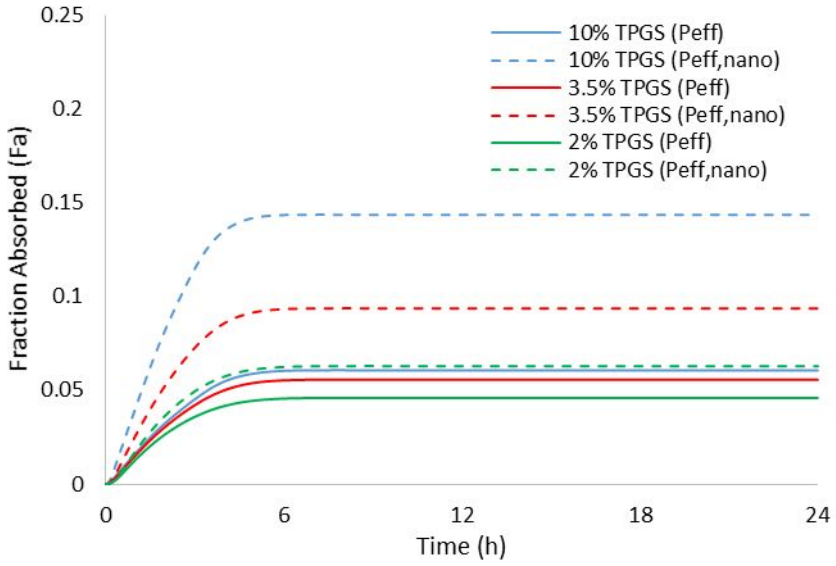

Figure S2. Simulated fraction dose absorbed vs. time for anacetrapib formulations comparing P_{eff} and $P_{eff,nano}$ at a 4 mg dose to beagle dogs. Y-axis adjusted for clarity.

Table S2. Tabulated regional absorption simulations for anacetrapib formulations comparing P_{eff} and $P_{eff,nano}$ at a 4 mg dose.

Compartment	10% TPGS, P_{eff}	10% TPGS, $P_{eff,nano}$	3.5% TPGS, P_{eff}	3.5% TPGS, $P_{eff,nano}$	2% TPGS, P_{eff}	2% TPGS, $P_{eff,nano}$
Stomach	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Duodenum	0.7%	1.6%	0.6%	1.0%	0.4%	0.6%
Jejunum 1	3.7%	8.8%	3.4%	5.7%	2.7%	3.8%
Jejunum 2	1.6%	3.5%	1.5%	2.4%	1.3%	1.7%
Ileum 1	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
Ileum 2	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
Ileum 3	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
Caecum	0.1%	0.2%	0.1%	0.1%	0.1%	0.1%
Asc Colon	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total	6.1%	14.4%	5.6%	9.3%	4.6%	6.3%

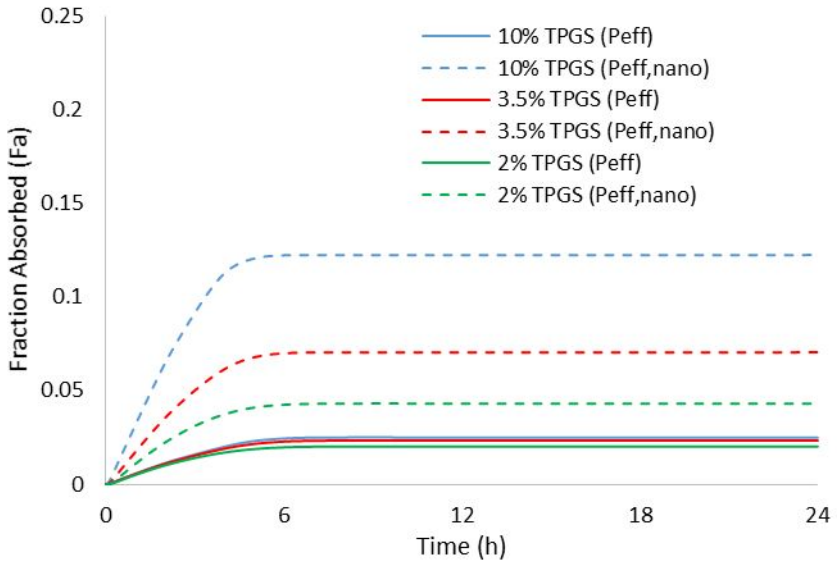

Figure S3. Simulated fraction dose absorbed vs. time for anacetrapib formulations comparing P_{eff} and $P_{eff,nano}$ at a 12 mg dose to beagle dogs. Y-axis has been adjusted for clarity.

Table S3. Tabulated regional absorption simulations for anacetrapib formulations comparing P_{eff} and $P_{eff,nano}$ at a 12 mg dose.

Compartment	10% TPGS, P_{eff}	10% TPGS, $P_{eff,nano}$	3.5% TPGS, P_{eff}	3.5% TPGS, $P_{eff,nano}$	2% TPGS, P_{eff}	2% TPGS, $P_{eff,nano}$
Stomach	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Duodenum	0.3%	1.5%	0.2%	0.8%	0.2%	0.4%
Jejunum 1	1.5%	7.7%	1.4%	4.4%	1.2%	2.6%
Jejunum 2	0.6%	2.8%	0.6%	1.7%	0.5%	1.1%
Ileum 1	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%
Ileum 2	0.0%	0.1%	0.0%	0.0%	0.0%	0.0%

Ileum 3	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Caecum	0.0%	0.1%	0.0%	0.1%	0.0%	0.1%
Asc Colon	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total	2.5%	12.2%	2.3%	7.1%	2.0%	4.3%

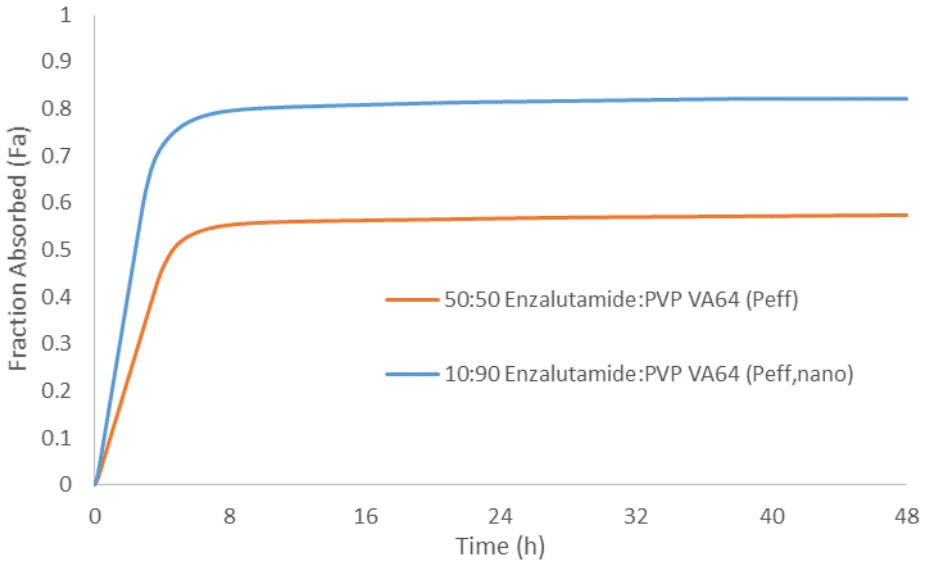

Figure S4. Simulated fraction dose absorbed vs. time for 50:50 enzalutamide:PVP VA64 (using P_{eff}) and 10:90 enzalutamide:PVP VA64 ASDs (using $P_{eff,nano}$). Dose was 100 mg/kg to a 0.5 kg rat.

Table S4. Tabulated regional absorption simulations for 50:50 enzalutamide:PVP VA64 (using P_{eff}) and 10:90 enzalutamide:PVP VA64 ASDs (using $P_{eff,nano}$).

Compartment	50:50 enzalutamide:PVP VA64, P_{eff}	10:90 enzalutamide:PVP VA64, $P_{eff,nano}$
Stomach	0.0%	0.0%
Duodenum	11.0%	18.4%
Jejunum 1	32.0%	45.1%
Jejunum 2	12.0%	15.3%
Ileum 1	0.2%	0.2%
Ileum 2	0.1%	0.1%
Ileum 3	0.1%	0.1%
Caecum	0.8%	1.2%
Asc Colon	1.2%	1.7%
Total	57.4%	82.1%

Table S5. Tabulated parameters for calculating $P_{eff,nano\ (n)}$ for enzalutamide in rats in each individual compartment in GastroPlus using Eq 9-10 in the main text. The P_{eff} was adjusted in each compartment under the physiology tab of GastroPlus.

Parameter	Duodenum	Jejunum 1	Jejunum 2	Illeum 1	Illeum 2	Illeum 3	Caecum	Asc Colon
P_{eff} (cm/s)	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}	1.03×10^{-4}
D_u (cm^2/s)	6.33	6.33	6.33	6.33	6.33	6.33	6.33	6.33

C_u (µg/mL)	42	42	42	42	42	42	42	42
C_{SIF} (µg/mL)	680	588	237	96	44	42	42	42
C_{nano} (µg/mL)	10393	9036	3986	2259	2236	2225	2081	1882
$d_{nano(n)}$ (nm)	100	93	71	59	60	59	58	56
Fa (prior compartment)	0	0.184	0.456	0.156	0.002	0.001	0.013	0.018
$P_{eff,nano(n)}$ (cm/s)	**1.87×10^{-4}**	**1.90×10^{-4}**	**1.93×10^{-4}**	**1.93×10^{-4}**	**2.09×10^{-4}**	**2.10×10^{-4}**	**2.05×10^{-4}**	**1.99×10^{-4}**

Figure S5. Simulated blood plasma profiles comparing P_{eff}, $P_{eff,nano}$ and $P_{eff,nano\ (n)}$ for 10:50 enzalutamide:PVP VA64. Dose was 100 mg/kg to a 0.5 kg rat.