Supporting information

Effect of piperine co-delivery on the oral bioavailability of cannabidiol: Insights from *in vitro* digestion and *in vivo* pharmacokinetics

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Table S1: Composition (mmol/L) of simulated digestive fluids according to recommended by Brodkorb et al. [*Nature Protocols*, 14, (2019) p. 991–1014].

Salt	Simulated salivary fluid (SSF)	Simulated gastric fluid (SGF)	Simulated intestinal fluid (SIF)
KCl	15.1	6.9	6.8
KH_2PO_4	3.7	0.9	0.8
$NaHCO_3$	13.6	25.0	85.0
NaCl	-	47.2	38.4
$MgCl_2(H_2O)_6$	0.15	0.12	0.33
$(NH_4)_2CO_3$	0.06	0.5	-
$CaCl_2(H_2O)_2$	1.5	0.15	0.6

Table S2: Protocol for blood collection via mandibular vein.

	Mice code									
Collection time (h)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
0										
0.5										
1										
2										
3										
4 (cardiac punch)										
6 (cardiac punch)										

Table S3: Entrapment efficiency of PIP into the NLCs during 28 days of storage at 4 °C.

Sample	Day 0	14 days	28 days
NLC-PIP-CBD_{ext}	99.7 ± 0.3	99.80 ± 0.03	99.80 ± 0.01
NLC-PIP-CBD_{iso}	99.7 ± 0.2	99.82 ± 0.02	99.80 ± 0.01