Electronic Supplementary Information

Enhanced hepatic targeted delivery via oral administration using nanoliposomes functionalized with novel DSPE-PEG-cholic acid conjugate

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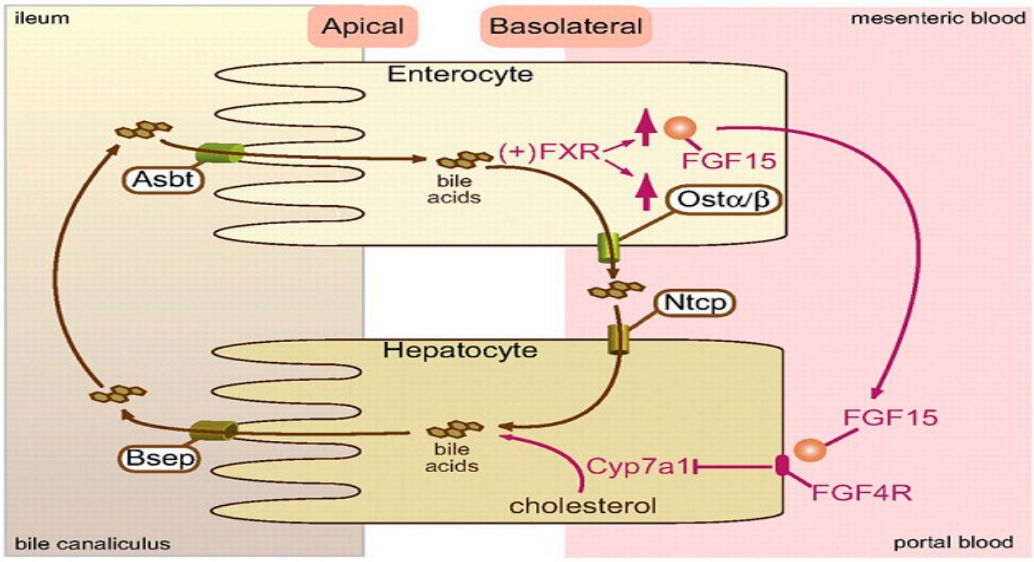


Fig. S1 The vivo fate of cholic acid after oral administration

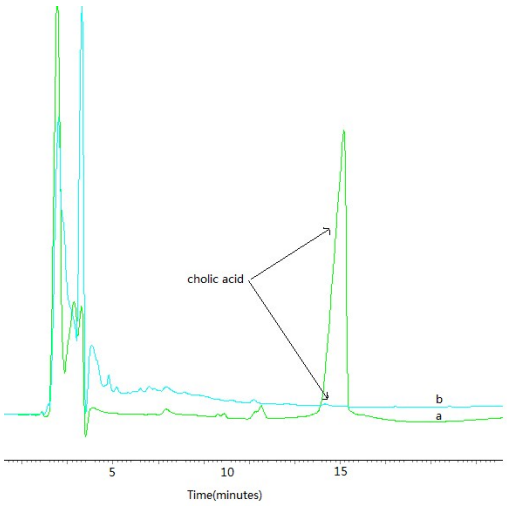
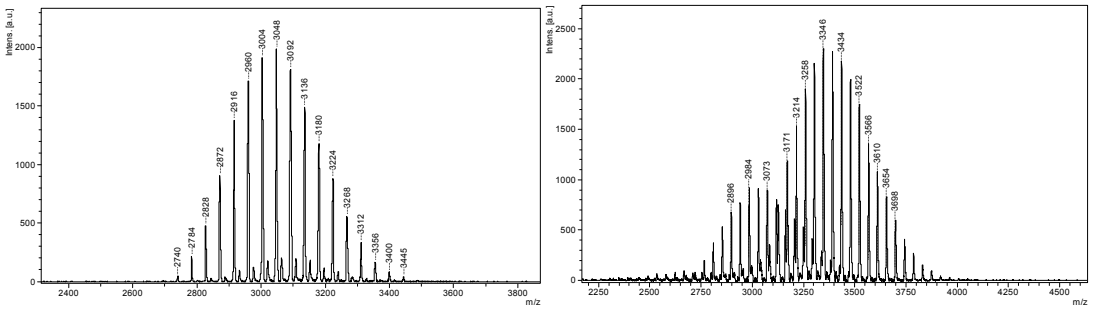


Fig. S2 HPLC of cholic acid and DSPE-PEG-cholic acid. a:cholic acid,b: DSPE-PEG-cholic acid.



a b

Fig. S3 MALDI-TOF MS spectra of DSPE-PEG-cholic acid. a:cholic acid,b: DSPE-PEG-cholic acid.

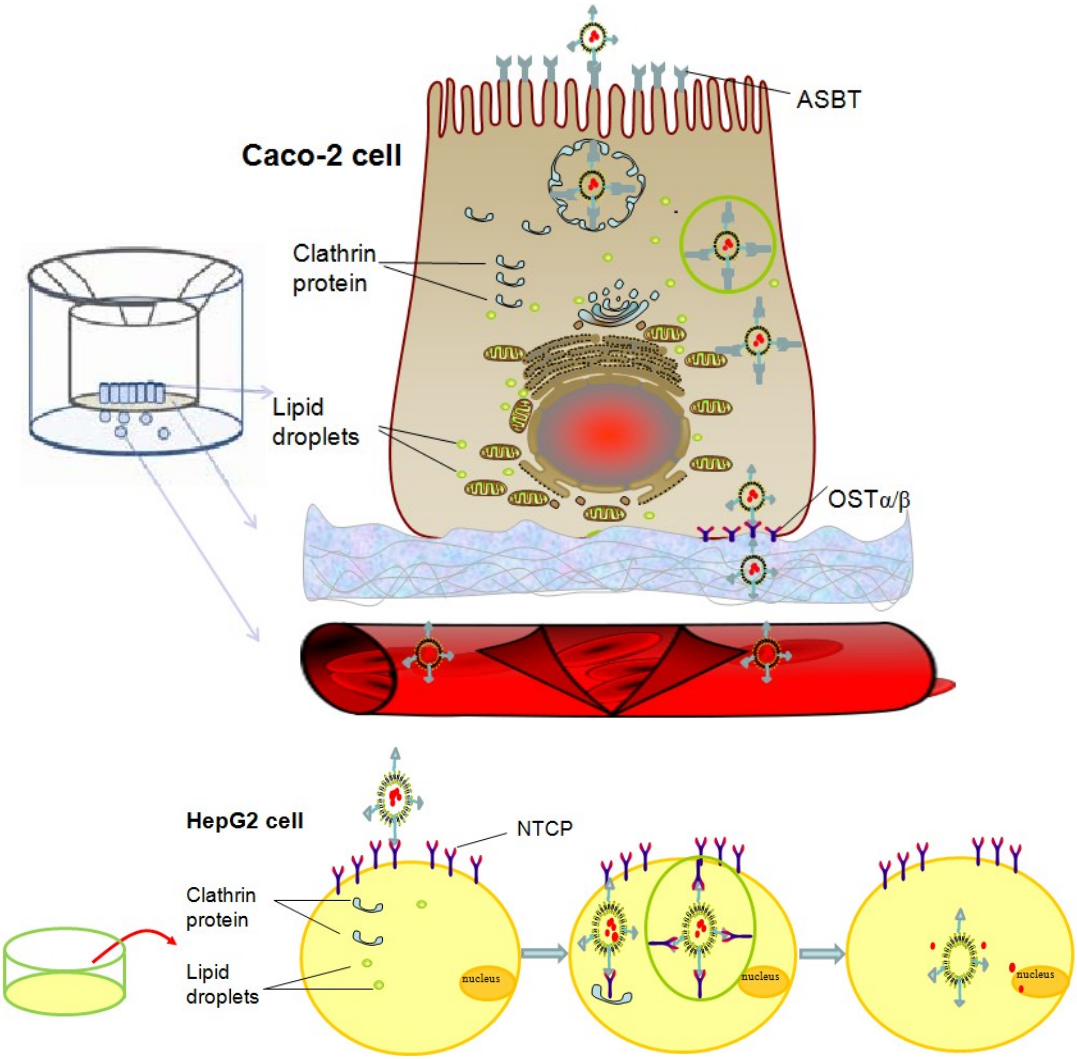


Fig. S4 A.Schematic diagram of the transcellular process CA-LPs on Caco-2 monolayer; B. Schematic diagram of the CA-LPs targeting to NTCP and the intracellular trafficking.

Table S1 Characteristics of silybin-loaded functional nanoliposomes and the control(n=3)

Characterizations loaded contents	Particle size (nm)	PDI	Zeta potential (mV)	Encapsulation ratio(%)	Loading efficiency(%)
LPs-silybin	96.07±1.14	0.207±0.0135	-11.67±1.25	99.93±0.0049	7.46±0.65
CA-LPs-silybin	94.65±0.73	0.179±0.007	-4.02±0.62	99.86±0.0049	6.56±0.72

Table S2 The percent of free drug and drug loaded in nanoliposomes among all drugs in basolateral chamber(n=3)

groups	% free drug in basolateral chamber	% drug loaded in nanoliposomes in basolateral chamber
LPs-silybin	10.95±4.01	89.05±4.01
CA-LPs-silybin	3.17±1.29	96.83±1.29

Table S3 Pharmacokinetic parameters in blood silybin after oral administration of free drug, LPs-silybin or CA-LPs-silybin to rats; mean F S.E. (n=6)

Parameter	Free drug	LPs-silybin	CA-LPs-silybin
C_{max}(ug/mL)	0.12±0.014	0.12±0.019	0.16±0.019
T_{max}(min)	30±6.12	30±18.37	30±17.54
AUC_{0-240}(μg/ml*min)	21.40±1.15	#23.39±3.48	**#28.29±3.86
MRT(min)	380.18±74.84	732.39±432.32	546.08±93.69
F_r(%)	-	109.30	132.18

Fr: relative bioavailability=($AUC_{0-240(Test)}$×100)/($AUC_{0-240(silybin)}$).Comparative Pharmacokinetics profile in blood of silybin solution, LPs-silybin and CA-LPs-silybin 4h post administration (mean±S.E., n=6, ** p<0.01 between silybin solution and other formulations, # P<0.05 between LPs-silybin and CA-LPs-silybin).

Table S4 Pharmacokinetic parameters in liver silybin after oral administration of free drug, LPs-silybin or CA-LPs-silybin to rats; mean F S.E.(n=6)

Parameter	Free drug	LPs-silybin	CA-LPs-silybin
C_{max}(ng/g)	352.43±69.01	**## 1238.506±270.48	**## 3874.399±1283.71
T_{max}(min)	30±0	30±0	30±0
AUC0-	58379.33±7836.90	**##	**##

240(ng/g*min)		125867.7±22975.6	253823±24135.35
MRT(min)	455.89±121.76	132.09±33.81	107.34±21.07
F_r(%)	-	215.60	434.78

F_r: relative bioavailability=$(AUC_{0\text{-}240(Test)} \times 100)/(AUC_{0\text{-}240(silybin)})$.Comparative Pharmacokinetics profile in blood of silybin solution, LPs-silybin and CA-LPs-silybin 4h post administration (mean±S.E., n=6, $^{**}p<0.01$ between silybin solution and other formulations, $^{\#\#}P<0.01$ between LPs-silybin and CA-LPs-silybin).