

Supporting information

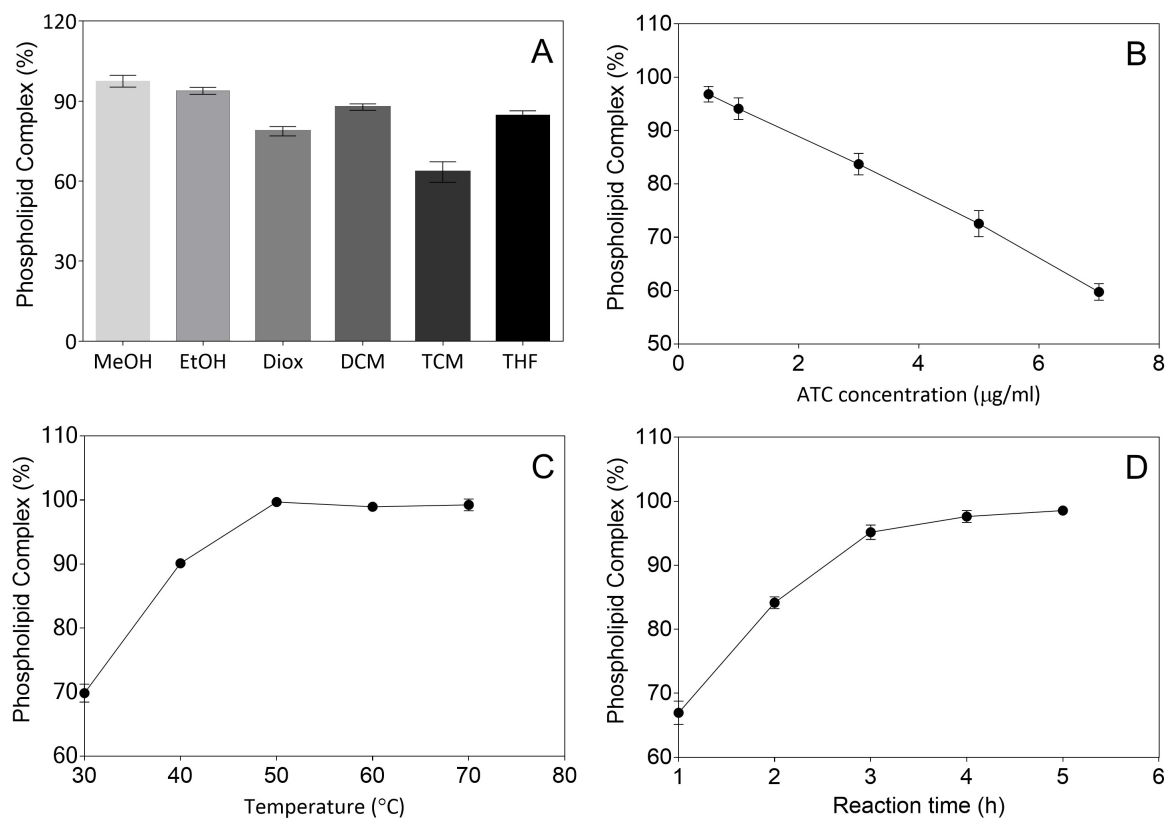


Figure S1 Optimization of the reaction parameters by single factor investigation. (A) Reaction solvent. (B) ATC concentration. (C) Reaction temperature. (D) Reaction time.

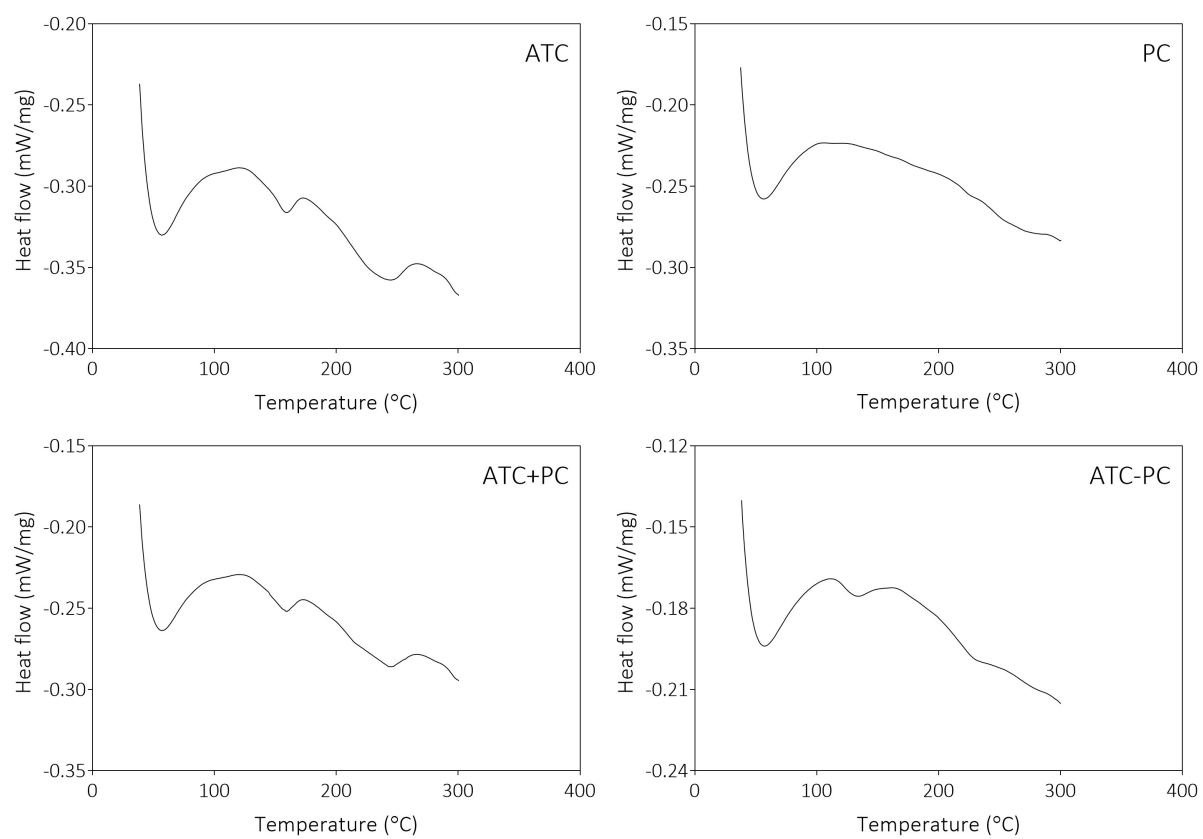


Figure s2 DSC thermograms of ATC, PC, ATC+PC and ATC-PC

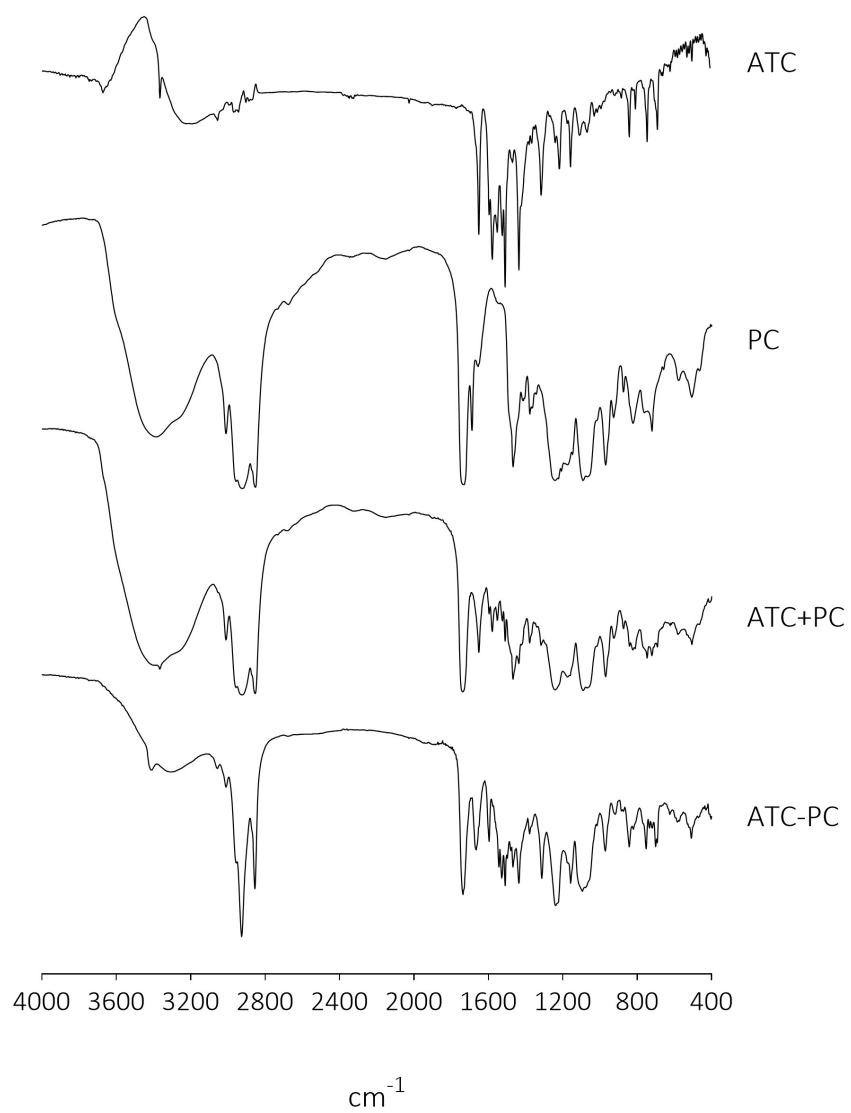


Figure s3 FT-IR spectra of ATC, PC, ATC+PC and ATC-PC

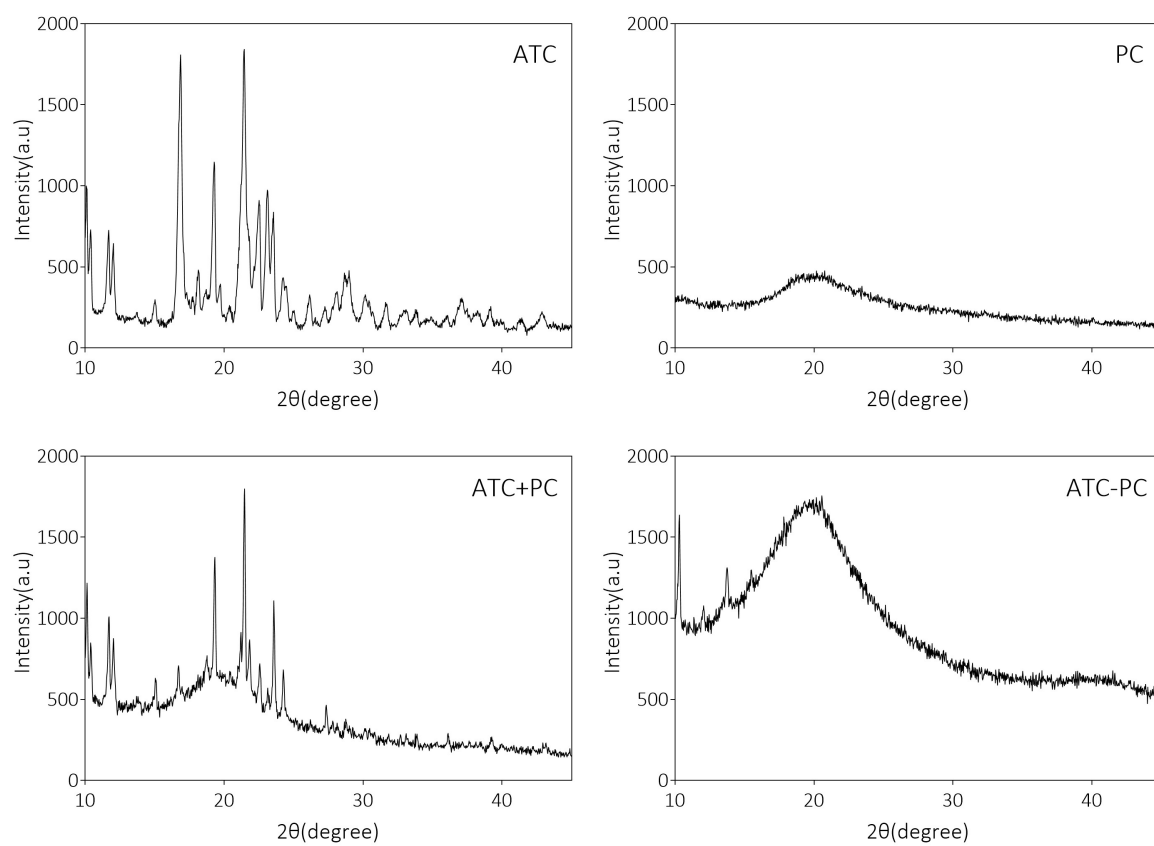


Figure s4 X-ray diffraction patterns of ATC, PC, ATC+PC and ATC-PC

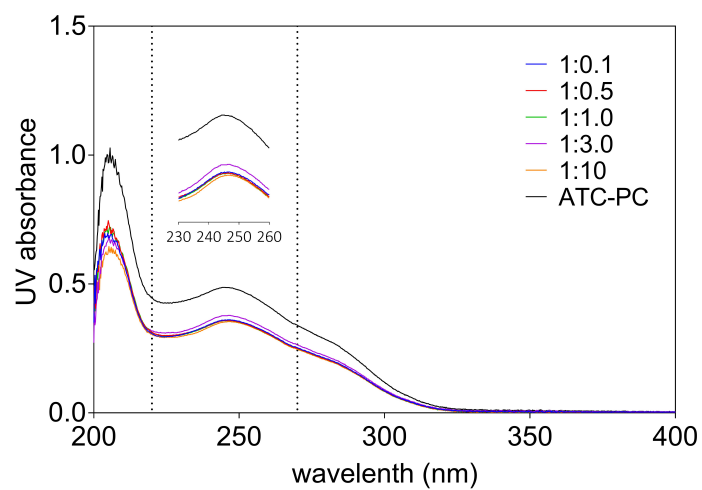


Figure s5 UV-vis absorbance of ATC+ PC mixture (molar ratio from 1:0.1 to 1:10) and ATC-PC complex (1:1).

Table s1 Factors and levels of L₁₆ (4⁵) orthogonal test

Levels	Influence factors				
	Lecithin (A)	Sodium oleate (B)	Tween-80 (C)	Poloxamer (D)	Soybean oil (E)
1	0.8%	0.00%	0.2%	0.6%	5%
2	1.0%	0.05%	0.4%	0.8%	7%
3	1.2%	0.07%	0.6%	1.0%	9%
4	1.4%	0.09%	0.8%	1.2%	11%

Table s2 Evaluation index of L₁₆ (4⁵) orthogonal design

Test No.	Evaluation index		
	Particle size (nm)	PDI	Ke
1	145.8	0.237	0.259
2	159.1	0.193	0.294
3	141.6	0.23	0.279
4	153.5	0.169	0.304
5	134.2	0.207	0.263
6	185.4	0.168	0.357
7	178.9	0.165	0.399
8	169.7	0.199	0.351
9	169.9	0.165	0.416
10	186.9	0.133	0.429
11	169.9	0.193	0.399
12	177.2	0.148	0.386
13	200.3	0.129	0.488
14	160.6	0.166	0.301
15	150.3	0.243	0.026
16	154.7	0.133	0.219

* Scores = [(Particle size/200.3) + (PDI/0.243) + (Ke/0.488)] ×100

Table s3 Fitting results for drug release curve of ATC submicron emulsion

Release curve fitting model		R^2
First-order release rate equation	$Q=21.37\ln t+7.916$	0.921
Higuchi equation	$Q=18.96t^{1/2}-5.337$	0.958
Ritger-Peppas equation	$\ln Q=0.614\ln t+3.149$	0.977

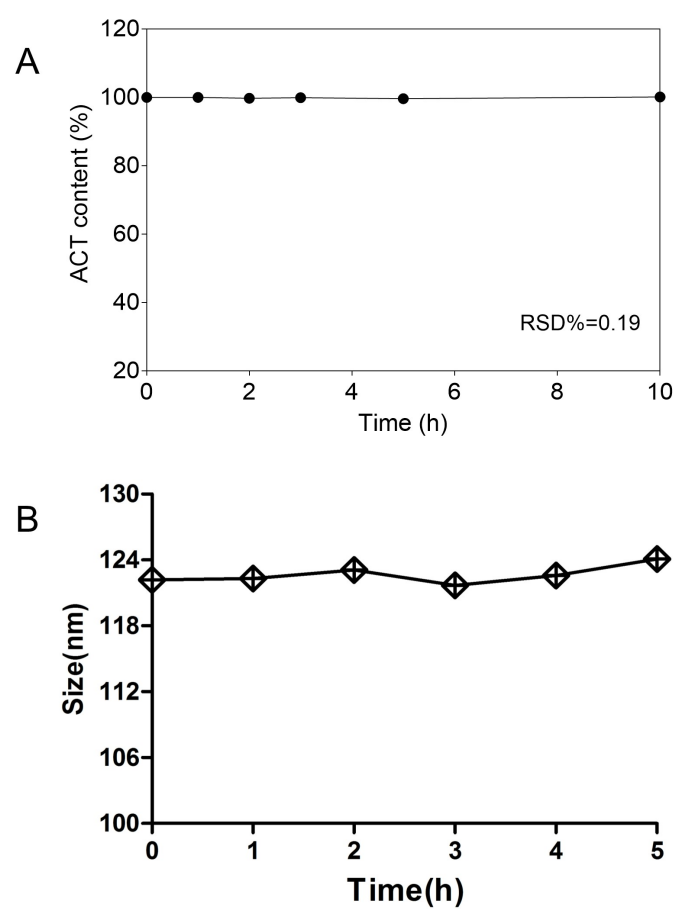


Figure s6 The stability of ATC submicron emulsion in K-R solution. (A) Drug content variation in K-R solution within 10h. (B) Particle size changes in K-R solution within 5h.

Lymphatic transportation of ATC submicron emulsion

To study the lymphatic transportation of ATC submicron emulsion, experiment was performed as following. The selecting duodenum, jejunum, ileum and colon segments (about 10 cm) were washed using saline and ligated at two ends. 2ml of 1 mg/ml free ATC solution or ATC submicron emulsion was injected. After 2h, mesenteric lymph duct cannulation was performed to collect lymph fluid for determination of ATC concentration by HPLC method.

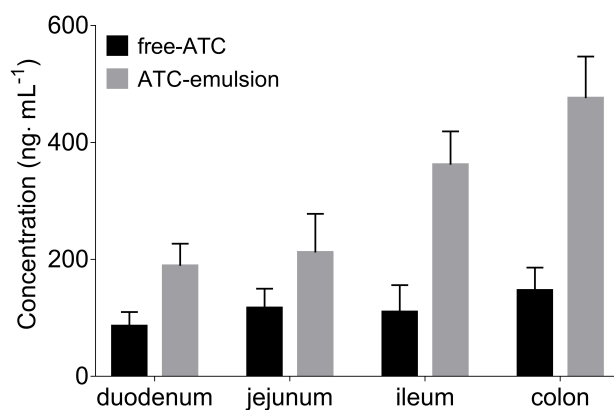


Figure s7 Drug concentration of free ATC solution or ATC submicron emulsion in lymph fluid absorbed from different intestinal segments after 2h.