

Supplementary Table S1 : The plasma samples were analyzed by liquid phase mass spectrometry. The pharmacokinetic parameters are determined based on the average concentration-time data in the research-oriented test drug. Use WinNonlin® Professional 6.3 non-isolated module to calculate parameters (drug peak concentration, peak time and final elimination rate, etc.). The calculation of PK parameters does not include any BLQ (10ng/mL) concentration.

#### LC-MS methods

LC method (HPLC: Shimadzu LC20AD)				
Column:	Waters ACQUITY BEH C8 1.7um 2.1*50mm			
Mobile Phase:	A:	0.1% formic acid (FA) aqueous solution	B:	0.1% FA in acetonitrile (CAN)
HPLC Gradient				
Total time (min)	Flow rate (µL/min)	A (%)	B (%)	
0.01	500	70	30	
0.3	500	70	30	
1.3	500	2	98	
2	500	2	98	
2.2	500	70	30	
2.7	500	70	30	
Mass Spectrometer Conditions (Mass Spectrometer: API4000)				
Ionization Mode:	ESI			
Mass Spectrometer Conditions:				
Compound ID:	Q1	Q3	DP	CE
Dic	296	250.1	50	17
Simvastatin-1	419.2	199.5	100	15
Sample processing:				
For rabbit plasma samples: In an EP tube, 5 µL of duplicate samples, QC samples and rabbit plasma samples with 150 µL ACN (50 ng / mL propranolol and 200 ng / mL tolbutamide and 500 ng / mL diisopropylcarbodiimide). Vortex the mixture for 1 minute, centrifuge for 10 minutes (13,000 rpm, 4 ° C), transfer 50 µL of the supernatant to a 96-well plate containing 150 µL of pure water, shake for 10 minutes, and finally inject 10 µL into the liquid phase. Grade mass spectrometry system.				

Supplementary Table S2 : Cerebrospinal fluid-liquid phase mass spectrometry. Rabbit cerebrospinal fluid before, 3h, 5h, 8h, 24h, 3, 7, 14 and 28 days after the operation were tested.

Cerebrospinal fluid-liquid phase mass spectrometry

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HPLC:	Shimadzu LC20AD		
Autosampler:	CTC PAL		
Mass Spectrometer:	API4000		
	LC Method		
Column:	Thermo Hypersil Gold 1.9um 50*2.1mm		
Mobile Phase:	A:	0.1%FA in water	B: 0.1%FA in ACN
	HPLC Gradient		
Total Time(min)	Flow Rate( $\mu$ L/min)	A(%)	B(%)
0.01	500	70	30
0.30	500	70	30
0.90	500	40	60
2.00	500	5	95
2.40	500	5	95
2.50	500	70	30
3.00	500	70	30
	Mass Spectrometer Conditions		
Ionization Mode:	ESI		
	Mass Spectrometer Conditions:		
Compound ID:	Q1	Q3	DP CE
Tol	271.0	74.2	70 22
Simvastatin-1	419.2	199.5	100 15
	Sample processing:		
Rabbit cerebrospinal fluid samples: In an EP tube, duplicate samples of 10 $\mu$ L, duplicate QC samples and rabbit cerebrospinal fluid samples with 60 $\mu$ L ACN (50 ng/mL propranolol and 200 ng/mL tolbutamide and 500 ng/mL diisopropylcarbodiimide). Vortex the mixture for 1 minute, centrifuge for 10 minutes (13,000 rpm, 4 ° C), transfer 50 $\mu$ L of the supernatant to a 96-well plate containing 150 $\mu$ L of pure water, shake for 10 minutes, and finally inject 10 $\mu$ L into the liquid phase. Grade mass spectrometry system.			

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