

Table S1. Optimizing TFS using BBD ($n=3$, mean \pm SD).

Formulation		Factors			Responses		
Std	Run	X1	X2	X3	EE _{IMP} (%)	EE _{FU} (%)	Y (%)
1	1	1:12.5	6:4	40 °C	84.69 \pm 3.6	73.72 \pm 2.7	79.21
12	2	1:15.0	8:2	45 °C	86.49 \pm 2.5	76.57 \pm 1.4	81.53
3	3	1:12.5	8:2	40 °C	85.26 \pm 3.7	76.24 \pm 3.1	80.75
17	4	1:15.0	7:3	40 °C	89.94 \pm 4.4	81.74 \pm 2.9	85.84
4	5	1:17.5	8:2	40 °C	84.10 \pm 1.8	75.87 \pm 3.7	79.99
8	6	1:17.5	7:3	45 °C	85.88 \pm 0.9	76.41 \pm 2.2	81.14
11	7	1:15.0	6:4	45 °C	83.75 \pm 7.1	75.94 \pm 2.2	79.84
7	8	1:12.5	7:3	45 °C	87.71 \pm 6.3	77.35 \pm 2.2	82.53
9	9	1:15.0	6:4	35 °C	83.21 \pm 3.0	70.55 \pm 2.9	76.88
14	10	1:15.0	7:3	40 °C	88.79 \pm 2.9	79.98 \pm 2.6	84.39
16	11	1:15.0	7:3	40 °C	89.73 \pm 2.7	80.58 \pm 0.4	85.15
15	12	1:15.0	7:3	40 °C	89.30 \pm 1.6	80.21 \pm 3.6	84.75
13	13	1:15.0	7:3	40 °C	87.82 \pm 1.2	79.50 \pm 5.7	83.66
6	14	1:17.5	7:3	35 °C	83.19 \pm 6.4	70.80 \pm 3.8	76.99
5	15	1:12.5	7:3	35 °C	81.41 \pm 7.6	72.83 \pm 2.4	77.12
2	16	1:17.5	6:4	40 °C	84.64 \pm 2.2	73.60 \pm 2.9	79.12
10	17	1:15.0	8:2	35 °C	80.67 \pm 8.5	71.96 \pm 5.6	76.31

Table S2. ANOVA for Response Surface Quadratic Model.

Source	Squares	df	Mean Square	F-Value	P-Value
Model	0.015	9	1.686*10 ⁻³	37.20	<0.0001
X_1	7.011*10 ⁻⁵	1	7.011*10 ⁻⁵	1.55	0.2537
X_2	1.557*10 ⁻⁴	1	1.557*10 ⁻⁴	3.43	0.1063
X_3	3.929*10 ⁻³	1	3.929*10 ⁻³	86.66	<0.0001
X_1X_2	1.159*10 ⁻⁵	1	1.159*10 ⁻⁵	0.26	0.6286
X_1X_3	3.950*10 ⁻⁵	1	3.950*10 ⁻⁵	0.87	0.3817
X_2X_3	1.265*10 ⁻⁴	1	1.265*10 ⁻⁴	2.79	0.1388
X_1^2	1.846*10 ⁻³	1	1.846*10 ⁻³	40.71	0.0004
X_2^2	3.539*10 ⁻³	1	3.539*10 ⁻³	78.05	<0.0001
X_3^2	4.362*10 ⁻³	1	4.362*10 ⁻³	96.20	<0.0001
Residual	3.174*10 ⁻⁴	7	4.534*10 ⁻⁵		
Lack of Fit	5.040*10 ⁻⁵	3	1.680*10 ⁻⁵	0.25	0.8569
Pure Error	2.670*10 ⁻⁴	4	6.674*10 ⁻⁵		
Cor Total	0.015	16	1.686*10 ⁻³		

Table S3. Encapsulation Rate of TFS

Number	EE _{IMP}	EE _{FU}	EE _{5-FU/IMP}	EE _{5-FU/IMP} (projected value)	Absolute deviation	RSD
1	88.49%	80.23%	84.36%		0.99%	
2	88.80%	79.92%	84.36%	85.20%	0.99%	0.9%
3	92.38%	78.98%	85.68%		0.56%	

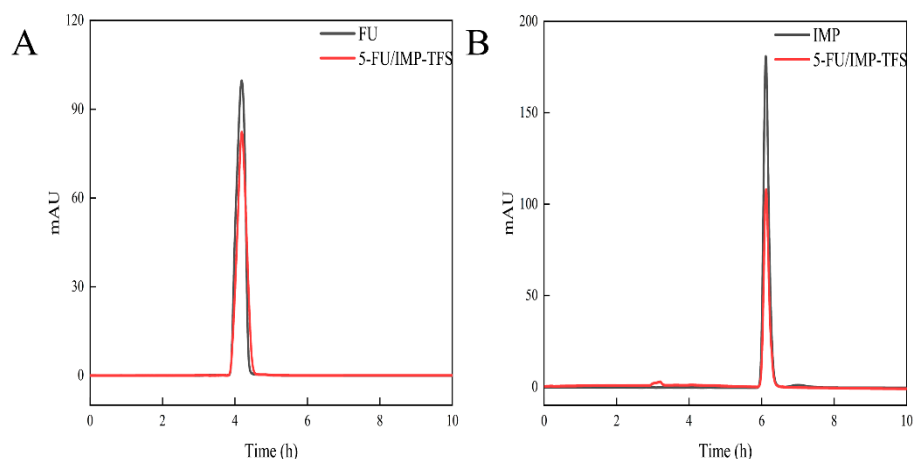


Fig. S1. The HPLC Chromatograms. (A) 5-FU, (B) IMP.

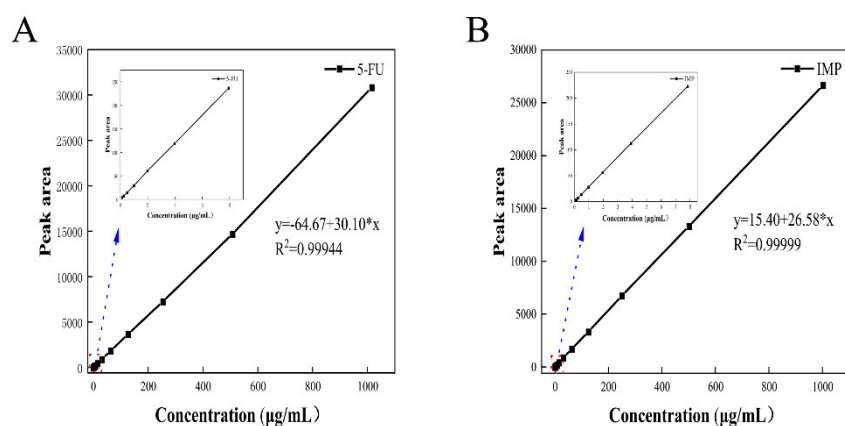


Fig. S2. The HPLC Standard Curves. (A) 5-FU, (B) IMP.

Table S4. HPLC Precision Test

	Concentration (µg)	Peak area						Average peak area	RSD (%)
		1	2	3	4	5	6		
IMP	125.63	3212.6	3207.6	3205.4	3205.7	3205.3	3206.4	3207.17±2.55	0.08
	251.25	6498.5	6501.1	6489.0	6496.8	6495.5	6498.6	6496.58±3.81	0.06
	502.50	12666.2	12667.2	12646.9	12661.0	12678.3	12653.0	12662.10±10.17	0.08
	132.75	4028.5	4031.7	4033.5	4029.7	4033.3	4034.4	4031.85±2.13	0.05
FU	265.50	7998.9	8114.6	8112.8	8121.4	8126.7	8080.1	8092.42±44.38	0.55
	531.00	16709.0	16731.6	16704.2	16720.8	16494.2	16524.1	16647.32±98.46	0.59

Table S5. HPLC Stability Test

	Concentration (µg)	Peak area						Average peak area	RSD (%)
		0 h	3 h	6 h	12 h	18 h	24 h		
IMP	62.81	1627.5	1609.4	1615.9	1612.4	1646.4	1616.2	1621.30±12.55	0.77
FU	66.38	1970.5	1975.5	1940.6	1930.8	1970.2	1975.3	1960.48±17.87	0.91

Table S6. HPLC Repeatability Test

	Concentration	Peak area						Average peak area	RSD (%)
	(µg)	1	2	3	4	5	6		
IMP	62.81	1616.5	1617.4	1614.0	1613.1	1612.1	1611.4	1614.08±2.20	0.14
FU	66.38	1963.5	1970.4	1968.6	1965.9	1973.0	1970.7	1968.68±3.17	0.16

Table S7. IMP Sample HPLC Recovery Rate

	Preparat ions	Concent ration (µg)	Preparation peak area	Control peak area	Recovery rate (%)	Average recovery rate (%)	RSD (%)
IMP	TFS	255.50	659.7	655.1	100.71	99.37±1.28	1.29
			653.4		99.75		
			639.6		97.64		
		127.75	325.8	338.5	96.25	96.16±0.74	0.77
			322.3		95.21		
			328.4		97.01		
	TFS	63.88	161.1	167.1	96.42	97.27±1.43	1.47
			160.6		96.12		
			165.9		99.29		
		251.25	613.5	632.3	97.02	99.96±2.13	2.13
			645.0		102.00		
			637.7		100.85		
	TFS gel	125.63	313.5	324.5	96.63	96.58±1.08	1.12
			317.6		97.89		
			309.0		95.24		
		62.81	159.5	160.4	99.46	99.11±0.31	0.31
			158.3		98.72		
			159.0		99.15		

Table S8. 5-FU Sample HPLC Recovery Rate

	Preparat ions	Concent ration (µg)	Preparation peak area	Control peak area	Recovery rate (%)	Average recovery rate (%)	RSD (%)
FU	TFS	259.00	775.4	789.5	98.21	98.92±0.58	0.59
			781.0		98.92		
			786.6		99.63		
		129.50	381.0	390.6	97.53	97.71±0.45	0.46
			380.0		97.28		
			384.1		98.33		
	TFS	64.75	192.3	189.2	101.63	99.16±1.95	1.96
			183.3		96.87		
			187.3		98.99		
		251.25	801.3	824.7	97.16	100.49±2.53	2.52
			851.8		103.28		
			833.2		101.03		
	TFS gel	125.63	386.1	399.9	96.54	96.81±0.54	0.55
			390.2		97.56		
			385.3		96.34		
		62.81	209.0	201.4	103.76	102.21±1.14	1.11
			205.0		101.77		
			203.6		101.08		