SUPPORTING INFORMATION

Folic acid modified erythrocyte membrane loading dual drug for targeted and chemo-photothermal synergistic cancer therapy

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Optimization of preparation parameters. Single influence factor experiment was used to optimize the preparation parameters, the entrapment efficiency (EE%)，drug loading efficiency (LE%), particle diameter and polydispersity index (PDI) were used as indexes to investigate several single influence factors. The results were shown in Table 1s and the EE% and LE% of drugs in different nanoformulation using the optimal parameters were shown in Table2s.

Table 1s Preparation optimization of drug loaded nanoparticles.

		LE%	EE%	Diameter(nm)	PDI
Organic solvents	Acetone	4.23	42.56	100.7	0.280
	Acetone:CH2Cl2 =1:1	8.54	85.38	112.3	0.096
	CH2Cl2	8.62	86.16	131.1	0.204
PLGA concentration	5mg/ml	8.54	85.38	112.3	0.096
	10mg/ml	6.25	62.54	119.0	0.141
	15mg/ml	5.96	59.583	138.1	0.150
	20mg/ml	6.35	63.47	144.1	0.184
Drug loading ratio	10:1	8.54	85.38	112.3	0.096
	5:1	17.02	85.12	111.3	0.252
	2:1	33.83	65.66	100.5	0.258
Oil/water ratio	1:10	1.64	16.35	134.9	0.173
	1:5	8.54	85.38	112.3	0.096
	1:4	5.09	50.89	106.1	0.229
	1:2	5.94	59.43	163.7	0.223
PVA concentration	0.5%	5.79	57.89	134.9	0.173
	1.0%	8.54	85.38	112.3	0.096
	1.5%	5.79	57.89	108.6	0.396
	2%	4.68	46.82	60.9	0.323
	3%	5.32	53.24	108.5	0.528
Ultrasonic power	95w	3.19	31.89	125.8	0.253
	142.5w	2.61	26.11	144.2	0.253
	190w	8.54	85.38	112.3	0.096
	237.5w	4.54	45.40	157.1	0.317
	285w	5.38	53.79	130.8	0.271
Ultrasound time	5min	5.99	59.89	163.4	0.232
	8min	4.44	44.41	138.9	0.155
	10min	3.07	30.71	140.6	0.221
	15min	8.54	85.38	112.3	0.096
	18min	6.33	63.31	105.9	0.252
M_W of PLGA	10000	8.54	85.38	112.3	0.096
	20000	8.12	81.15	176.4	0.230

Table 2s. The EE% and LE% of drugs in nanoformulations.

	DOX		ICG	
	LE%	EE%	LE%	EE%
DNPs	8.54±0.24	85.38±2.39	/	/
DRNPs	6.61±0.22	64.91±2.11	/	/
DINPs	3.93±0.12	81.49±2.41	4.09±0.27	83.23±1.74
DIRNPs	2.98±0.07	61.78±1.37	3.07±0.18	62.41±3.73
INPs	/	/	8.69±0.99	86.90±6.12

FA modification efficiency. Coupling efficiency of folic acid on the surface of RBC membrane was analyzed using fluorescence spectrophotometry. FA coupling efficiency was calculated using the following equations: CE%= $(M_{FA}-M_{filtrate})/MFA\times$ 100% (where M_{FA} = the amount of added FA, $M_{filtrate}$= the amount of FA in filtrate after ultrafiltration). The FA coupling efficiency versus ligand amount curve was shown in Figure1s.

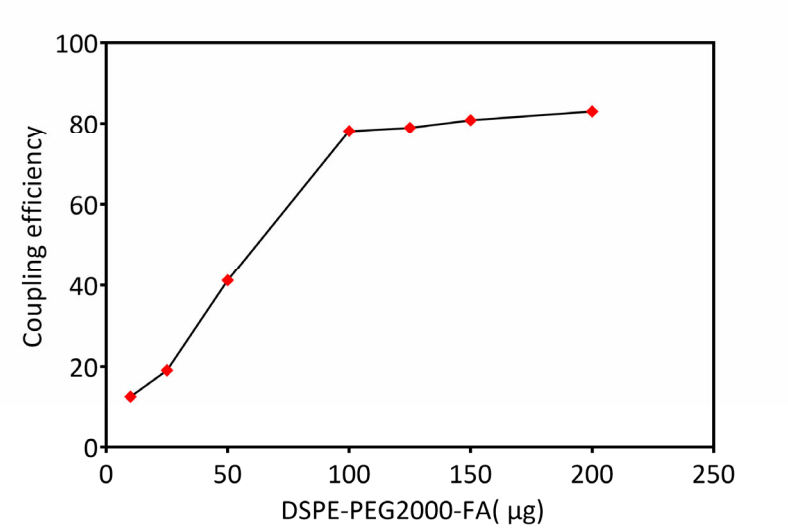

Figure 1s The FA coupling efficiency versus ligand amount curve.

Centrifugal and turbulence stability of different nanoformulations. Centrifugal stability and turbulence stability were evaluated by analyzing drug leakage under different test conditions. For centrifugal stability study, DIRNPs was centrifuged at 1000，4000，8000，12000 rpm for 10 min. The turbulence stability was assessed by passing samples through 1ml needle with different times (5, 10, 15, 20 and 25 times).

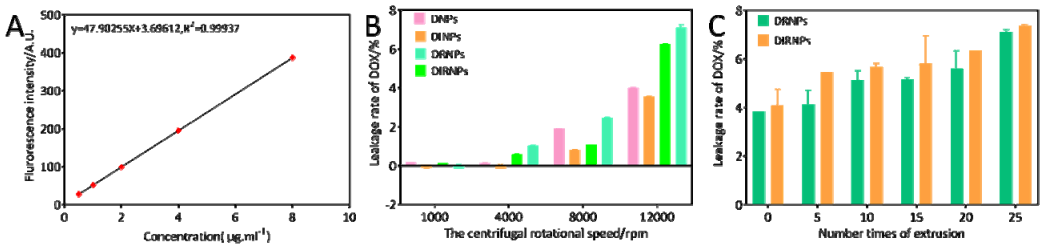

Figure 2s. (A) Standard curve of DOX. (B) Centrifugation stability of DOX loaded nanoformulations. (C) Turbulence stability DOX loaded nanoformulations

Hemolysis test. Hemolysis test and were performed to assess the biocompatibility of DIRNPs. Briefly, red blood cells were obtained by centrifuging the rabbit blood at 4000 rpm for 10 min and diluted with 0.9% saline to prepare 2% RBC suspension. Hemolysis was observed by adding different volume of DIRNPs sample into 2ml RBC suspension at 37 °C for 4 hours.

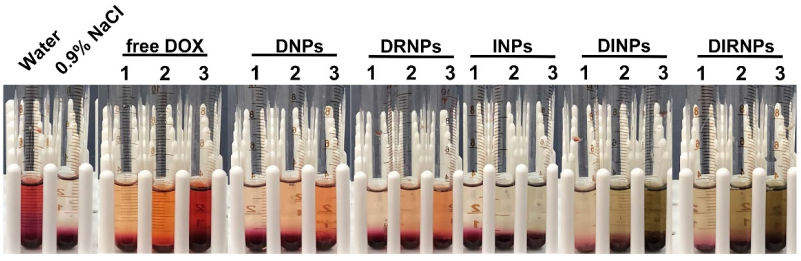

Figure 3s. Hemolysis test of different nanoformulations in 2% rabbit red blood cell solution (1, 2, 3 represents low, medium and high drug concentration, respectively).

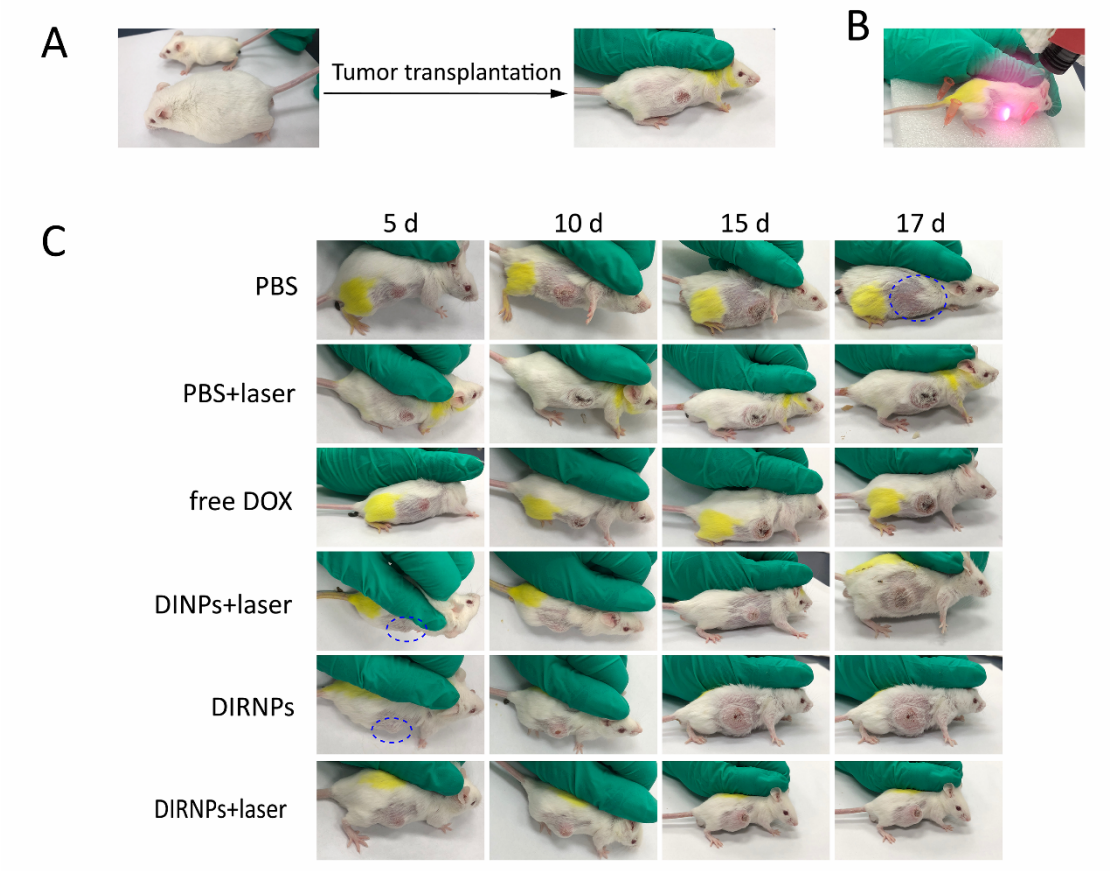

Figure 4s (A) The construction of H22 tumor-bearing mice. (B) The process of laser therapy in tumor-bearing mice. (C) Tumor growth of different test groups during treatment.