Supplementary Materials for

A prebiotic inulin derivative-containing liposome for oral berberine delivery improves the orthotopic colorectal cancer chemotherapy

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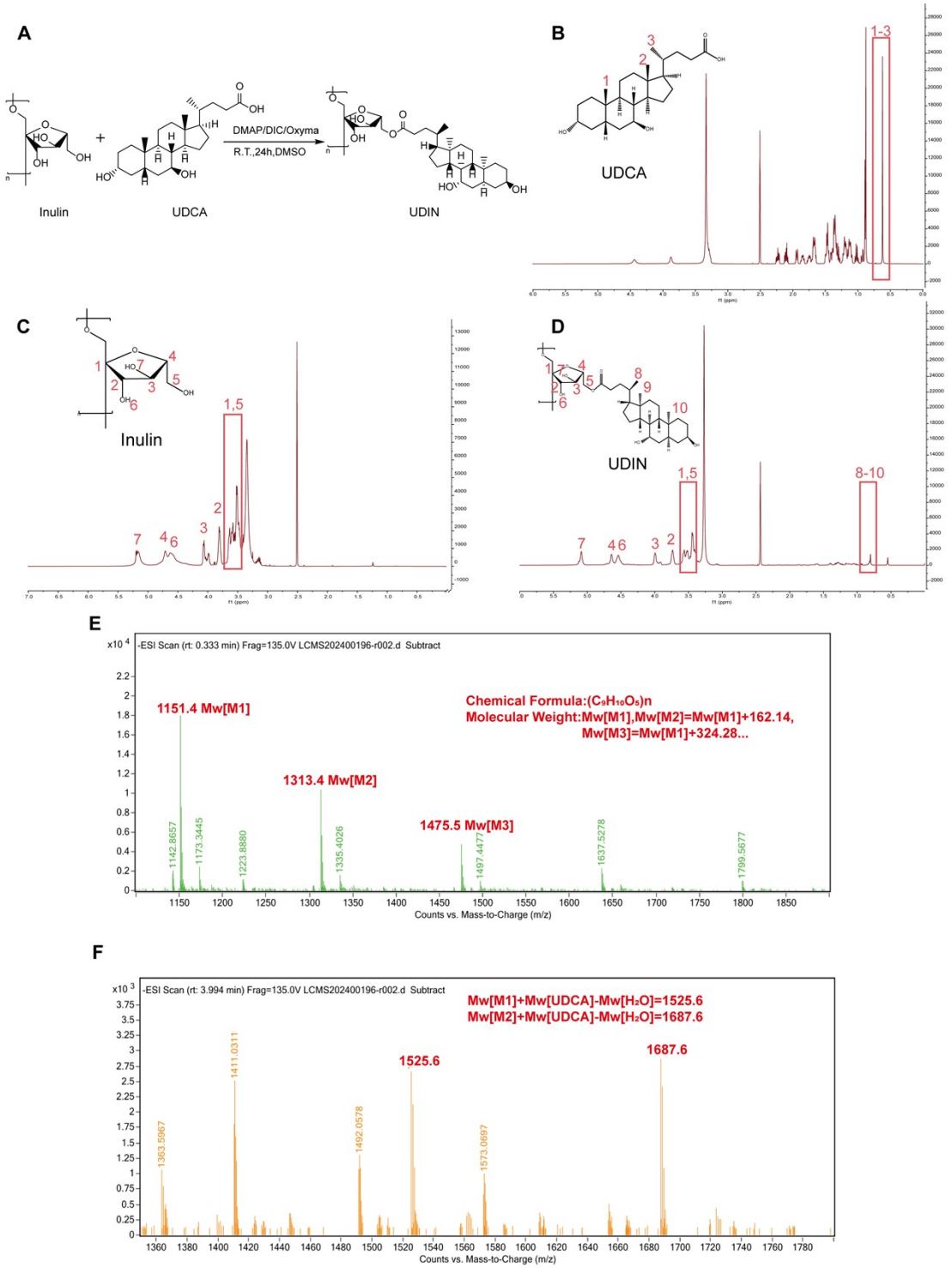

Figure S1. Synthesis and characterization of UDIN. (A) Synthesis flow chart. (B-D) ^{1}H NMR spectra of UDIN (B), IN (C), and UDCA (D). (E-F) LC/MS spectra of IN (E) and UDIN (F).

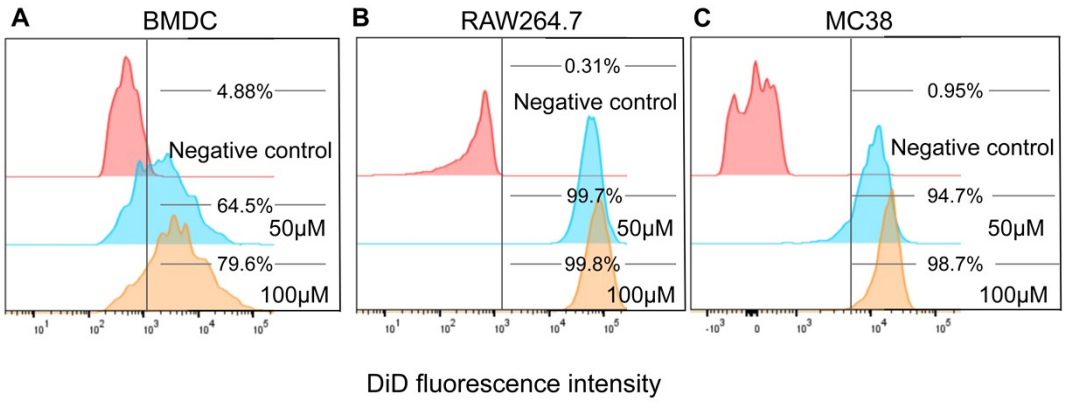

Figure S2. Cellular uptake efficiency of BLPN in different cells. Intracellular fluorescence intensity of BMDC (A), RAW264.7 (B) and MC38 cells (C) incubated with BLPN for 4 h.

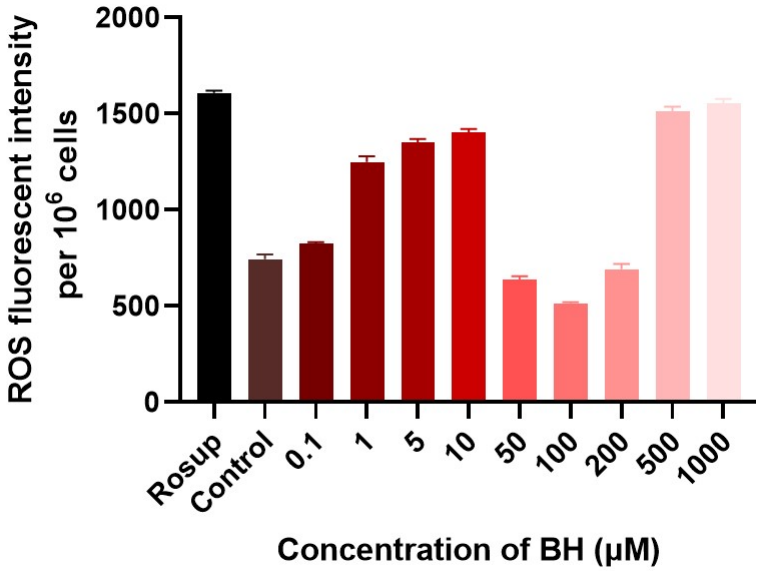

Figure S3. ROS fluorescent intensity in MC38 cells after treated with BLPN for 24 h.

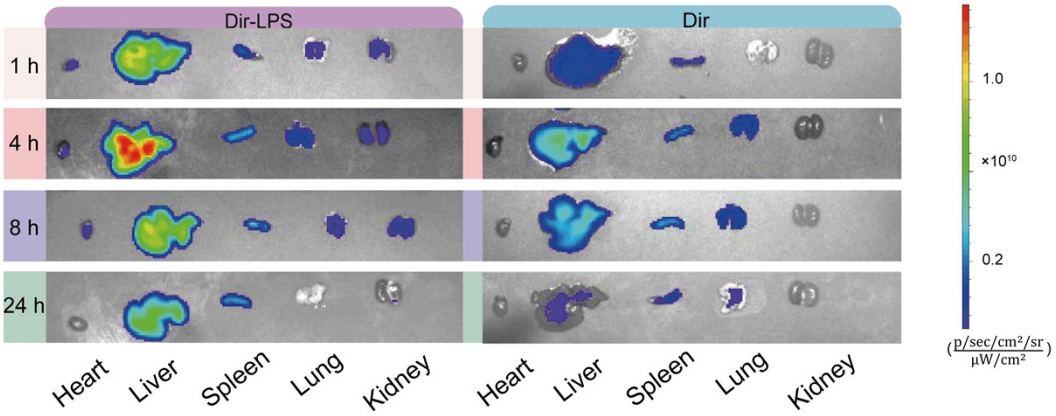

Figure S4. Ex vivo fluorescence images of major organs (heart, liver, spleen, lungs, kidneys) at different time after intravenous injection of free Dir and Dir-LPS in MC38 tumor-bearing mice.

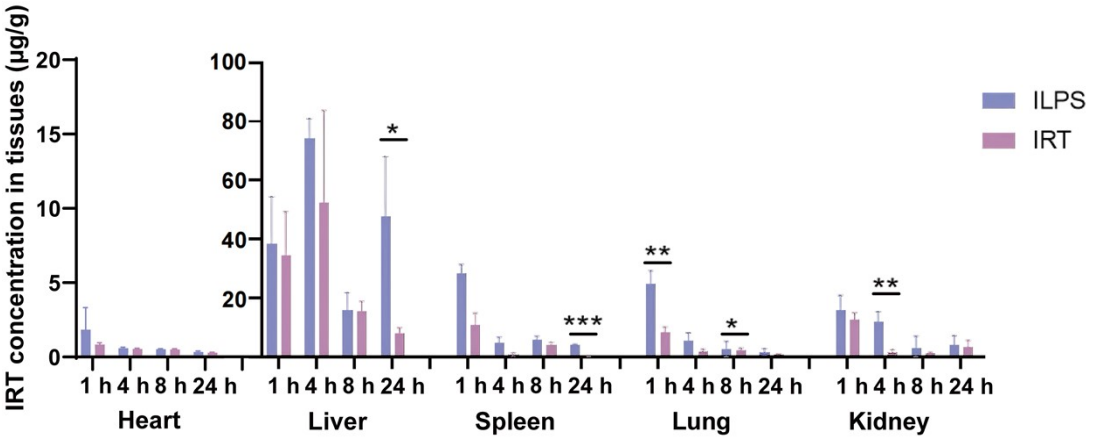

Figure S5. Concentrations of IRT in major organs at 1, 4, 8, and 24 h after intravenous injection of free IRT and ILPS in MC38 tumor-bearing mice. Data are presented as mean ± SD (n=3), $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

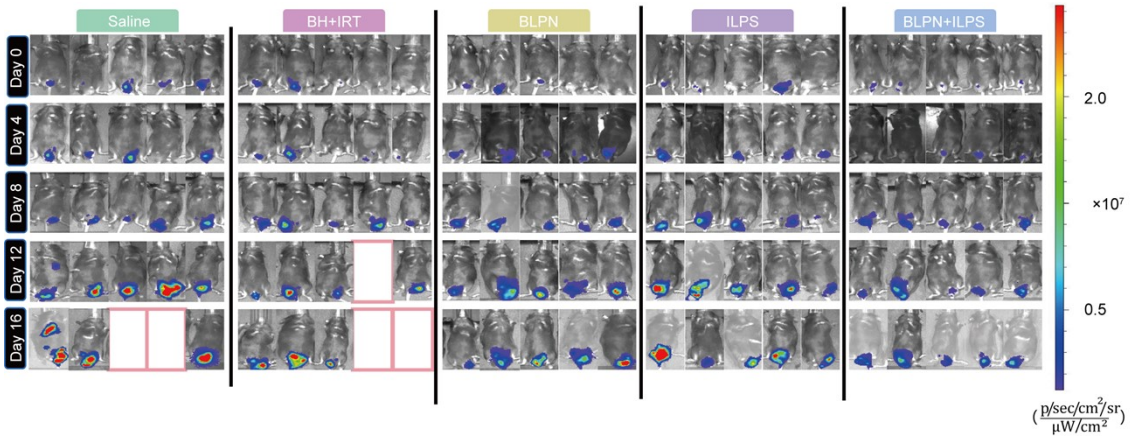

Figure S6 All bioluminescent images of MC38-luc tumor-bearing mice within 16 d of treatment (n=5). The red box indicates dead mice.

Figure S7. Individual tumor volume variation in MC38-luc tumor-bearing mice after receiving multiple doses of different formulations.

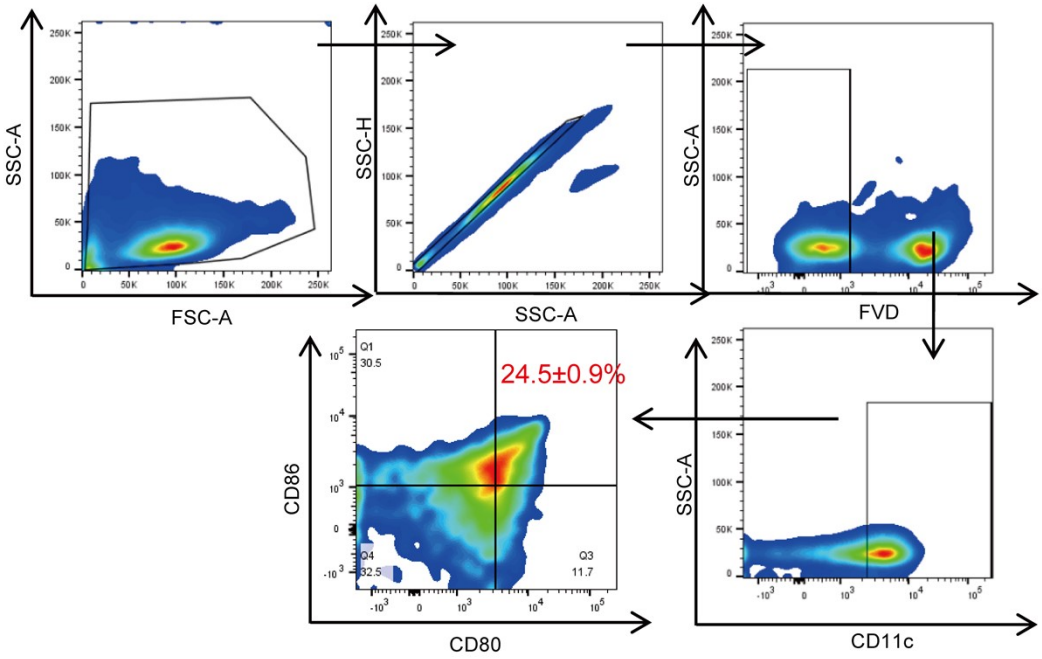

Figure S8. Gating strategies for mature DCs in tumor-draining lymph nodes in Fig. 5A.

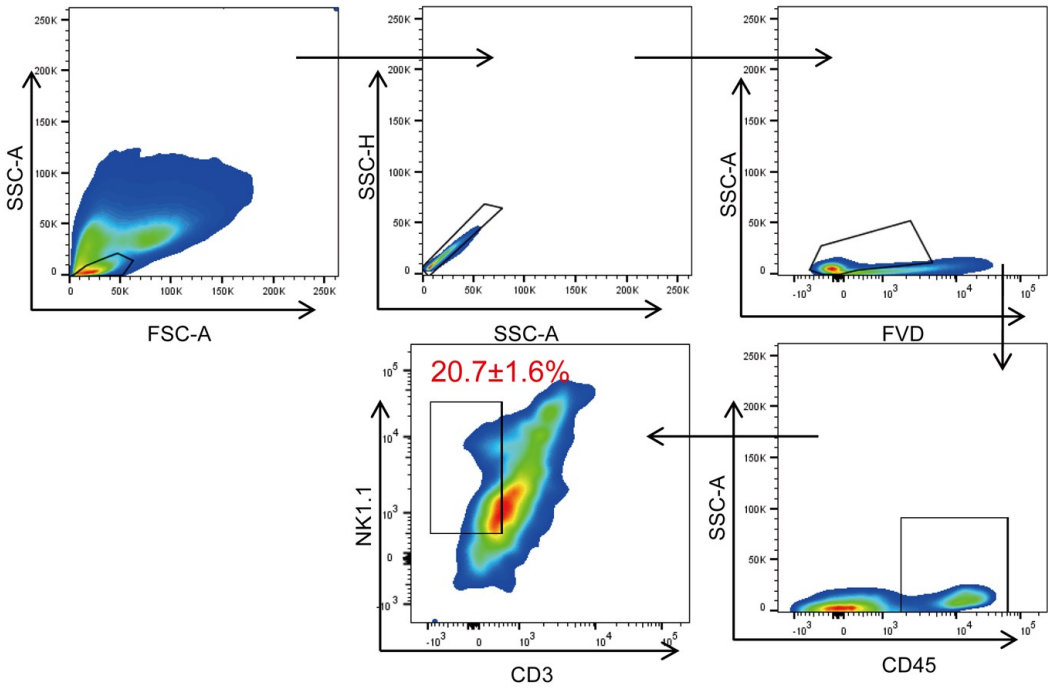

Figure S9. Gating strategies for NK cells in Fig. 5C.

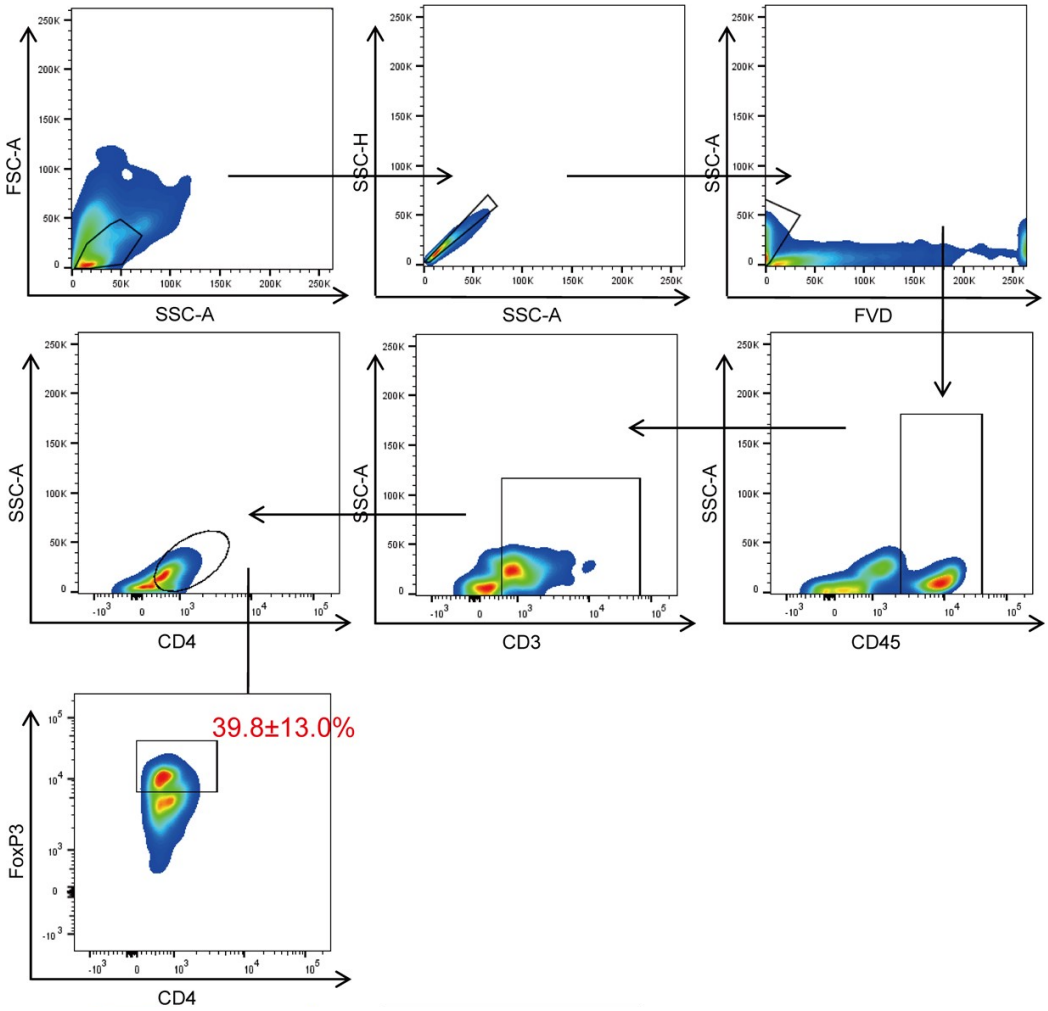

Figure S10. Gating strategies for Tregs in Fig. 5E.

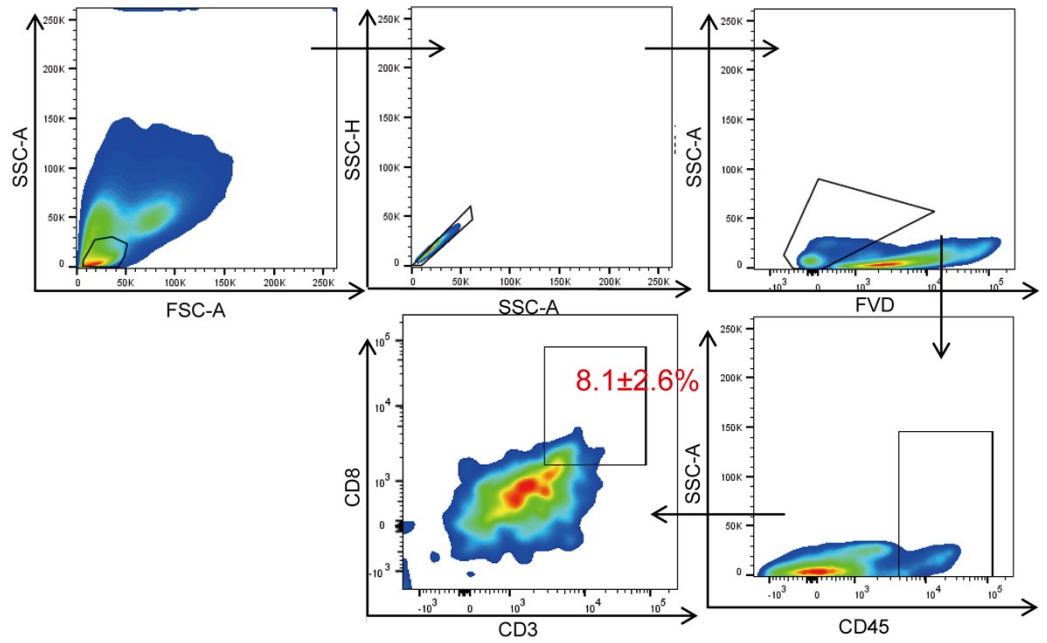

Figure S11. Gating strategies for $CD8^+$ T cells in Fig. 5G.

Figure S12. Gating strategies for TAMs in Fig. 5J.

Table S1 IC_{50} values of MC38 cells after treated with different formulations. For BH and BLPN groups, IC50 values of BH were shown; for ILPS and BLPN+ILPS groups, IC50 values of IRT were shown.

Treatment	IC_{50} (μM)
BH	242.7
BLPN	199.0
ILPS	7.697
BLPN+ILPS	45.36

Table S2 Pharmacokinetic parameters of orally administered free BH and BLPN in healthy C57BL/6 mice

Parameter	**BH**	**BLPN**
$T_{1/2}$ (h)	6.80018	49.4648
C_{max} (μg/mL)	2.92086	7.03145
$MRT_{0-\infty}$ (h)	10.6893	58.2786
AUC_{0-t} (h·μg/mL)	12.8873	29.6786
$AUC_{0-\infty}$ (h·μg/mL)	19.0751	70.5945

Table S3 Pharmacokinetic parameters of free IRT and ILPS administered intravenously in healthy C57BL/6 mice

Parameter	**IRT**	**ILPS**
$T_{1/2}$ (h)	0.721546	1.09939
$MRT_{0-\infty}$ (h)	0.852563	1.30939
AUC_{0-t} (h·μg/mL)	2.53227	6.22028
$AUC_{0-\infty}$ (h·μg/mL)	2.85718	6.64591

Table S4 The tumor inhibition rates and median survival time of all groups

	Saline	BH+IRT	BLPN	ILPS	BLPN+ILPS
Tumor inhibition rate (%)	-	22.23	34.87	19.99	69.51
Median survival time (d)	13.00	17.00	18.00	15.00	38.00

Table S5 Blood routine parameters of healthy mice receiving multi-doses of different formulations. Data are presented as mean ± SD (n=3).

Group	RBC (10^{12} L^{-1})	WBC (10^{9} L^{-1})	Gran (10^{9} L^{-1})	MCV (fL)	RDW (%)	PLT (10^{9} L^{-1})
Saline	7.3±0.2	5.8±3.0	1.0±0.6	41.0±3.4	16.3±3.1	386.0±6.0
BH+IRT	7.6±0.2	2.3±0.5	0.5±0.2	39.1±2.2	14.0±0.2	392.0±42.0
BLPN	8.2±0.4	4.8±1.2	1.3±0.2	39.7±0.2	13.1±0.3	482.7±47.7
ILPS	7.6±0.7	3.3±1.4	0.6±0.5	38.7±1.6	17.4±4.6	502.3±25.3
BLPN+ILPS	9.2±1.5	5.4±1.4	0.8±0.3	39.9±3.6	16.5±6.2	685.0±115.0

RBC: red blood cells; PLT: platelets.

WBC: white blood cells;

GRAN: granulocytes;

MCV: mean corpuscular volume;

RDW: red cell distribution width;