

Acute animal toxicity test

According to the LD_{100} and LD_0 from preliminary experiment, the administration dosage of oridonin was determined by a geometric series of 1:0.76 (21.40, 16.26, 12.36, 9.39, 7.14, 5.42, 4.11, 3.12, 2.37, 1.79 $mg/kg \cdot d^{-1}$). 55 female and 55 male BALB/c nude mice (6 weeks of age, 18~20 g) were purchased from The Laboratory Animal Center of Dalian Medical University (Dalian, China). All of BALB/c nude mice were randomly divided into 11 groups by their weight and sex: 10 dose groups of oridonin and a control group. 10 BALB/c nude mice were included in each group. After 12-hour fasting but drinking, different dose of oridonin or 0.5% dimethyl sulfoxide were respectively injected into all of mice in administered group or control group via intraspleen or intraportal vein. Then the common status including active state, weight, fur color, toxic reaction, death etc were recorded during the 2-weeks observation period. Last but not least, the half lethal dose (LD_{50}) was determined using probit analysis,

meanwhile the maximum safe concentration of intraportal oridonin were determined, which was used as the dosage of subsequent treatment group and preventive group.

The acute toxicity evaluation of intraportal oridonin

To better pinpoint the toxicity, maximum safe concentration of intraportal oridonin, 11 groups of BALB/c nude mice were treated using the acute animal toxicity test. In order from top to bottom, all of BALB/c nude mice administrated with 21.4 $mg/kg \cdot d^{-1}$ oridonin via intraspleen or intraportal vein died during 2 weeks experiment. Then, 7.14 $mg/kg \cdot d^{-1}$ was the maximum dose in this experiment, where no mice died. Thus, the maximum safe dose of intraportal oridonin were respectively 7.14 $mg/kg \cdot d^{-1}$, which can be used as the administrated dose of treatment group and preventive group. On the other hand, LD_{50} of intraportal oridonin was calculated using probit analysis and it was 13.61 $mg/kg \cdot d^{-1}$ (Table S1).

Table S1 The acute toxic effect of intraportal oridonin on BALB/c nude mouse

Drug	Groups	Route of exposure	Dose $mg/kg \cdot d^{-1}$	Mortality	LD_{50} $mg/kg \cdot d^{-1}$
oridonin	1	Intraspleen or intraportal	21.40	10	13.61
	2		16.26	8	
	3		12.36	4	
	4		9.39	1	
	5		7.14	0	
	6		5.42	0	
	7		4.11	0	
	8		3.12	0	
	9		2.37	0	
	10		1.79	0	

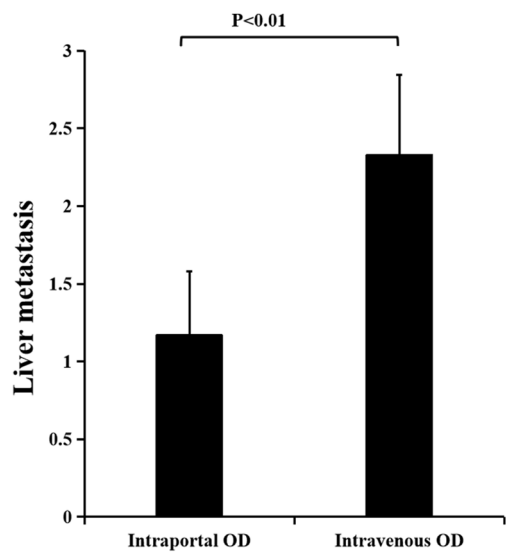


Figure S1 The comparison of liver metastasis scores between intraportal and intravenous OD. Values are the means \pm SD from three independent determinations. OD, oridonin.