Supporting Information:

Sinapultide-loaded lipid microbubbles and the stabilization effect of sinapultide on the shell of lipid

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Table S1. The number ratio comparsion of sinapultide to lipid between simulation and experiment.

Agents	Simulation Number	Sinapultide/lipid number ratio**	Experiments Number*	Sinapultide/lipid number ratio**
DPPC	300			
POPG Na	92			
Total lipid	392		1.6×10^{7}	
Sinapultide	0	**0**	0	**0**
	2	**0.0051**	6.06×10^{4}	**0.0038**
	4	**0.010**	1.41×10^{5}	**0.0088**
	8	**0.020**	3.00×10^{5}	**0.019**
	16	**0.041**	6.64×10^{5}	**0.042**
	24	**0.061**	1.47×10^{6}	**0.092**

**Note: The sinapultide number was caculated according to the experimental result in the following derivation process(1).

*Note: The sinapultide/ lipid number ration was caculated as equation (1):

$$\text{Number ration} = \frac{Number_{Sinalpultide}}{Number_{total\ lipid}} \quad (1)$$

Derivation process of sinapultide number caculation according to the experimental result:

Based on the surface area of one PC molecule （A_0 = 0.65 nm^2）, the determined size of sinapultide loaded microbubbles (r = 1820/2 nm), The count of phospholipids in a monolayer encapsulated bubble （N_{lipid}） was calculated using the follow equation (2):

$$N_{lipid} = 4\pi r^2/A_0 \quad (2)$$

Thus, the total phospholipids numbers for one microubbble are 1.60×10^{7}.

And the number of sinapultide in one microbubbles was calculated using the follow equation (3):

$$N_1 = (\frac{C \times V \times LCs}{M_W} \times N_A)/C_{MBs} \quad (3)$$

where, C was added sinapultide concentration in the solution. V was the volume of the solution, LCs was the sinapultide loading capacity (mass %), M_w was the molecular weight of sinalputide (2466), and N_A was the Avogadro's constant, equally to 6.02×10^{23}. The C_{MBs} was the concentration of the prepared MBs in the experiment, which is measured as 6.37×10^{9}.

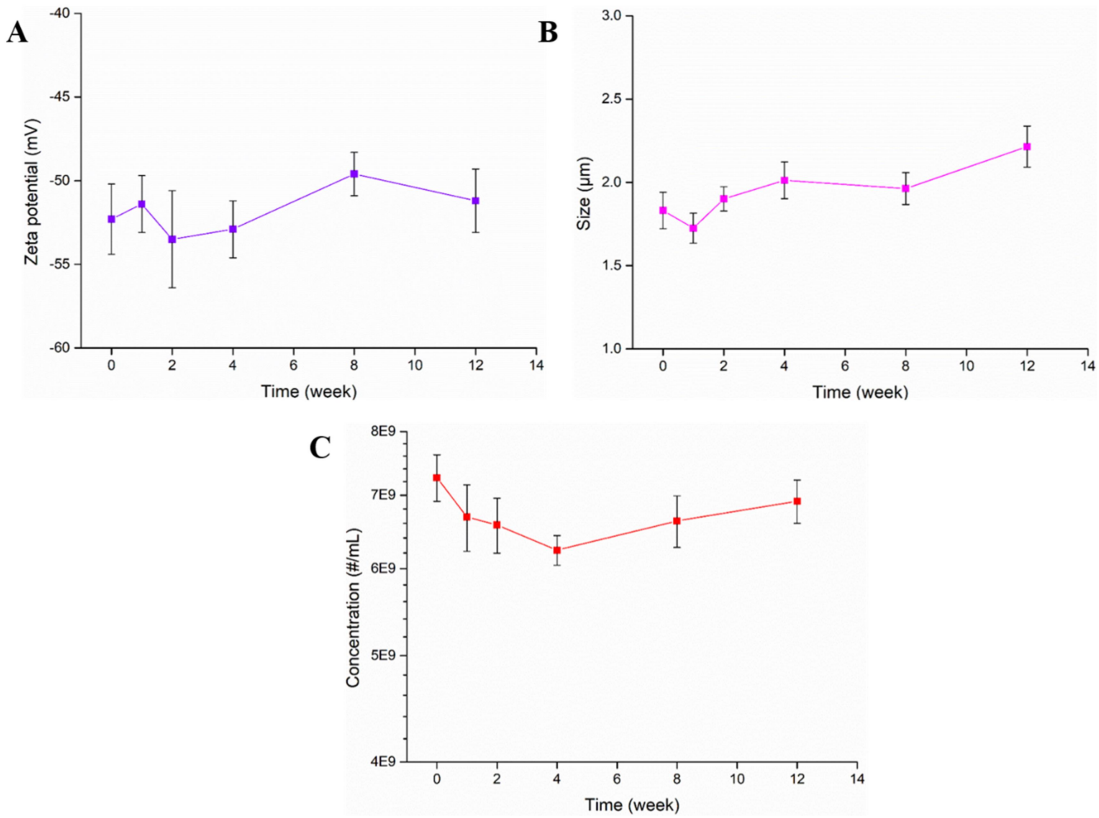

Fig. S1 Stability test for (a) zeta potential, (b) mean diameter, and (c) microbubble yields of microbubble with the sinapultide concentration of 0.1 mg/mL after keeping mother liquor of sinapultide suspension in different period.

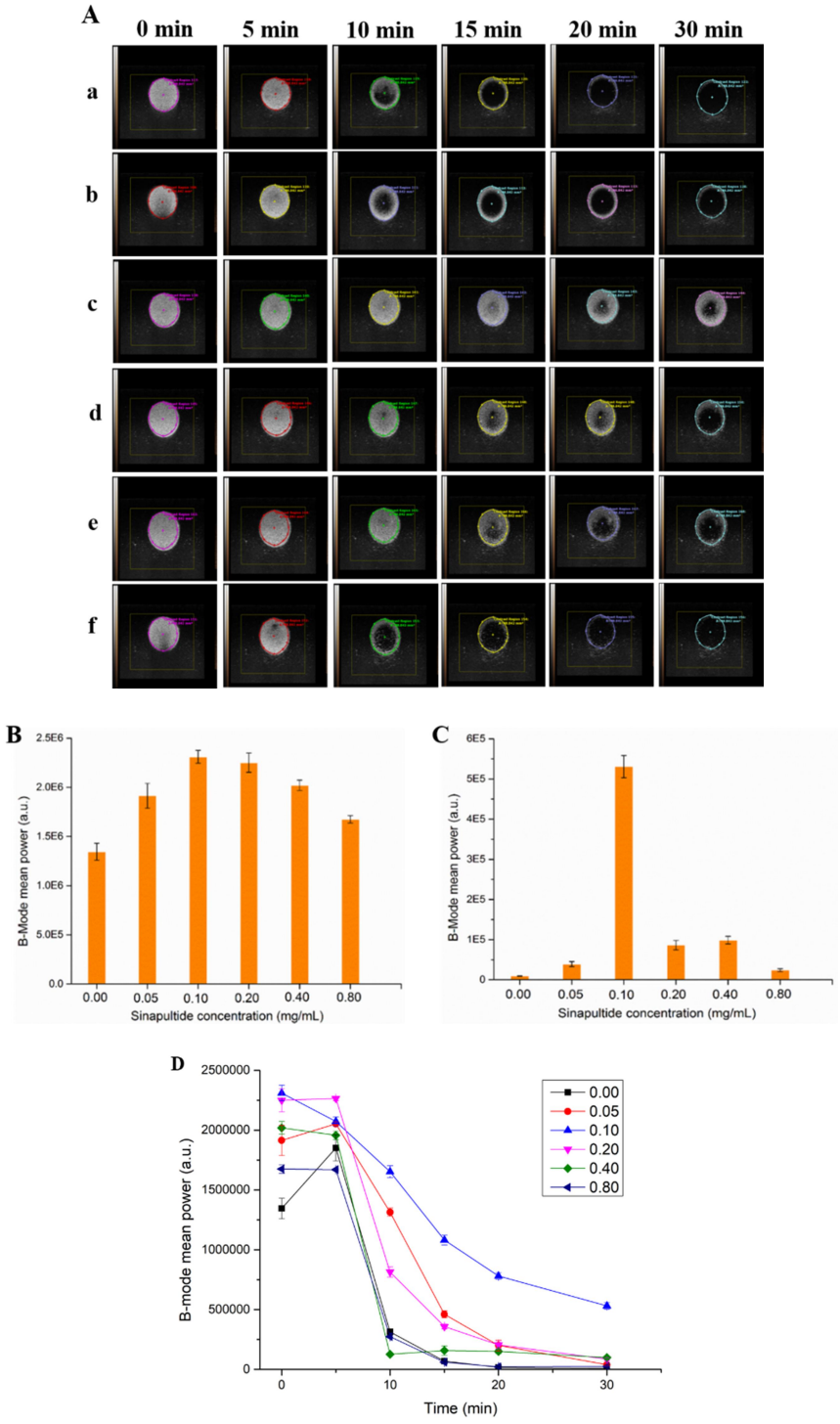

Fig. S2 Ultrasonic evaluation in vitro of sinapultide-loaded lipid microbubbles. (A) The images of the six groups at different period, and the formulations with different concentrations of sinapultide for a-f are 0.0, 0.05, 0.10, and 0.20, 0.40 and 0.80 mg/mL, respectively. All samples were diluted 40 times. The B-mode mean power change of microbubbles after 0 min (B) and 30 mins (C). Average mean B-mode enhanced grayscale of US imaging to sinapultide microbubble of different concentrations at different time courses (0, 5, 10, 15, 20, 30 min) (D).