Appendix 1. Electronic Supplementary Information (ESI)

Cerasome versus liposome: A comparative pharmacokinetic analysis following intravenous administration into rats

1. Synthesis of Ag_2S Qds

The Ag_2S Qds were prepared based on the previous report (1) with a little modification. Briefly, 15 mg of AgNO3 was dissolved in 15 ml of a mixed solution of the glycerin and deionized water (1: 2 *v*/*v*) in an amber beaker. Then the system was heated to 100 ℃ and stirred at 800 rpm by a thermostatic magnetic stirrer (Heidolph Instruments, Germany) for 0.5 h. Next, 100 µl of thioglycolic acid was dropwise added (at a rate of 10 µl/min) to the previous Ag^+ solution. As soon as the first drop was added, the system's color rendered cloudy white, then gray, and finally clear yellow after 1 h. The color of Qds got reddish brown by continuing heating and stirring the system for 2 h. After cooling to room temperature, the prepared Qds was stored in an amber beaker at 4 ℃.

2. Synthesis of Cerasome Forming Lipid (CFL)

2.1. Synthesis of dihexadecylamine (the intermediate compound)

For synthesizing the intermediate of dihexadecylamine, hexadecylamine (246.6 mg, 1 mmol) was dissolved in 10 ml acetonitrile in a 50 ml round bottom balloon. Then hexadecylbromide (315 µl, 1 mmol) was added dropwise to the previous solution. Finally, the mixture was refluxed in an oil bath at 80 ℃ for 6 hours. After cooling the mixture, the final product precipitates and the residual acetonitrile were removed by a Büchner funnel under avacuum.

For purification of the intermediate, the product was dissolved in CH_2Cl_2 and extracted twice with the mixture 15 ml 6 M NaOH. After evaporating the solvent, the precipitate was washed with 10 ml MeOH to remove the residual of hexadecylamine. For final purification, the washed precipitate was recrystallized from n-hexane to obtain a clear white powder (% Ra: % 44) (2-4).

2.2. Synthesis of CFL (the final product)

For synthesizing the CFL, 100 mg (0.21 mmol) of the n-dihexadecylamine (the intermediate product) and 56 µl (0.27 mmol) of 3-triethoxysilyl propylisocyanate were dissolved in 30 ml dichloromethane and refluxed in an oil bath at 60 ℃ for 5 hours. Finally, the solvent residual was evaporated to obtain the final colorless oil (3, 5).

References

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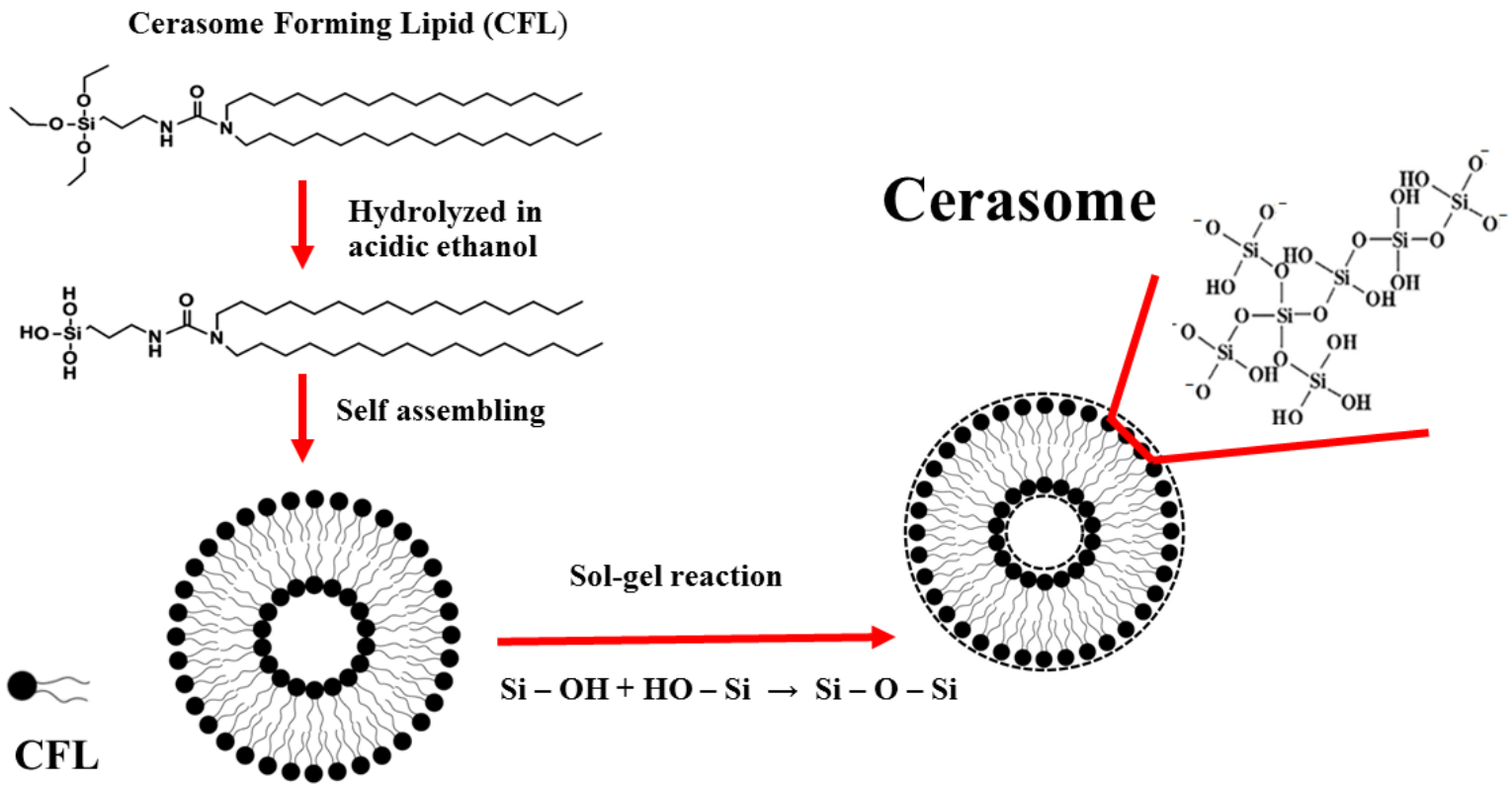

Appendix 2. Schematic illustration of a molecule of cerasome forming lipid (CFL) and a cerasome vesicle

Appendix 3. In vitro stability of Qds-loaded nanocarriers (Cer5, Cer6, and Lip) upon storage at 4 °C (n=3, Mean ± SD)

Time (day)	Formulation											
	Cer5				Cer6				Lip			
	Size (nm)	PDI	ζ-Potential (mV)	Qds retention%	Size (nm)	PDI	ζ-Potential (mV)	Qds retention%	Size (nm)	PDI	ζ-Potential (mV)	Qds retention%
0	134.7 ± 3.4	0.21 ± 0.03	-31.5 ± 0.2	99.8 ± 1.6	117.1 ± 1.7	0.28 ± 0.04	-24.6 ± 0.5	99.8 ± 0.0	126.3 ± 3.6	0.22 ± 0.02	-25.6 ± 7.4	98.7 ± 0.5
2	134.3 ± 4.5	0.21 ± 0.02	-32.1 ± 0.6	n.d.	118.1 ± 1.8	0.26 ± 0.00	-25.9 ± 0.5	n.d.	124.4 ± 3.9	0.30 ± 0.30	-26.8 ± 1.2	n.d.
3	131.2 ± 2.8	0.21 ± 0.01	-33.1 ± 0.1	n.d.	113.9 ± 2.4	0.26 ± 0.00	-20.3 ± 0.1	n.d.	126.1 ± 2.7	0.45 ± 0.03	-26.4 ± 1.2	n.d.
7	137.9 ± 1.9	0.22 ± 0.02	-30.2 ± 0.3	n.d.	116.6 ± 2.4	0.26 ± 0.01	-22.9 ± 0.6	n.d.	124.2 ± 1.6	0.50 ± 0.03	-23.8 ± 1.5	n.d.
15	128.5 ± 0.4	0.22 ± 0.02	-31.5 ± 0.5	n.d.	117.1 ± 1.7	0.27 ± 0.00	-26.0 ± 0.1	n.d.	148.5 ± 4.6	0.45 ± 0.42	-21.6 ± 2.0	n.d.
30	131.1 ± 2.6	0.22 ± 0.03	-31.6 ± 0.7	99.7 ± 0.6	116.5 ± 2.0	0.26 ± 0.01	-24.3 ± 0.6	98.8 ± 1.6	222.2 ± 5.7	0.83 ± 0.00	-18.7 ± 2.2	81.4 ± 1.0

Abbreviation: n.d., was not determine.

Appendix 4. Percentage of Qds retention in the prepared nanocarriers (Cer5, Cer6, and Lip) upon incubation in human plasma at 37 ^{o}C (n = 3, Mean ± SD).

Incubation time (h)	**Qd-retention (%)**		
	Cer5	**Cer6**	**Lip**
1	96.52 ± 1.07	98.73 ± 1.25	97.81 ± 1.05
4	98.30 ± 0.97	99.56 ± 1.78	96.86 ± 1.78
8	99.30 ± 1.10	98.97 ± 1.59	94.18 ± 1.77
24	99.66 ± 1.04	98.52 ± 1.88	95.52 ± 1.50