

Electronic Supplementary Material for:

Stable DOPG/glycyrrhizin vesicles with a wide  
range of mixing ratios:

Structure and stability as seen by  
scattering experiments and cryo-TEM

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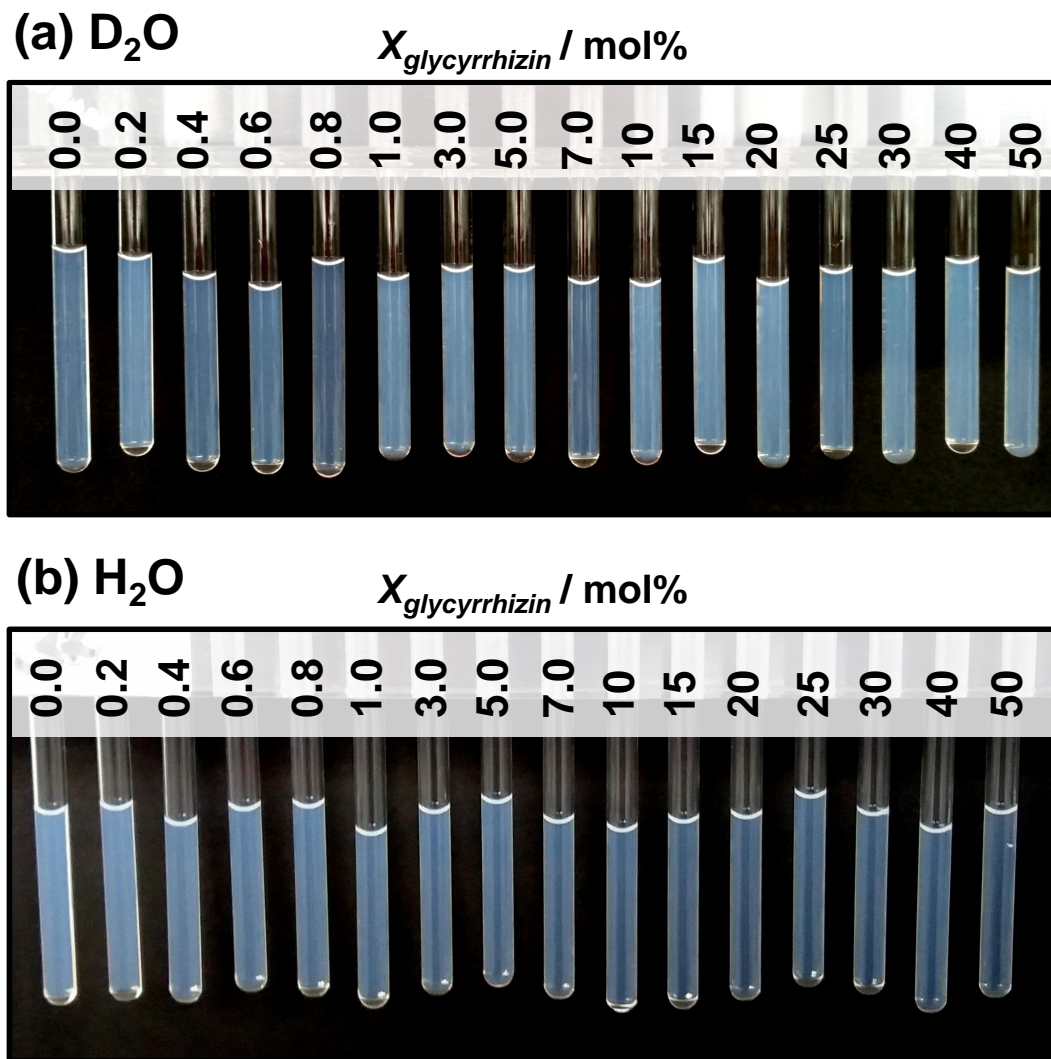


Figure S1. Photographs of mixtures of DOPG and glycyrrhizin in (a) D<sub>2</sub>O and (b) H<sub>2</sub>O at room temperature ( $\approx 25^\circ\text{C}$ ). The samples were extruded (with increasing  $x_{\text{glycyrrhizin}}$ ) through a membrane with a pore size of  $500\text{ \AA}$ . All samples exhibit a bluish color and are stable for at least six month. By eye no significant difference in appearance of the samples can be observed.

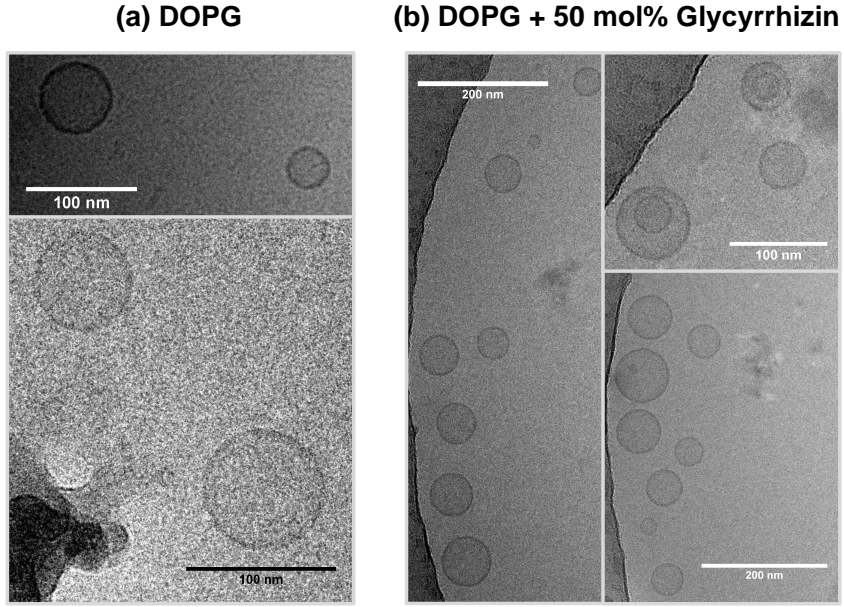


Figure S2. Cryo-TEM images of (a) DOPG and (b) DOPG with 50 mol% glycyrrhizin in H<sub>2</sub>O buffer solution. The samples were diluted to a DOPG mass concentration of 0.5 g·L<sup>-1</sup> and were kept at room temperature ( $\approx 25^\circ\text{C}$ ) before freezing. In both cases, unilamellar vesicles are observed.

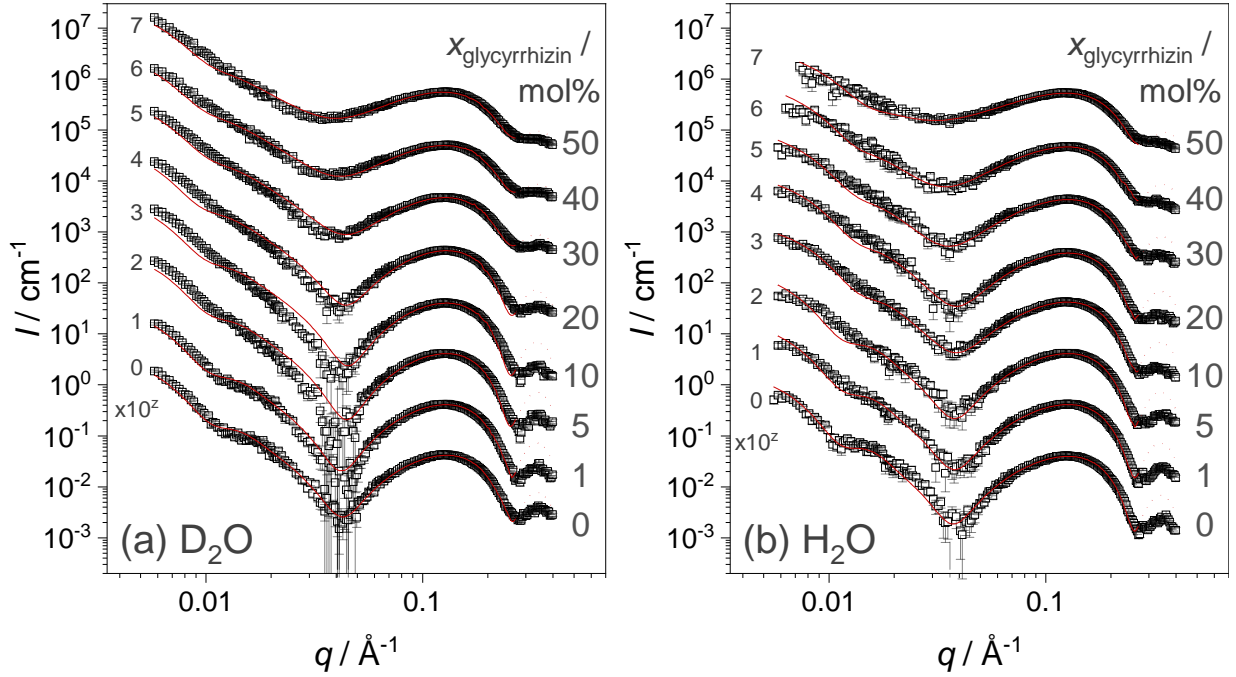


Figure S3. Comparison of X-ray scattering data for samples with different  $x_{\text{glycyrrhizin}}$  in (a) D<sub>2</sub>O and (b) H<sub>2</sub>O buffer as solvent. The glycyrrhizin content  $x_{\text{glycyrrhizin}}$  is denoted by the numbers on the right. For better readability, the data are scaled by different power of 10 indicated by the exponent  $z$  given as numbers on the left side of the graphs. Solid lines are CMS model fits from SASView [59]. Dotted lines are extensions of the CMS fits beyond the fit range.

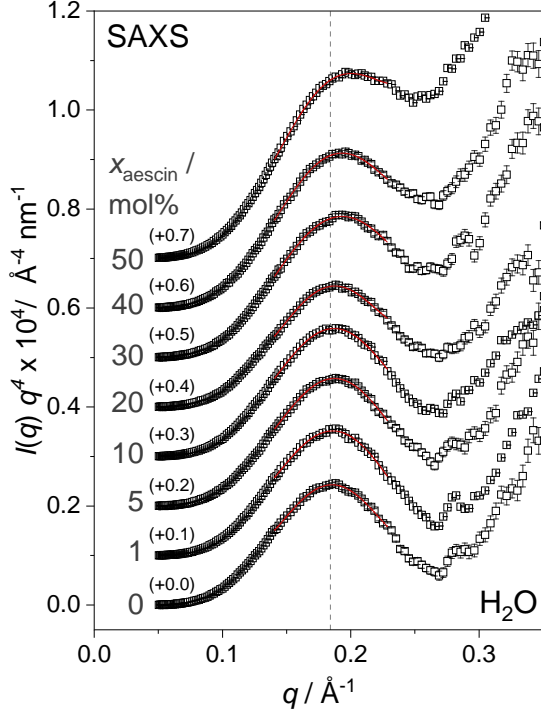


Figure S4. Modified Kratky-Porod (MKP) plots for SAXS data obtained for samples with different  $x_{\text{glycyrrhizin}}$  in  $\text{H}_2\text{O}$  buffer as solvent[54]. Solid lines are 4th order polynomial approximations. The maximum of these approximations was used to determine the membrane thickness  $d_{\text{MKP}}$ . The glycyrrhizin content  $x_{\text{glycyrrhizin}}$  is indicated by the numbers on the left. For better readability of the figure, the data is baseline-shifted by the numbers in brackets.

Table S1: Total membrane thickness  $d_{\text{MKP}}$  derived from the MKP plot of SANS and SAXS data of samples in  $\text{D}_2\text{O}$  and  $\text{H}_2\text{O}$ .

$x_{\text{glycyrrhizin}}$ mol%	$d_{\text{MKP,SANS,D}_2\text{O}}$ Å	$x_{\text{glycyrrhizin}}$ mol%	$d_{\text{MKP,SAXS,D}_2\text{O}}$ Å	$d_{\text{MKP,SAXS,H}_2\text{O}}$ Å
0	$30.5 \pm 0.3$	0	$33.3 \pm 0.4$	$34.1 \pm 0.4$
1	$30.9 \pm 0.3$	1	$33.7 \pm 0.4$	$34.0 \pm 0.4$
3	$30.7 \pm 0.3$	5	$33.7 \pm 0.4$	$33.8 \pm 0.4$
10	$30.4 \pm 0.3$	10	$33.5 \pm 0.4$	$33.8 \pm 0.4$
20	$29.4 \pm 0.3$	20	$33.0 \pm 0.3$	$33.7 \pm 0.4$
30	$29.6 \pm 0.3$	30	$31.9 \pm 0.3$	$32.7 \pm 0.3$
40	$29.6 \pm 0.3$	40	$31.7 \pm 0.3$	$32.7 \pm 0.3$
50	$28.0 \pm 0.4$	50	$30.9 \pm 0.3$	$31.6 \pm 0.3$

Table S2: Parameters to determine *NSLDs* and *XSLDs* of DOPG and glycyrrhizin at a temperature of 30 °C.  $M$ : molar mass,  $V_{mol}$ : molar volume,  $V$ : molecular volume,  $\rho$ : density.

	molecular formular	$M$ g mol <sup>-1</sup>	$V_{mol}$ cm <sup>3</sup> mol <sup>-1</sup>	$V$ Å <sup>3</sup>	$\rho$ g cm <sup>-3</sup>	$NSLD$ 10 <sup>-6</sup> Å <sup>-2</sup>	$XSLD$ 10 <sup>-6</sup> Å <sup>-2</sup>
DOPG	C <sub>42</sub> H <sub>78</sub> O <sub>10</sub> P	773.53	761.78	1265.00 [53]	0.978	0.385	9.15
DOPG, head	C <sub>8</sub> H <sub>12</sub> O <sub>10</sub> P	299.03	175.24	291.00 [53]	1.706	2.45	15.1
DOPG, tail	C <sub>34</sub> H <sub>66</sub>	474.50	586.54	974.00 [53]	0.809	-0.214	7.82
glycyrrhizin	C <sub>42</sub> H <sub>62</sub> O <sub>16</sub>	822.93	572.6 [73]	950.85 [73]	1.44 [73]	1.48	13.2

Table S3: Core radii  $R_c$  obtained from CMS fits to SANS and SAXS data. In the case of samples in D<sub>2</sub>O values were determined from SANS and in the case of H<sub>2</sub>O values were derived from SAXS. In the latter case, the minimal  $q$ -value was not small enough for exact determination of  $R_c$  values and the uncertainty of these values might be larger than the depicted error. Values in brackets denote polydispersities of  $R_c$  ( $\sigma_{R_c}$ ) in %.

$x_{\text{glycyrrhizin}}$ mol%	$R_c$ , SANS, D <sub>2</sub> O Å	$x_{\text{glycyrrhizin}}$ mol%	$R_c$ , SAXS, H <sub>2</sub> O Å
0	207 ± 2 (37)	0	204 ± 7 (32)
1	208 ± 3 (39)	1	191 ± 5 (36)
3	203 ± 3 (42)	5	172 ± 5 (38)
10	202 ± 3 (45)	10	142 ± 5 (46)
20	205 ± 3 (48)	20	138 ± 5 (50)
30	176 ± 3 (55)	30	131 ± 1 (56)
40	172 ± 3 (61)	40	124 ± 1 (59)
50	156 ± 2 (64)	50	108 ± 5 (60)

Table S4: Scattering length densities for neutrons ( $NSLD_{\text{tail}}$ ) and X-rays ( $XSLD_{\text{tail}}$ ) for the hydrophobic membrane part. Values were determined by fitting SAXS data of samples in D<sub>2</sub>O and H<sub>2</sub>O buffer by the CMS model.  $NSLD$  values for samples in D<sub>2</sub>O (indicated in italic letters) were calculated based on the corresponding  $XSLD$  values. Additionally, calculated values for the head group region are listed for comparison and were taken from Table S2.

$x_{\text{glycyrrhizin}}$ mol%	$NSLD_{\text{tail, D}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$	$x_{\text{glycyrrhizin}}$ mol%	$XSLD_{\text{tail, D}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$	$XSLD_{\text{tail, H}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$
0	<i>-0.23 ± 0.01</i>	0	8.23 ± 0.01	8.18 ± 0.01
1	<i>-0.21 ± 0.01</i>	1	8.23 ± 0.01	8.19 ± 0.01
3	<i>-0.16 ± 0.01</i>	5	8.28 ± 0.01	8.18 ± 0.01
10	<i>-0.05 ± 0.01</i>	10	8.28 ± 0.01	8.18 ± 0.01
20	<i>0.11 ± 0.01</i>	20	8.24 ± 0.01	8.87 ± 0.01
30	<i>0.28 ± 0.02</i>	30	8.20 ± 0.01	8.11 ± 0.01
40	<i>0.37 ± 0.02</i>	40	8.09 ± 0.01	8.06 ± 0.01
50	<i>0.48 ± 0.02</i>	50	8.02 ± 0.01	7.89 ± 0.01
$NSLD_{\text{head, D}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$		$XSLD_{\text{head, D}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$		$XSLD_{\text{head, H}_2\text{O}}$ $10^{-6}\text{\AA}^{-2}$
2.45		15.1		15.1

Table S5: Thickness of the hydrophobic membrane part  $d_{\text{tail}}$  obtained from CMS fits to SANS and SAXS data of samples prepared in D<sub>2</sub>O and H<sub>2</sub>O buffer. Values in brackets denote polydispersities of  $d_{\text{tail}}$  ( $\sigma_{d_{\text{tail}}}$ ) in %.

$x_{\text{glycyrrhizin}}$ mol%	$d_{\text{tail, SANS, D}_2\text{O}}$ $\text{\AA}$	$x_{\text{glycyrrhizin}}$ mol%	$d_{\text{tail, SAXS, D}_2\text{O}}$ $\text{\AA}$	$d_{\text{tail, SAXS, H}_2\text{O}}$ $\text{\AA}$
0	26.3 ± 0.1 (-)	0	31.3 ± 0.1 (3)	31.0 ± 0.2 (0)
1	25.9 ± 0.1 (-)	1	31.4 ± 0.1 (1)	31.1 ± 0.2 (0)
3	25.9 ± 0.1 (-)	5	31.7 ± 0.1 (1)	31.0 ± 0.1 (0)
10	25.9 ± 0.1 (-)	10	31.5 ± 0.1 (4)	30.9 ± 0.2 (6)
20	25.9 ± 0.1 (-)	20	31.2 ± 0.2 (6)	30.9 ± 0.2 (4)
30	26.0 ± 0.1 (-)	30	30.8 ± 0.2 (10)	30.4 ± 0.2 (5)
40	26.0 ± 0.1 (-)	40	30.0 ± 0.1 (12)	30.1 ± 0.1 (7)
50	25.6 ± 0.1 (-)	50	29.7 ± 0.2 (13)	28.9 ± 0.2 (9)