Supporting Information

Solubility of Lanosterol in Organic Solvents and in Water-Alcohol Mixtures at 101.8 kPa

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Table S1. Solubility Parameters, Polarities and Polarizabilities of Solvents

solvent	solubility parameter[a] $(J/cm^3)^{0.5}$	polarity[a] (water =100)	polarizability [b] ($Å^3$)
methanol	29.52	76.2	3.26
ethanol	26.58	65.4	5.13
isopropanol	23.8	54.6	7.14
n-propanol	24.5	61.7	7.23
acetone	20.05	35.5	6.47
acetonitrile	24.09	46	4.44
DMF	23.97	40.4	7.93
DMSO	26.33	44.4	8.03
ethyl acetate	18.35	23	8.87
n-hexane	14.9	0.9	11.94

[a] Taken from References 1 and 2.

[b] Taken from Reference 3.

Table S2. Interaction Parameters for the NRTL and UNIQUAC Models

Solvent	NRTL		
	Δg_{12}	Δg_{21}	a
methanol	3786.04	-1893.02	0.20
ethanol	5866.49	-2933.24	0.20
isopropanol	5929.32	-2964.66	0.20
n-propanol	5389.93	-2694.96	0.20
acetone	4027.24	-2013.62	0.20
acetonitrile	6080.32	-3040.16	0.20
ethyl acetate	3866.78	-1933.39	0.20
solvent	UNIQUAC		
	Δu_{12}	Δu_{21}	
methanol	162.67	-81.34	
ethanol	90.00	-45.00	
isopropanol	153.36	-76.68	
n-propanol	147.01	-73.51	
acetone	83.04	-41.53	
acetonitrile	136.14	-68.07	
ethyl acetate	62.43	-31.22	

Table S3. Calculated Values for Gibbs Free Energy of Mixing (ΔG_{mix}), Enthalpy of Mixing (ΔH_{mix}) and Entropy of Mixing (ΔS_{mix})

T (K)	ΔG_{mix} (J/mol)	ΔH_{mix} (J/mol)	ΔS_{mix} (J/mol K)
methanol			
277.78	-1.19	0.00040	0.0043
288.15	-2.16	0.00072	0.0070
298.15	-3.93	0.0013	0.013
303.05	-4.82	0.0016	0.016
307.55	-5.70	0.0019	0.019
312.15	-7.11	0.0024	0.023
316.95	-9.54	0.0032	0.030
321.65	-14.28	0.0048	0.044
ethanol			
277.95	-14.16	0.013	0.051
285.74	-21.25	0.020	0.074
293.45	-30.10	0.028	0.10
298.25	-37.17	0.035	0.12
302.85	-47.83	0.045	0.15
307.15	-54.82	0.051	0.17
312.35	-68.29	0.064	0.21
318.05	-87.13	0.082	0.27
isopropanol			
278.07	-18.45	0.014	0.066
287.81	-23.84	0.018	0.083
298.84	-38.05	0.029	0.13
307.27	-63.57	0.048	0.21

318.93	-92.89	0.069	0.29
n-propanol			
278.07	-32.16	0.033	0.12
287.81	-51.60	0.052	0.18
298.84	-75.64	0.076	0.25
307.27	-110.31	0.11	0.36
318.93	-174.39	0.17	0.55
acetone			
278.65	-19.19	0.015	0.070
283.75	-25.20	0.020	0.090
288.45	-30.50	0.024	0.11
293.25	-36.92	0.029	0.13
298.05	-45.56	0.036	0.15
302.75	-55.89	0.044	0.18
307.55	-68.47	0.054	0.22
318.36	-103.74	0.082	0.33
acetonitrile			
277.09	-1.38	-0.00021	0.0050
288.55	-2.80	-0.00041	0.010
293.35	-4.10	-0.00060	0.014
298.15	-5.45	-0.00080	0.018
303.05	-6.75	-0.0010	0.022
307.55	-8.48	-0.0012	0.028
312.25	-11.33	-0.0016	0.036
317.05	-16.49	-0.0024	0.052
ethyl acetate			
277.67	-21.42	-0.0060	0.077

288.55	-35.80	-0.010	0.12
293.25	-46.22	-0.013	0.16
298.05	-52.65	-0.015	0.18
302.85	-65.88	-0.019	0.22
307.45	-79.45	-0.022	0.26
318.64	-123.16	-0.035	0.39

Table S4-a. Parameters for the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree Models, Root Mean Square Deviation (*RMSD*) and Relative Average Deviation (*RAD*) for the Solubility of Lanosterol (x_3) in Water-Methanol Binary Mixtures[a]

water(1)-methanol(2)								
T (K)	w_2	x_3^{exp}	$x_3^{cal\text{-}apb}$	$x_3^{cal\text{-}van}$		Apelblat–Jouyban-Acree		van't Hoff–Jouyban-Acree
296.67	0.00	3.25E-09	2.27E-09	5.44E-10	A_1	-497.83	A_1	10.81
306.81	0.00	5.30E-09	2.51E-09	1.57E-09	B_1	20730.00	B_1	-9537.74
316.94	0.00	9.33E-09	2.97E-09	4.25E-09	C_1	71.67	A_2	9.36
328.97	0.00	1.75E-08	3.92E-09	1.28E-08	A_2	-823.63	B_2	-5620.29
338.78	0.00	2.81E-08	5.19E-09	2.96E-08	B_2	32600.00	J_0	-5277.64
296.67	0.04	3.53E-09	3.55E-09	1.14E-09	C_2	123.70	J_1	126.75
306.81	0.04	5.95E-09	3.99E-09	3.22E-09	J_0	-4922.56	J_2	8573.20
316.94	0.04	1.33E-08	4.80E-09	8.47E-09	J_1	-685.88		
328.97	0.04	3.02E-08	6.48E-09	2.48E-08	J_2	6864.09		
338.78	0.04	6.56E-08	8.74E-09	5.62E-08				
296.67	0.16	3.66E-09	4.37E-09	2.04E-09				
306.81	0.16	6.34E-09	5.34E-09	5.62E-09				
316.94	0.16	1.51E-08	7.01E-09	1.45E-08				
328.97	0.16	3.70E-08	1.05E-08	4.12E-08				
338.78	0.16	7.33E-08	1.54E-08	9.16E-08				
296.67	0.44	3.83E-09	3.69E-09	1.34E-09				
306.81	0.44	7.91E-09	5.62E-09	3.68E-09				
316.94	0.44	2.06E-08	9.21E-09	9.48E-09				
328.97	0.44	4.72E-08	1.80E-08	2.70E-08				

338.78	0.44	1.01E-07	3.27E-08	6.01E-08
296.67	0.65	6.49E-08	8.24E-08	3.46E-08
306.81	0.65	1.01E-07	1.33E-07	8.45E-08
316.94	0.65	1.98E-07	2.33E-07	1.95E-07
328.97	0.65	4.74E-07	4.97E-07	4.92E-07
338.78	0.65	1.00E-06	9.79E-07	9.98E-07
296.67	0.88	1.30E-05	1.77E-05	1.45E-05
306.81	0.88	2.94E-05	2.86E-05	2.87E-05
316.94	0.88	5.47E-05	5.08E-05	5.43E-05
328.97	0.88	0.00011	0.000111	0.00011
277.78	1.00	2.70E-05	3.69E-05	1.9E-05
288.15	1.00	4.86E-05	5.03E-05	3.93E-05
298.15	1.00	8.83E-05	7.7E-05	7.56E-05
303.05	1.00	0.00011	9.87E-05	0.000103
307.55	1.00	0.00013	0.00013	0.00013
312.15	1.00	0.00016	0.00017	0.00018
316.95	1.00	0.00021	0.00023	0.00023
321.65	1.00	0.00032	0.00031	0.00030
Apelblat–Jouyban-Acree	*RAD*	0.39		
	RMSD	1.88E-06		
van't Hoff–Jouyban-Acree	*RAD*	0.21		
	RMSD	2.59E-06		

[a] w_2 is the mass fraction of alcohols in a water-alcohol binary system free of lanosterol; $x_3^{cal\text{-}apb}$ and $x_3^{cal\text{-}van}$ are calculated lanosterol mole fractions by the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree models respectively.

Table S4-b. Parameters for the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree Models, Root Mean Square Deviation (*RMSD*) and Relative Average Deviation (*RAD*) for the Solubility of Lanosterol (x_3) in Water-Ethanol Binary Mixtures[a]

water(1)-ethanol(2)								
T (K)	w_2	x_3^{exp}	$x_3^{cal\text{-}apb}$	$x_3^{cal\text{-}van}$		Apelblat–Jouyban-Acree		van't Hoff–Jouyban-Acree
278.15	0.00	1.43E-09	4.37E-09	9E-09	A_1	-507.613	A_1	-9.35289
288.15	0.00	1.94E-09	6.33E-09	1.22E-08	B_1	19136.32	B_1	-2721.48
298.15	0.00	4.17E-09	9.68E-09	1.62E-08	C_1	74.45794	A_2	2.542052
308.15	0.00	6.21E-09	1.70E-08	2.22E-08	A_2	-727.768	B_2	-2785.93
318.15	0.00	1.25E-08	2.82E-08	2.81E-08	B_2	30018.84	J_0	-1969.19
278.15	0.04	1.73E-08	1.28E-08	1.19E-08	C_2	108.8534	J_1	-14.3242
288.15	0.04	2.79E-08	1.56E-08	1.65E-08	J_0	-2745.25	J_2	5998.03
298.15	0.04	4.57E-08	2.05E-08	2.24E-08	J_1	1714.521		
308.15	0.04	7.64E-08	2.88E-08	2.97E-08	J_2	10612.25		
318.15	0.04	1.06E-07	4.27E-08	3.88E-08				
278.15	0.25	6.07E-08	1.01E-07	6.54E-08				
288.15	0.25	8.96E-08	1.22E-07	9.31E-08				
298.15	0.25	1.35E-07	1.61E-07	1.29E-07				
308.15	0.25	1.80E-07	2.27E-07	1.76E-07				
318.15	0.25	2.25E-07	3.42E-07	2.35E-07				
278.15	0.54	1.73E-07	1.93E-07	4.74E-07				
288.15	0.54	2.87E-07	2.48E-07	7.10E-07				
298.15	0.54	4.42E-07	3.50E-07	1.03E-06				
308.15	0.54	8.38E-07	5.34E-07	1.47E-06				

318.15	0.54	1.20E-06	8.72E-07	2.05E-06
278.15	0.88	0.00022	0.00034	0.00025
288.15	0.88	0.00033	0.00038	0.00034
298.15	0.88	0.00047	0.00046	0.00047
308.15	0.88	0.00069	0.00063	0.00062
318.15	0.88	0.00077	0.00093	0.00081
318.05	1.00	0.0021	0.0021	0.0020
312.35	1.00	0.0017	0.0017	0.0017
307.15	1.00	0.0014	0.0014	0.0015
302.85	1.00	0.0012	0.0012	0.0013
298.25	1.00	0.0010	0.0010	0.0011
293.45	1.00	0.00092	0.00091	0.0010
285.74	1.00	0.00082	0.00080	0.00074
277.95	1.00	0.00073	0.00075	0.00056
Apelblat–Jouyban-Acree	*RAD*	0.32		
	RMSD	2.88E-05		
van't Hoff–Jouyban-Acree	*RAD*	0.38		
	RMSD	3.98E-05		

[a] w_2 is the mass fraction of alcohols in a water-alcohol binary system free of lanosterol; $x_3^{cal\text{-}apb}$ and $x_3^{cal\text{-}van}$ are calculated lanosterol mole fractions by the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree models respectively.

Table S4-c. Parameters for the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree Models, Root Mean Square Deviation (*RMSD*) and Relative Average Deviation (*RAD*) for the Solubility of Lanosterol (x_3) in Water-Isopropanol Binary Mixtures[a]

water(1)-isopropanol(2)								
T (K)	w_2	x_3^{exp}	$x_3^{cal\text{-}apb}$	$x_3^{cal\text{-}van}$		Apelblat–Jouyban-Acree		van't Hoff–Jouyban-Acree
278.15	0.00	1.43E-09	4.37E-09	8.43E-13	A_1	-507.61	A_1	5.759314
288.15	0.00	1.94E-09	6.33E-09	8.75E-13	B_1	19136.32	B_1	-3771.12
298.15	0.00	4.17E-09	9.68E-09	9.06E-13	C_1	74.45	A_2	-26.6873
308.15	0.00	6.21E-09	1.70E-08	9.41E-13	A_2	16.99	B_2	-330.517
318.15	0.00	1.25E-08	2.82E-08	9.69E-13	B_2	-4281.89	J_0	7328.281
278.15	0.04	8.79E-09	3.68E-09	1.55E-11	C_2	-1.67	J_1	-6306.84
288.15	0.04	1.23E-08	4.75E-09	1.53E-11	J_0	1632.95	J_2	3343.804
298.15	0.04	1.41E-08	6.56E-09	1.5E-11	J_1	-1464.48		
308.15	0.04	1.69E-08	9.59E-09	1.48E-11	J_2	-1554.38		
318.15	0.04	2.21E-08	1.47E-08	1.46E-11				
278.15	0.25	7.97E-08	7.64E-08	2.57E-07				
288.15	0.25	9.02E-08	1.02E-07	2.29E-07				
298.15	0.25	1.07E-07	1.42E-07	2.06E-07				
308.15	0.25	1.19E-07	2.06E-07	1.86E-07				
318.15	0.25	1.31E-07	3.10E-07	1.69E-07				
278.15	0.54	1.07E-05	8.03E-06	1.82E-05				
288.15	0.54	1.41E-05	1.10E-05	1.94E-05				
298.15	0.54	2.08E-05	1.53E-05	2.05E-05				
308.15	0.54	2.51E-05	2.17E-05	2.17E-05				

318.15	0.54	3.10E-05	3.10E-05	2.28E-05
278.15	0.88	0.00016	0.00019	0.00020
288.15	0.88	0.00030	0.00029	0.00028
298.15	0.88	0.00041	0.00044	0.00039
308.15	0.88	0.00052	0.00064	0.00053
318.15	0.88	0.00071	0.00093	0.00071
278.07	1.00	0.00047	0.00041	0.00041
287.81	1.00	0.00060	0.00065	0.0006
298.84	1.00	0.00095	0.00105	0.0010
307.27	1.00	0.0016	0.0015	0.0015
318.93	1.00	0.0023	0.0023	0.0023
Apelblat–Jouyban-Acree	*RAD*	0.36		
	RMSD	0.00037		
van't Hoff–Jouyban-Acree	*RAD*	0.23		
	RMSD	6.51E-06		

[a] w_2 is the mass fraction of alcohols in a water-alcohol binary system free of lanosterol; $x_3^{cal\text{-}apb}$ and $x_3^{cal\text{-}van}$ are calculated lanosterol mole fractions by the Apelblat–Jouyban-Acree and van't Hoff–Jouyban-Acree models respectively.

Table S5. Solubility of Lanosterol (3) in Water (1)-Methanol (2) Binary Mixtures Predicted by the Modified Wilson Compared with Experimental Data

	296.67 K			306.81 K			316.94 K		
w_2	$x^{exp}{}_3$	$x^{pre}{}_3$	*RD%*	$x^{exp}{}_3$	$x^{pre}{}_3$	*RD%*	$x^{exp}{}_3$	$x^{pre}{}_3$	*RD%*
0.04	3.53E-09	1.92E-09	45.55	5.95E-09	3.69E-09	37.89	1.33E-08	6.34E-09	52.17
0.16	3.66E-09	1.58E-09	56.76	6.34E-09	3.28E-09	48.17	1.51E-08	6.34E-09	0.58
0.44	3.83E-09	2.82E-08	636.15	7.91E-09	5.84E-08	638.05	2.06E-08	1.21E-07	4.90
0.65	6.49E-08	4.95E-07	662.08	1.01E-07	9.62E-07	851.77	1.98E-07	1.95E-06	8.88
0.88	1.30E-05	1.30E-05	0.34	2.94E-05	2.32E-05	21.07	5.47E-05	4.48E-05	0.18
	328.97 K			338.78 K					
w_2	$x^{exp}{}_3$	$x^{pre}{}_3$	*RD%*	$x^{exp}{}_3$	$x^{pre}{}_3$	*RD%*			
0.04	3.02E-08	1.33E-08	56.08	6.56E-08	2.36E-08	64.03			
0.16	3.70E-08	1.55E-08	57.98	7.33E-08	3.22E-08	56.11			
0.44	4.72E-08	3.30E-07	599.74	1.01E-07	7.73E-07	665.95			
0.65	4.74E-07	5.13E-06	982.59	1.00E-06	1.19E-05	1084.95			
0.88	0.00011	0.00011	1.16						

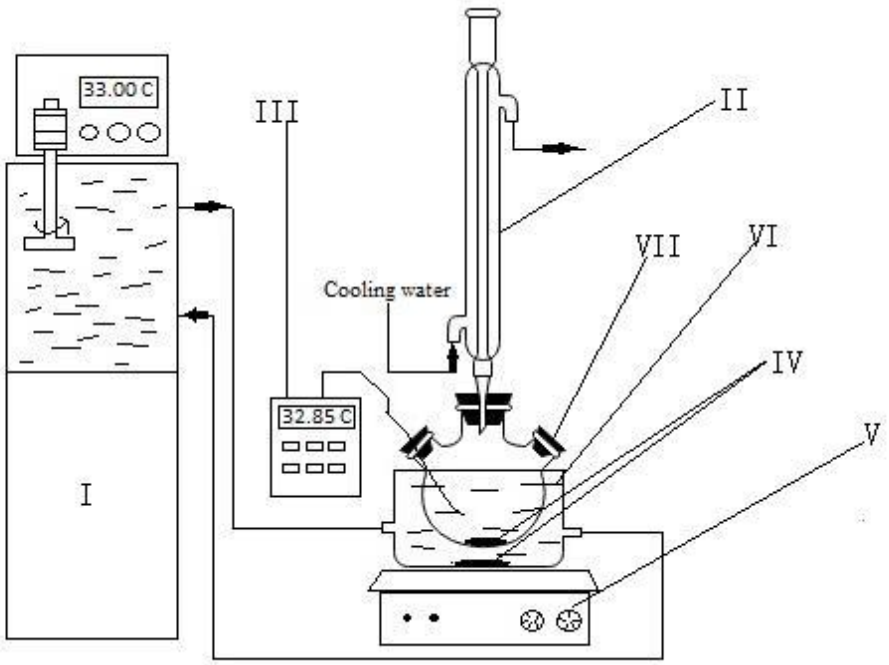


Figure S1. Schematic diagram of the experimental set up: I, water circulating bath; II, condenser; III, thermocouple; IV, magnetic stirrers; V, magnetic stirrer controller; VI, water jacketed three necks glass vessel; VII, sampling port.

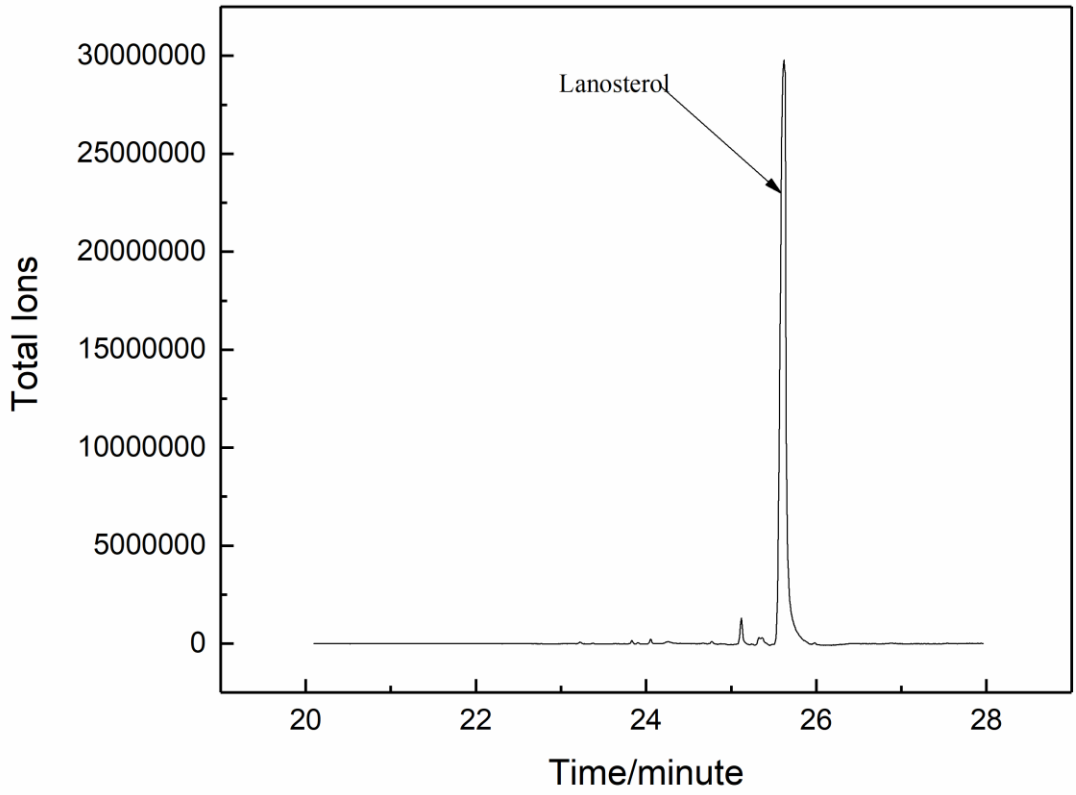


Figure S2. Total ions chromatogram of purified lanosterol in methanol by GC-MS. The retention time of lanosterol is 25.62 minutes and the purity of lanosterol is >95%.

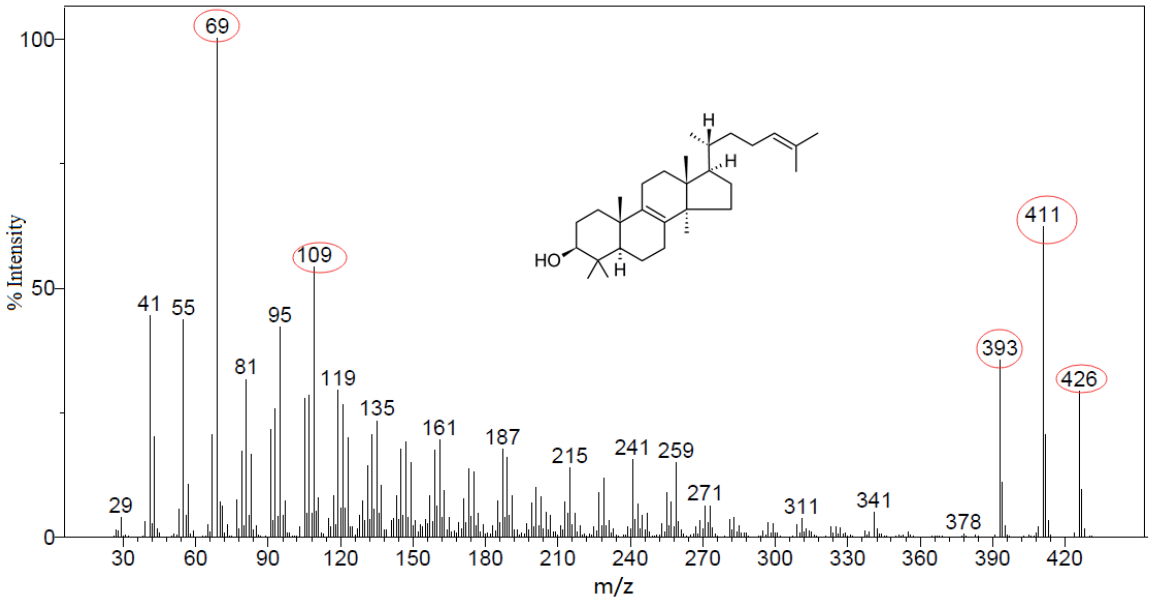


Figure S3. MS scan of lanosterol in methanol at 25.62 minutes. Ion groups (m/z) are found as 69, 109, 393, 411 and 426 (circled in red). MS scan results were compared with data from Reference 4 to confirm that the sample is lanosterol.

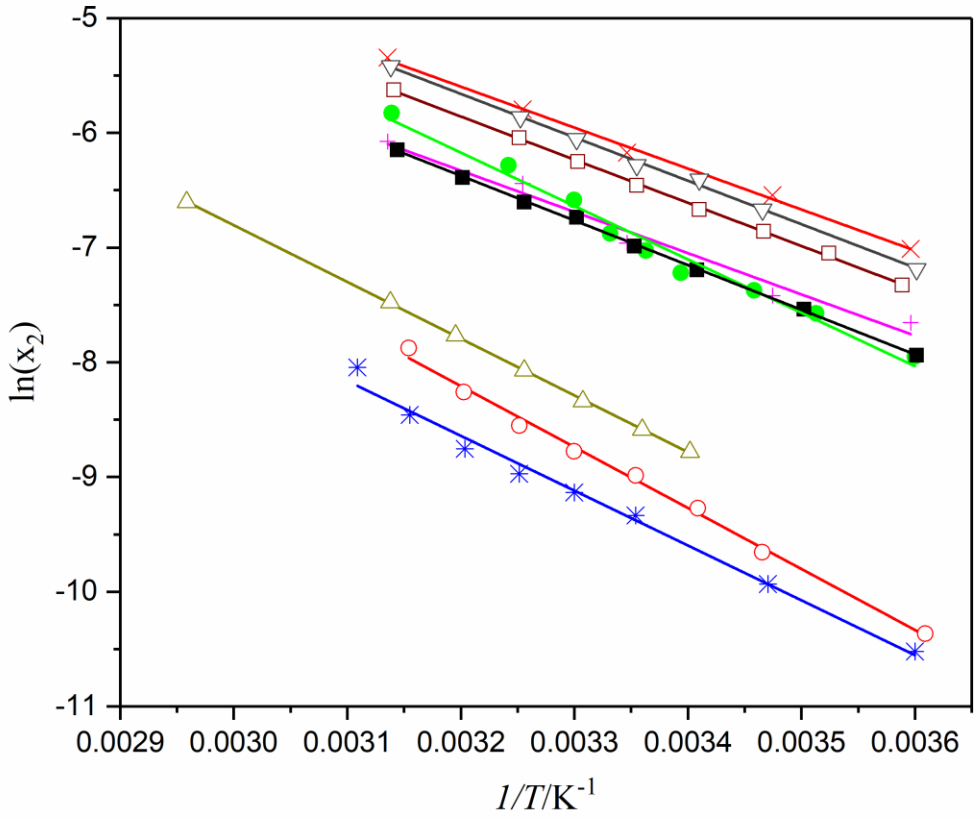


Figure S4. van't Hoff plots of ln(x_2) versus *1/T* in different solvents. ✳, methanol; ○, acetonitrile;△, DMSO; ●, DMF; ■, ethanol; □, acetone; ▽, ethyl acetate; ┼, isopropanol; and ×, *n*-propanol. The solid lines are the solubilities fitted by the modified Apelblat equation.

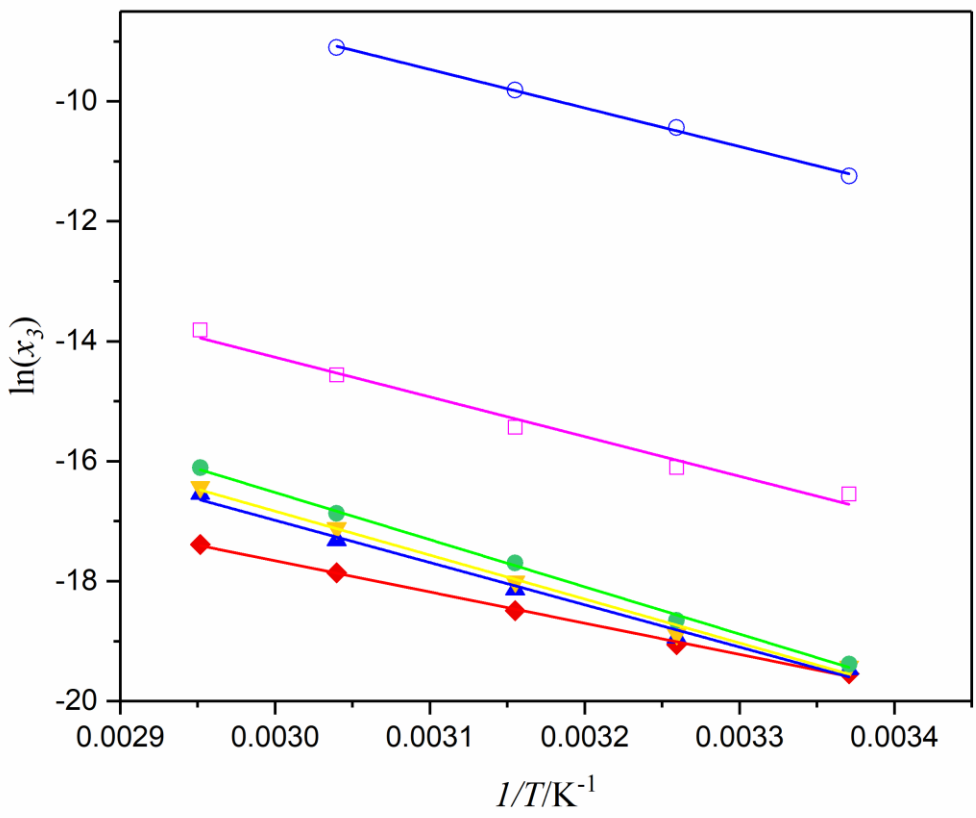


Figure S5. van't Hoff plots of ln(x_3) versus *1/T* in water (1)-methanol (2) mixtures. ◆, water; ▲, v_2=0.050; ▼, v_2=0.20; ●, v_2=0.50; □, v_2=0.70;and ○, v_2=0.90. The solid lines are the solubilities fitted by the modified Apelblat equation.

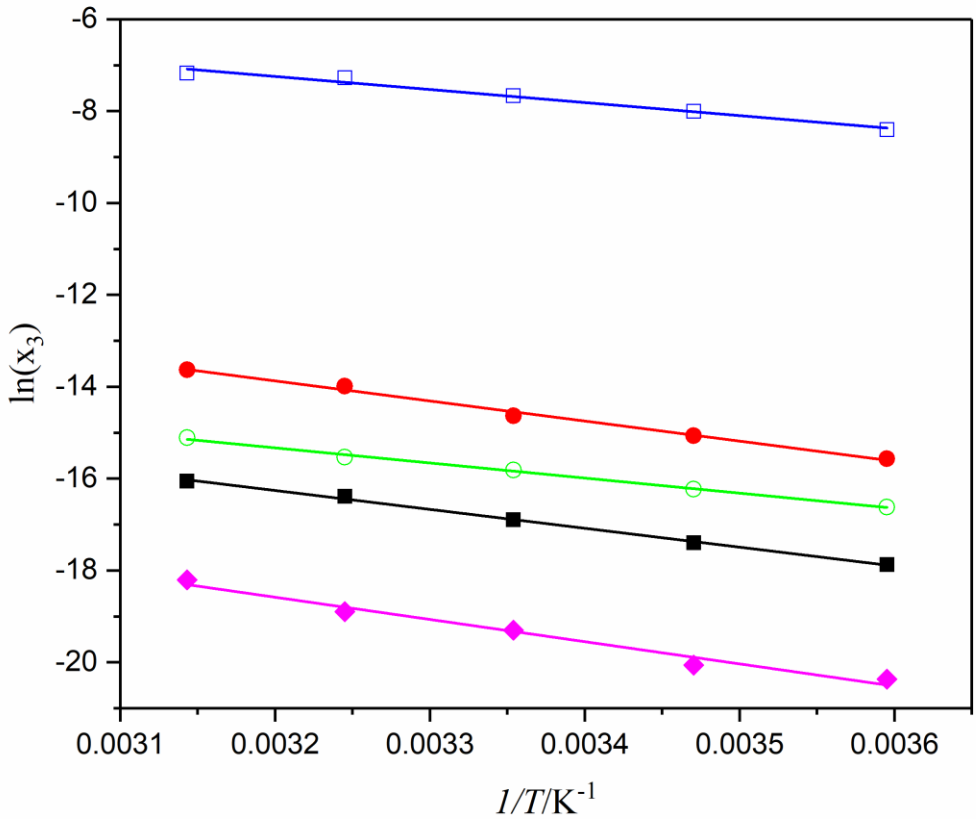


Figure S6. van't Hoff plots of ln(x_3) versus *1/T* in water (1)-ethanol (2) mixtures. ◆, water; ■, v_2=0.050; ○, v_2=0.30; ●, v_2=0.60; □, v_2=0.90. The solid lines are the solubilities fitted by the modified Apelblat equation.

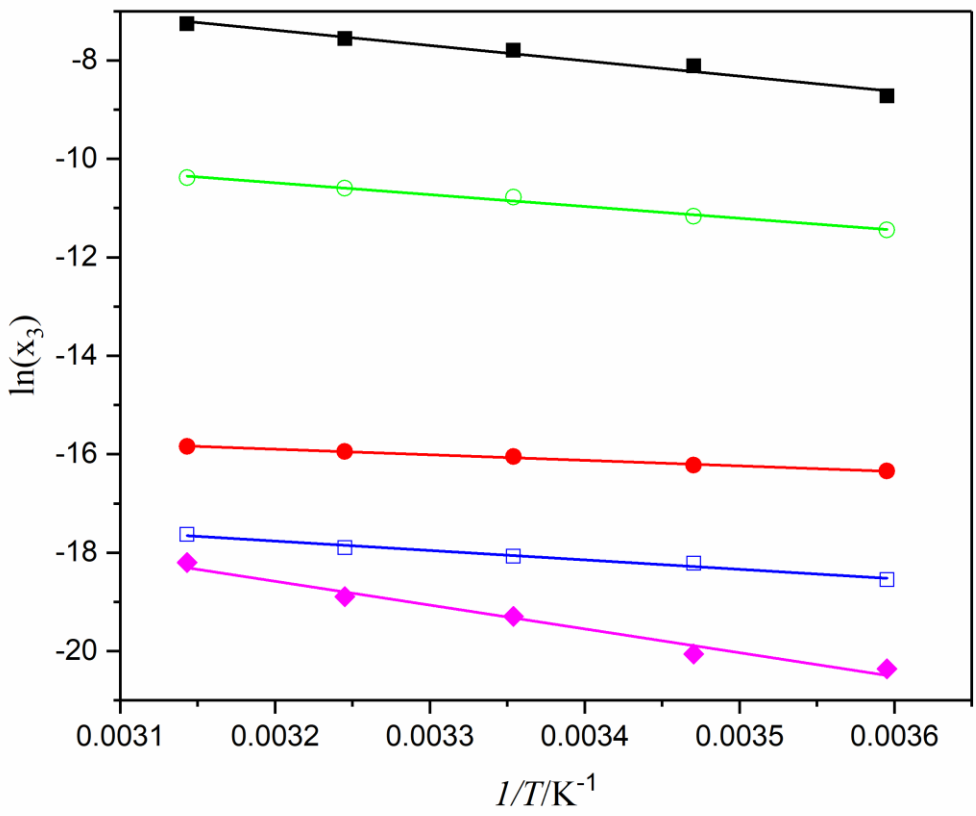
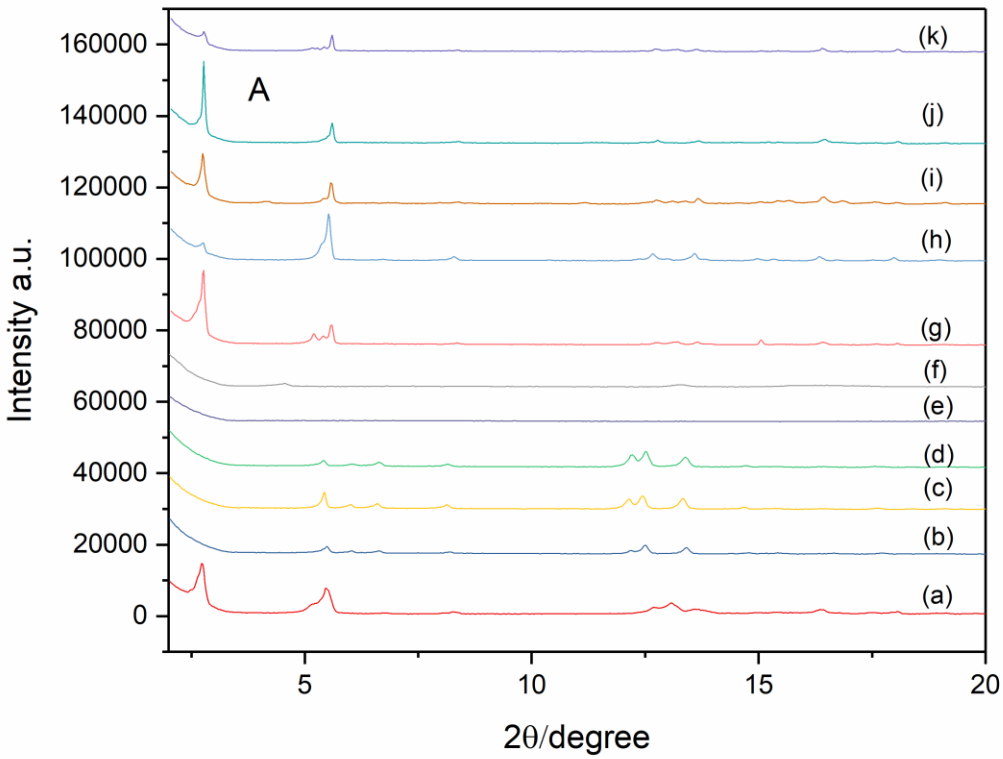
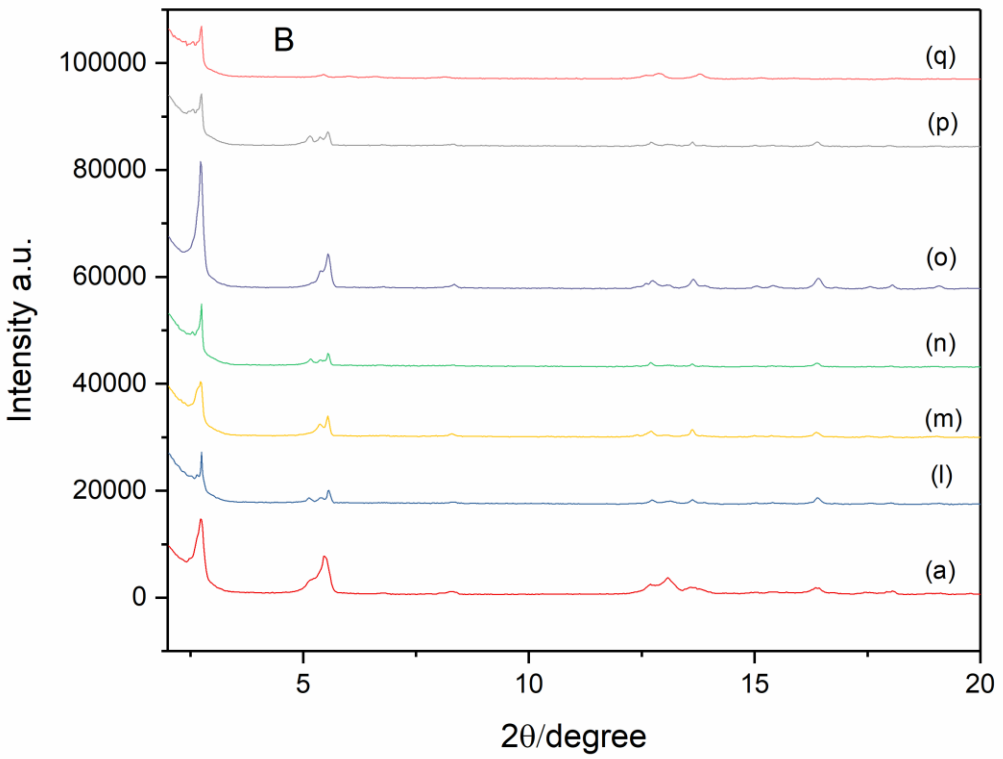


Figure S7. van't Hoff plots of ln(x_3) versus *1/T* in water (1)-isopropanol (2) mixtures. ◆, water; □ v_2=0.050; ●, v_2=0.30; ○, v_2=0.60;■, v_2=0.90. The solid lines are the solubilities fitted by the modified Apelblat equation.


A
Intensity a.u.
160000
140000
120000
100000
80000
60000
40000
20000
0
5
10
15
20
2θ/degree
(k)
(j)
(i)
(h)
(g)
(f)
(e)
(d)
(c)
(b)
(a)


B
Intensity a.u.
100000
80000
60000
40000
20000
0
5
10
15
20
2θ/degree
(q)
(p)
(o)
(n)
(m)
(l)
(a)

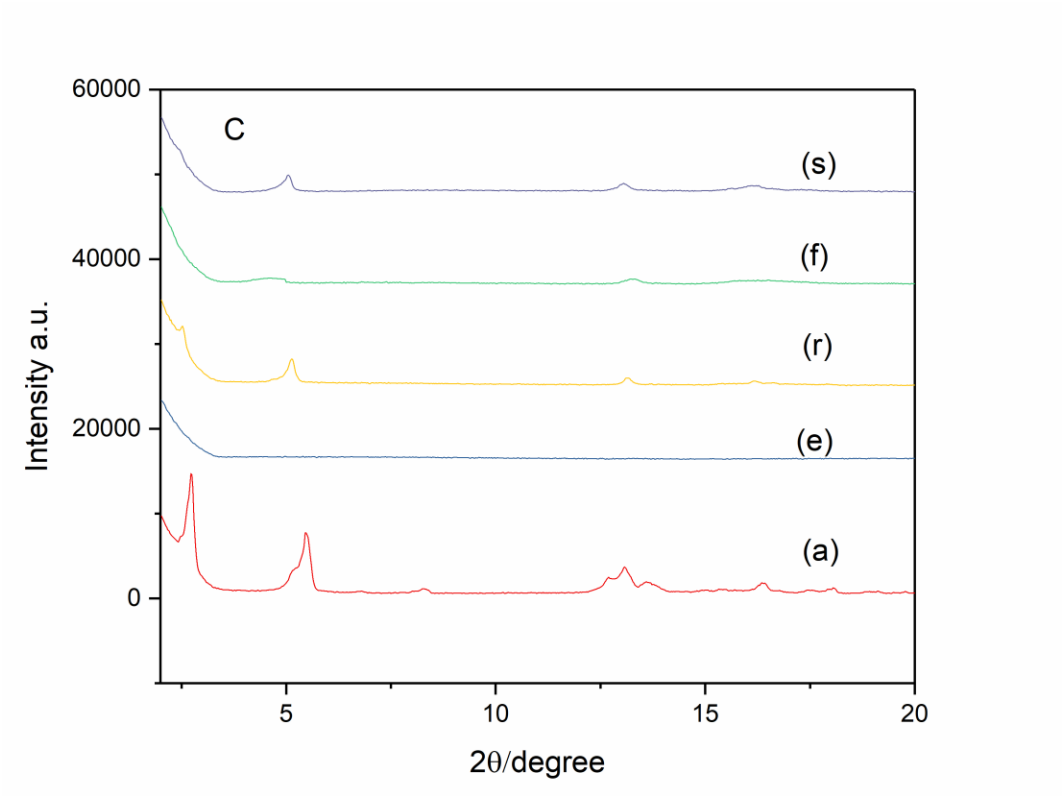


Figure S8. X-ray diffraction patterns from 2° to 20° 2θ/ degree of lanosterol powder and lanosterol precipitates at equilibrium with lanosterol solutions in pure solvents and water-alchol mixtures. A) (a) powder lanosterol before solubility experiments; (b) ethanol; (c) isopropanol; (d) *n*-propanol; (e) DMSO; (f) DMF; (g) actonitrile; (h) methanol; (i) acetone; (j) ethyl acetate; (k) water; B) (l) 5%(v/v) ethanol; (m) 90% ethanol; (n) 5% methanol; (o) 90% methanol; (p) 5% isopropanol; (q) 90% isopropanol; C) lanosterol precipitates at equilibrium with solutions of lanosterol in DMSO and DMF vacuum-oven dried 24 hours; (a) lanosterol powder before solubility experiments; (e) wet lanosterol at equilibrium with a lanosterol solution in DMSO; (r) dried lanosterol at equilibrium with a lanosterol solution in DMSO; (s), dried lanosterol at equilibrium with a lanosterol solution in DMF.

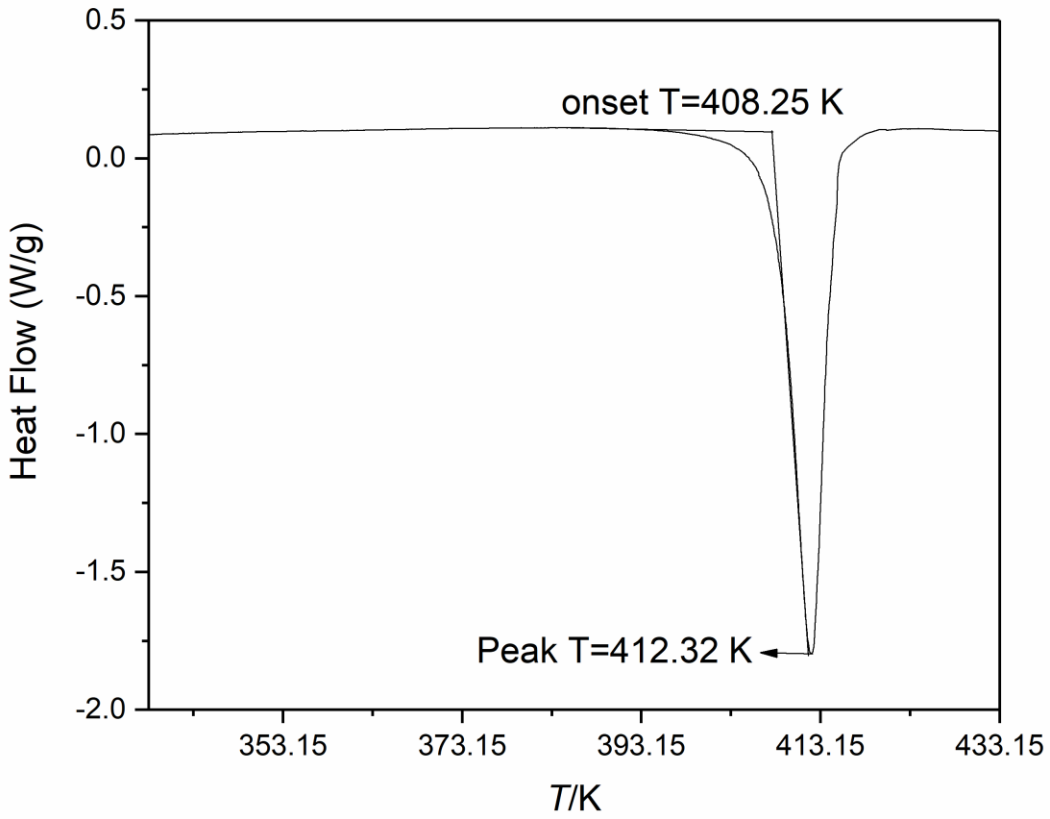


Figure S9. Differential scanning calorimetry (DSC) of lanosterol from 338.15 K-433.15 K. The onset T_m is 408.27 K with an uncertainty $u(T_m)$ = 0.50 K; the peak of T_m is 412.39 K with an uncertainty $u(T_m)$ = 0.60 K; the enthalpy of fusion ΔH_{fus} of lanosterol is 23.61 kJ with an uncertainty u (ΔH_{fus}) = 0.13kJ·mol^{-1}. DSC experiments were done in triplicate.

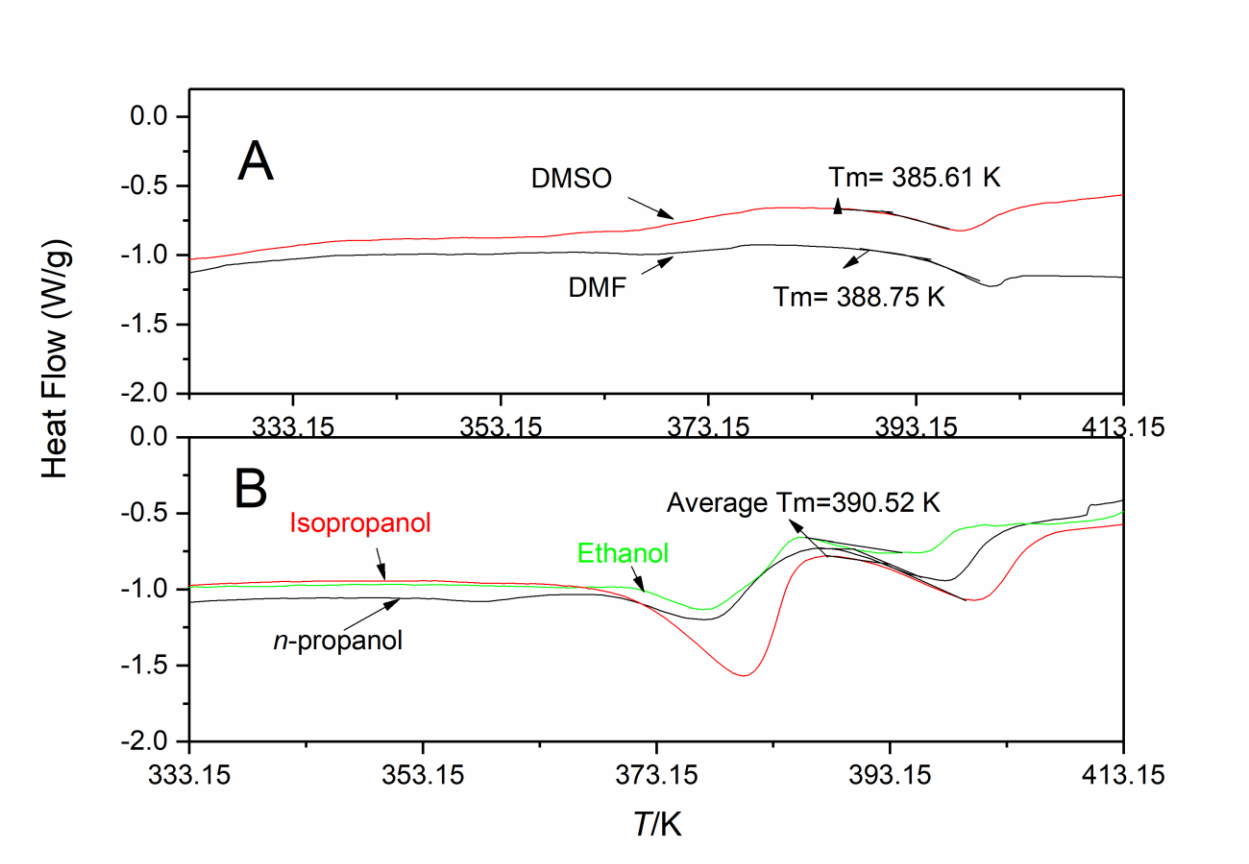


Figure S10. Differential scanning calorimetry (DSC) of lanosterol after solubility measurements. A), dried precipitate at equilibrium with a lanosterol solution in DMSO and DMF; B), dried precipitate at equilibrium with a lanosterol solution in ethanol, isopropanol and *n*-propanol.

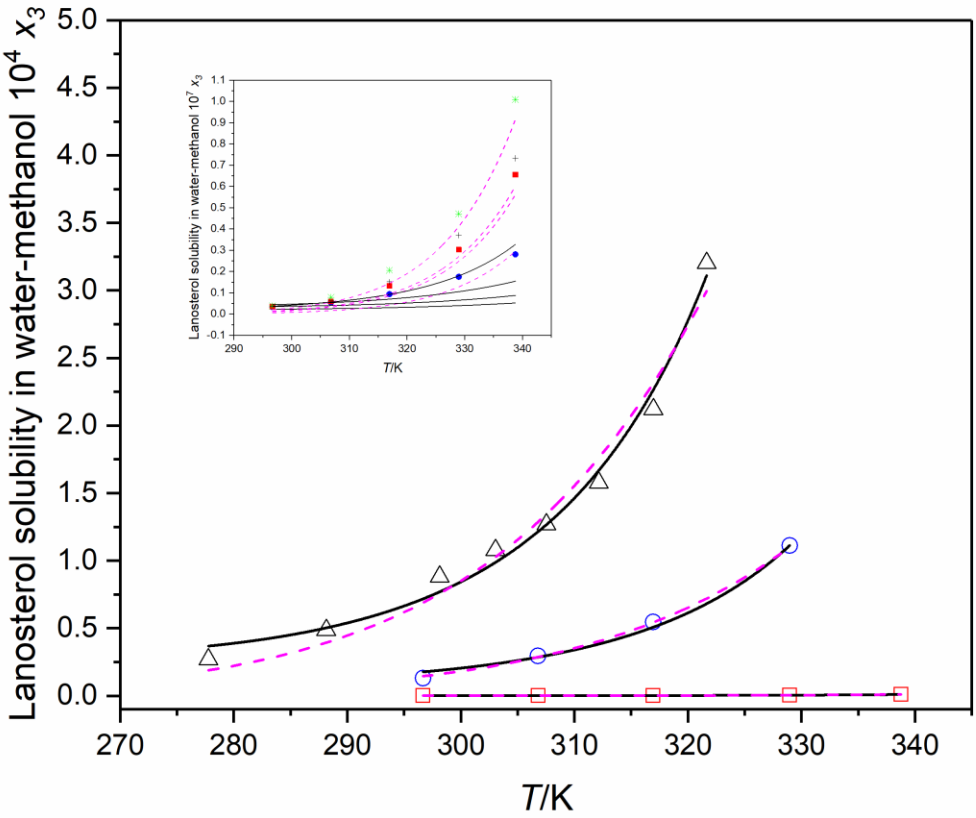


Figure S11. Mole fraction of lanosterol (3), x_3, in water and in water (1)-methanol (2) mixtures as a function of temperature. □, v_2=0.70; ○, v_2=0.90; △, v_2=1.00. The insert shows x_3 in ●, water v_2=0.00; ■, v_2=0.050; ＋, v_2=0.20; ✳, v_2=0.50; The solid lines are the solubilities fitted by the Apelblat–Jouyban-Acree model and the dash lines are the solubilities fitted by van't Hoff–Jouyban-Acree model.

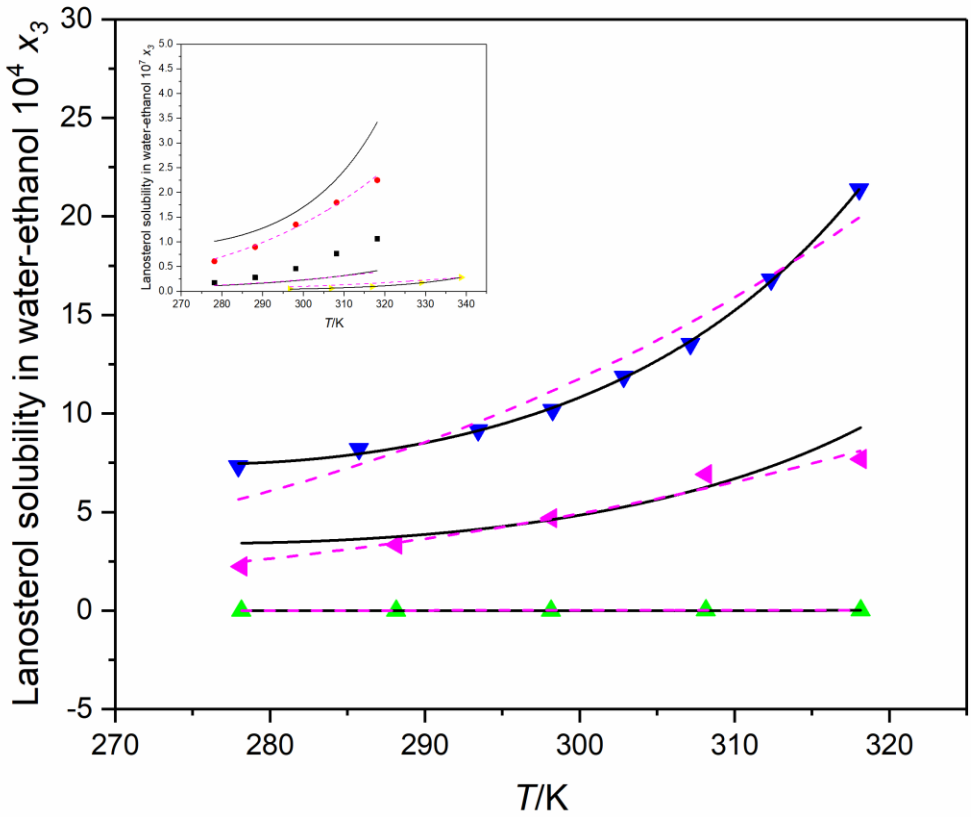


Figure S12. The mole fraction of lanosterol (3) x_3 in water and water (1)-ethanol (2) mixture as a function of temperature. ▲, v_2=0.60; ◀, v_2=0.90; ▼, v_2= 1.00. The insert shows x_3 in: ▶, water; ■, v_2=0.050; and ●, v_2=0.30. The solid lines are the solubilities fitted by the Apelblat–Jouyban-Acree model and the dash lines are the solubilities fitted by van't Hoff–Jouyban-Acree model.

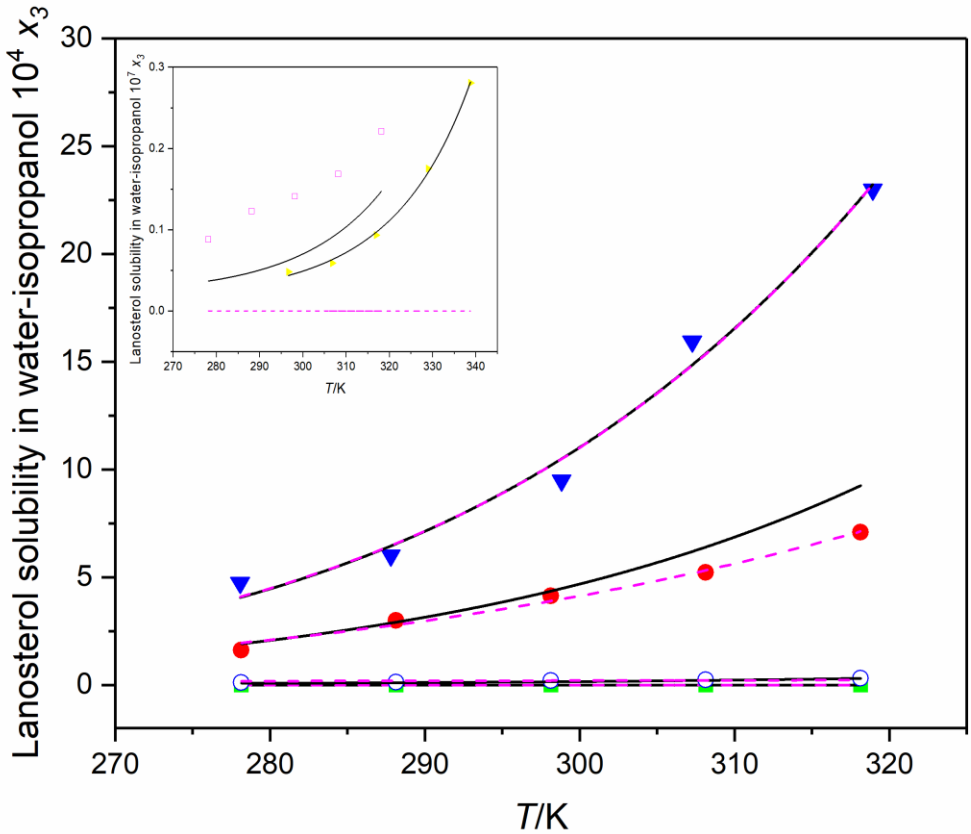


Figure S13. The mole fraction of lanosterol (3) x_3 in water and water (1)-isopropanol (2) mixtures as a function of temperature. ■, v_2=0.30; ○, v_2=0.60; ●, v_2=0.90; and ▼, v_2= 1.00. The insert shows x_3 in: ▶, water; and □, v_2=0.050. The solid lines are the solubilities fitted by the Apelblat–Jouyban-Acree model and the dash lines are the solubilities fitted by van't Hoff–Jouyban-Acree model.

References

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