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SUPPORTING INFORMATION

Comparative Study of Interactions of Aliskiren and

AT_1 Receptor Antagonists with Lipid Bilayers

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Table S1: Observed ^{13}C chemical shifts for the carbons of aliskiren in ^{13}C-CP/MAS spectra in the temperature range of 25-45 °C. On the right end column are shown the chemical shifts of aliskiren in CD_3OD solvent (for carbon identifiers of aliskiren refer to Fig. 1a).

Table S2: Observed ^{13}C chemical shifts for the carbons of cholesterol in ^{13}C-CP/MAS spectra at the temperature range of 25-45 °C (for carbon identifiers of cholesterol refer to Fig. 1c).

Table S3: Fitting parameters extracted from the diffraction data at 20ºC of the DPPC/aliskiren/cholesterol water system (refer to Fig. S1).

Table S3: Simulated properties of the DPPC/aliskiren bilayers.

Figure S1: Thermal scans of DPPC, DPPC/aliskiren, DPPC/cholesterol and DPPC/cholesterol/ aliskiren bilayers. Details of the sample concentrations are denoted on the left side of thermograms.

Figure S2: The smoothed X-ray diffraction peaks from the of the DPPC/aliskiren/ cholesterol water system at 20ºC (blue circles) and the corresponding Lorentzian fits (red lines). The fitting results are summarized in Table S3.

Figure S3: Electron density profile of the bilayer structure calculated from the scattering peaks of the DPPC/aliskiren/cholesterol water system resulting in a d_{HH} value of 50 Å. We remark that the d_{HH} value at 20 °C of pure DPPC bilayers with tilted chains is 44 Å [1], thus the chains in the DPPC/aliskiren/cholesterol bilayers are most probably untilted.

Table S1

	^{13}C-CP/MAS at 25°C		^{13}C-CP/MAS at 35 °C		^{13}C-CP/MAS at 45°C		^{13}C (CD_3OD)
Pos. ^{13}C	**DPPC/ aliskiren (80/20)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**DPPC/ aliskiren (80/20)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**DPPC/ aliskiren (80/20)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**aliskiren**
1	-	-	-	-	-	-	182.29
2	-	-	-	43.15	-	43.21	44.28
3	-	-	-	-	-	-	24.44
4	23.74	23.87	-	23.95	-	23.87	24.16
5	-	47.60	47.96	47.88	47.91	47.97	48.46
6	-	-	-	-	-	-	177.77
7	-	50.99	-	51.07	-	51.12	51.35
8	-	-	-	-	31.62	31.51	32.17
9	21.27	21.26	21.40	21.36	21.36	21.33	21.40
10	20.48	20.14	-	20.14	-	20.10	20.63
11	-	-	34.96	-	-	-	35.08
12	-	-	70.28	70.22	70.27 (or and C-28)	70.26 (or and C-28)	70.44
13	-	-	56.64 (or and C-34)	56.61 (or and C-34)	56.59 (or and C-30)	56.60 (or and C-30)	56.68
14	-	-	-	-	-	32.60	33.17
15	-	-	42.10	42.22	-	42.33	42.96
16	29.88 (ή/και C-27)	-	30.00 (or and C-27)	29.98 (or and C-27)	29.87 (or and C-27)	-	30.87
17	-	-	-	19.52	-	19.56	19.41
18	-	-	18.43	18.53	-	18.55	18.45
19	37.30	37.48	-	37.90	-	37.87	38.24
20	-	-	-	-	-	-	134.97
21	-	-	-	-	-	-	122.94
22	-	-	113.52	113.47	113.81	113.74	113.61
23	-	-	-	-	-	-	149.46
24	-	-	-	-	-	-	149.96

25	-	-	115.95	115.91	116.30	116.19	116.06
26	65.93	65.91	66.11	-	-	-	67.32
27	29.88 (or and C-16)	-	30.00 (or and C-16)	29.98 (or and C-16)	29.87 (or and C-16)	-	30.74
28	-	69.99	69.99	-	70.27 (or and C-12)	70.26 (or and C-12)	70.35
29	-	57.99	57.95	57.95	-	57.70	58.95
30	-	-	56.64 (or and C-13)	56.61 (or and C-13)	56.59 (or and C-13)	56.60 (or and C-13)	56.73
-CH-	-	-	-	-	-	-	137.02
-COOH	-	-	-	-	-	-	174.11

Table S2

	^{13}C-CP/MAS at 25°C		^{13}C-CP/MAS at 35°C		^{13}C-CP/MAS at 45°C		^{13}C-CP/ MAS
Pos. ^{13}C	**DPPC/ cholesterol (85/15)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**DPPC/ cholesterol (85/15)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**DPPC/ cholesterol (85/15)**	**DPPC/ cholesterol/ aliskiren (68/12/20)**	**cholesterol**
1	-	-	38.57	38.37	38.44	38.36	37.3
2	-	-	-	-	-	-	32.9, 32.4 and 32.0 (1:2:1)
3	-	-	-	-	-	-	71.8 and 70.9 (1:1)
4	43.66 (or C-13)	43.33 (or C-13)	43.37 (or C-13)	43.37 or 42.64	42.65 or 43.28	42.63 or 43.21	42.9
5	140-142	140.1-140.8	-	-	-	-	141.5 and 139.4 (2:1)
6	-	-	-	-	-	-	122.8 and 122.0 (1:1)
7	-	-	-	-	-	-	32.9, 32.4 and 32.0 (1:2:1)
8	-	-	-	-	-	-	32.9, 32.4 and 32.0 (1:2:1)
9	-	-	-	49.91	51.13, 49.95	49.93	51.6, 50.8 and 49.8 (2:1:2)
10	-	-	37.54 (or and C-22)	37.47 or37.32	37.38 (or and C-22)	37.27 (or and C-22)	36.6 (two peaks)
11	-	-	22.08	22.16	22.04	-	21.2 and 22.4
12	-	-	29.32	-	29.20	29.10	29.0
13	43.66 (or C-13)	43.33 (or C-4)	43.37 (or C-4)	43.37 or 42.64	42.65 or 43.28	42.63 or 43.21	42.9
14	57.37 (or C-17)	57.37 (or C-17)	57.63 (or C-17)	57.65 (or C-17)	57.72 (or C-17)	57.49 (or C-17)	58.1 and 57.6 (3:1)
15	25.68	-	-	-	25.39	25.19	25.3 και 24.6 (1:1)
16	-	-	40.97	40.86	40.94	40.86	40.7
17	57.37	57.53	57.63	57.65	57.72	57.49	58.1, 57.6, 56.7 (3:1:1)

	(or C-14)	(or C-14)	(or C-14)	(or C-14)	(or C-14)	(or C-14)	
18	-	13.39	13.25	13.36, 12.96, 12.70	12.93	12.71	13.7,13.2, 12.7, 12.1, 11.2
19	20.60	-	20.51	20.54	20.24	-	20.0 and 21.2 (1:2)
20	-	-	-	-	-	-	36.6 (two peaks)
21	-	-	20.08	-	19.74	-	18.8 (three peaks)
22	-	-	37.54 (or and C-10)	37.47 ήor 37.32	37.38 (or and C-10)	37.27 (or and C-10)	36.6 (two peaks)
23	-	-	-	-	-	-	24.6
24	-	40.47	40.51	40.40	40.37	40.37	39.3 and 38.8 (1:1)
25	29.08	28.96	29.00	-	28.77	28.78	29.0
26	23.08	-	23.07	23.26	23.26	23.24	23.0
27	-	-	-	-	-	-	24.5 and 25.3 (1:3)

Table S3

	x_c (10^{-2} Å^{-1})	w (10^{-4} Å^{-1})	A (10^{-4} a.u.)	F_h/F_1 (a.u.)
Peak 1	1.3913 ± 0.0003	9.6 ± 0.1	246.2 ± 2.4	1.000 ± 0.005
Peak 2	2.768 ± 0.002	11.0 ± 0.4	6.3 ± 2.2	1.009 ± 0.019
Peak 3	4.139 ± 0.002	40.3 ± 1.8	3.7± 0.2	0.369 ± 0.013
Peak 4	5.554 ± 0.001	41.4 ± 1.5	4.3 ± 0.3	0.527 ± 0.018

Table S4

Number of aliskirens	**A (Å^2)**	**θ(P-N) (º)**
1	64.9±0.2	79.8±0.8
5	65.0±0.3	78.8±1.2
11	65.8±0.2	78.9±1.1

Figure S1

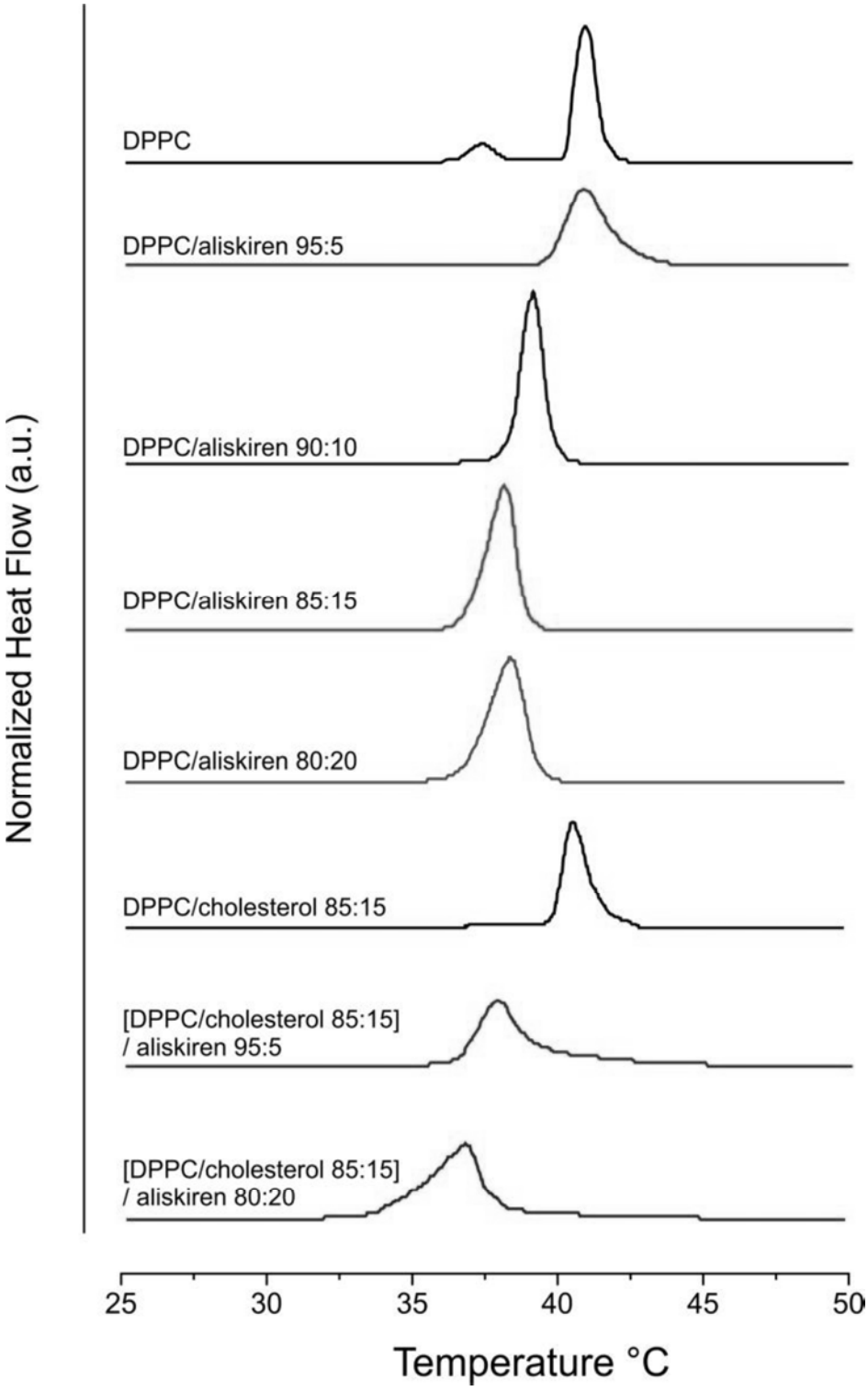

DPPC
DPPC/aliskiren 95:5
DPPC/aliskiren 90:10
DPPC/aliskiren 85:15
DPPC/aliskiren 80:20
DPPC/cholesterol 85:15
[DPPC/cholesterol 85:15]
/ aliskiren 95:5
[DPPC/cholesterol 85:15]
/ aliskiren 80:20
Normalized Heat Flow (a.u.)
25
30
35
40
45
50
Temperature °C

Figure S2

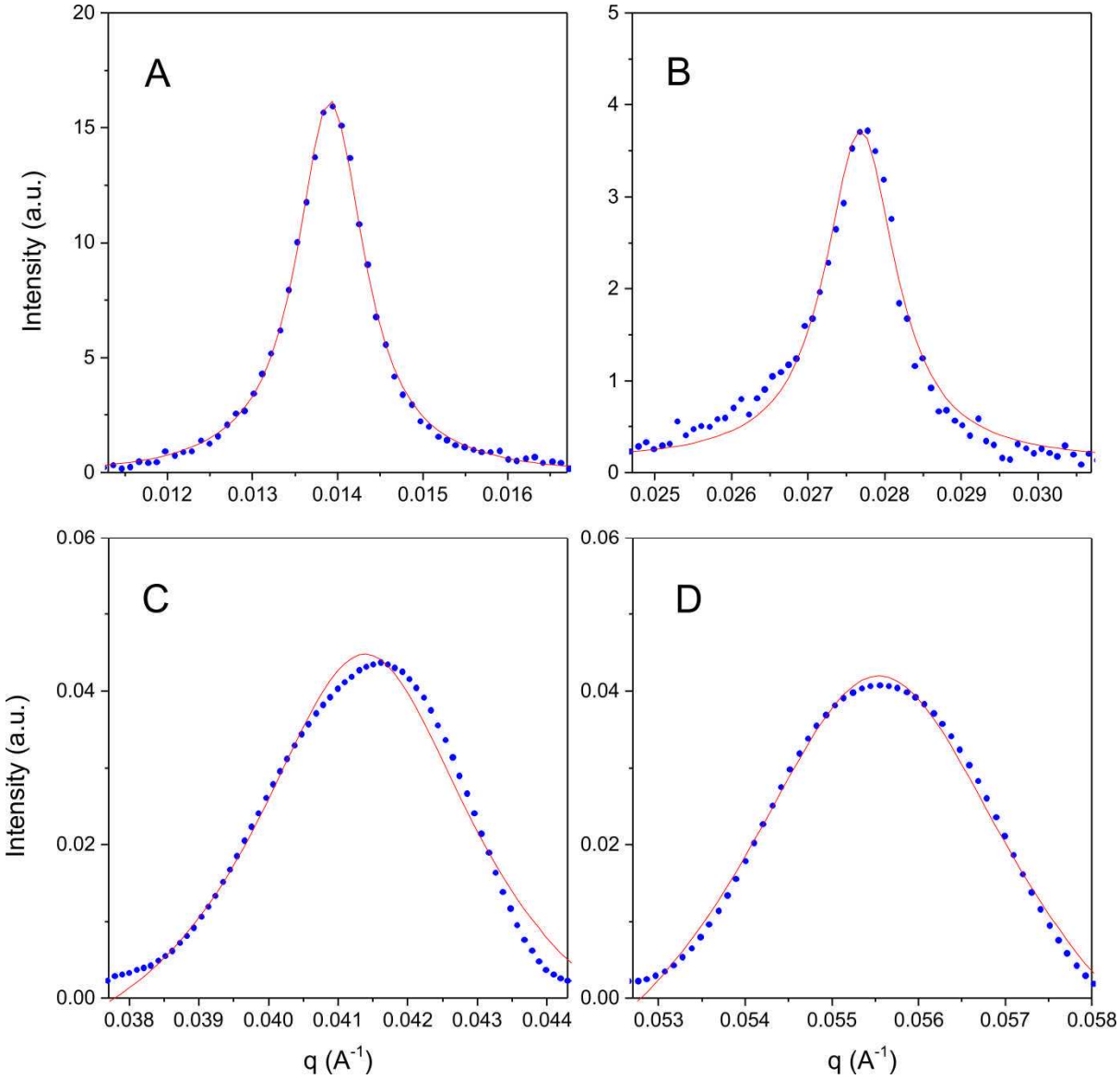
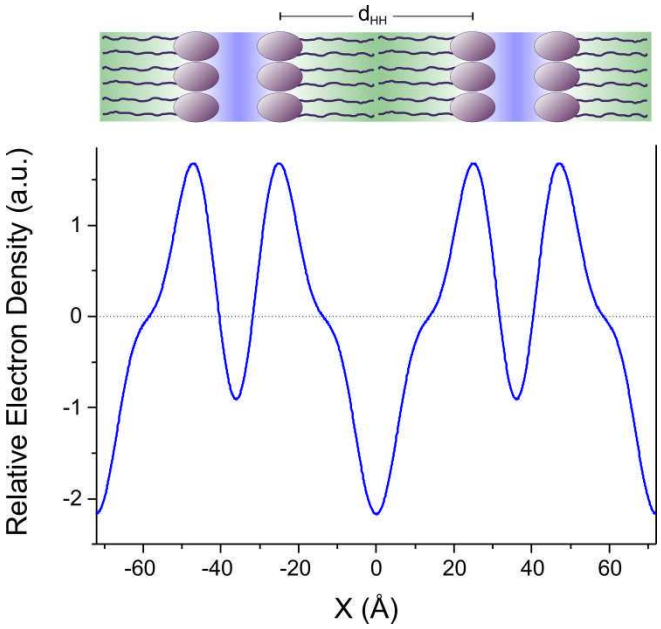


Figure S3



References

[1] J.F. Nagle, S. Tristram-Nagle, Structure of lipid bilayers, Biochimica Et Biophysica Acta-Reviews on Biomembranes, 1469 (2000) 159-195.