Electronic Supplementary Material

Spectroscopic studies on the molecular interactions of curcumin and piperine

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Table S1 Chemical shifts of curcumin (**1**) in methanol-d_4. Numbering of the positions is in accordance to those given in Fig. 1.

Position	δ_C/ppm	δ_H/ppm (*J* in Hz)
1	142.2	7.58 (1 H, d, 15.8)
2	122.3	6.64 (1 H, d, 15.8)
3	184.8	
4	102.0	5.97 (2 H, d, 6.6)
5	184.8	
6	122.3	6.64 (1 H, d, 15.8)
7	142.2	7.58 (1 H, d, 15.8)
8	128.6	
9	111.7	7.22 (1 H, d, 1.9)
10	149.4	
11	150.5	
12	116.6	6.83 (1 H, d, 1.8)
13	124.2	7.11 (1 H, dd, 8.3, 1.6)
14	128.6	
15	111.7	7.22 (1 H, d, 1.9)
16	149.4	
17	150.5	
18	116.6	6.83 (1 H, d, 1.8)
19	124.2	7.11 (1 H, dd, 8.3, 1.6)
OCH_3 (2x)	56.4	3.92 (2x3 H, s)

Table S2 Chemical shifts of piperin (**2**) in methanol-d_4. Numbering of the positions is in accordance to those given in Fig. 1.

Position	δ_C/ppm	δ_H/ppm (*J* in Hz)
1	167.8	
2	120.6	6.64 (1 H, d, 14.7)
3	144.6	7.33 (1 H, dd, 14.7, 10.7)
4	126.4	6.91 (1 H, ddd, 15.5, 10.6, 0.5)
5	140.2	6.84 (1 H, d, 15.5)
6	132.4	
7	106.7	7.10 (1 H, d, 1.7)
8	149.8	
9	102.7	5.97 (2 H, s)
10	149.8	
11	109.4	6.80 (1 H, d, 7.9)
12	123.9	6.97 (1 H, dd, 7.9, 1.7)
1', 5' *	44.6; 48.1	3.63 (2x2 H, t, 5.5)
2', 4' *	26.9; 27.9	1.59 (2x2 H, m)
3'	25.6	1.71 (2 H, m)

* Exact assignment of the respected signals was not determined

Table S3 Elemental analysis of curcumin (**1**) and piperine (**2**).

Curcumin (**1**)	C	H	N	O	S
calculated	68.47%	5.47%	0%	26.06%	0%
measured (averaged)*	67.69%	5.75%	0.11%	25.62%	0.03%
Sum of measured elements: 99.20					

Piperine (**2**)	C	H	N	O	S
calculated	71.56%	6.71%	4.91%	16.82%	0%
measured (averaged)*	71.74%	6.94%	5.01%	16.96%	<0.02%
Sum of measured elements: 100.66					

* Values are averaged over three (O) or four (CHNS) measurements for curcumin (**1**) and two measurements for piperine (**2**).

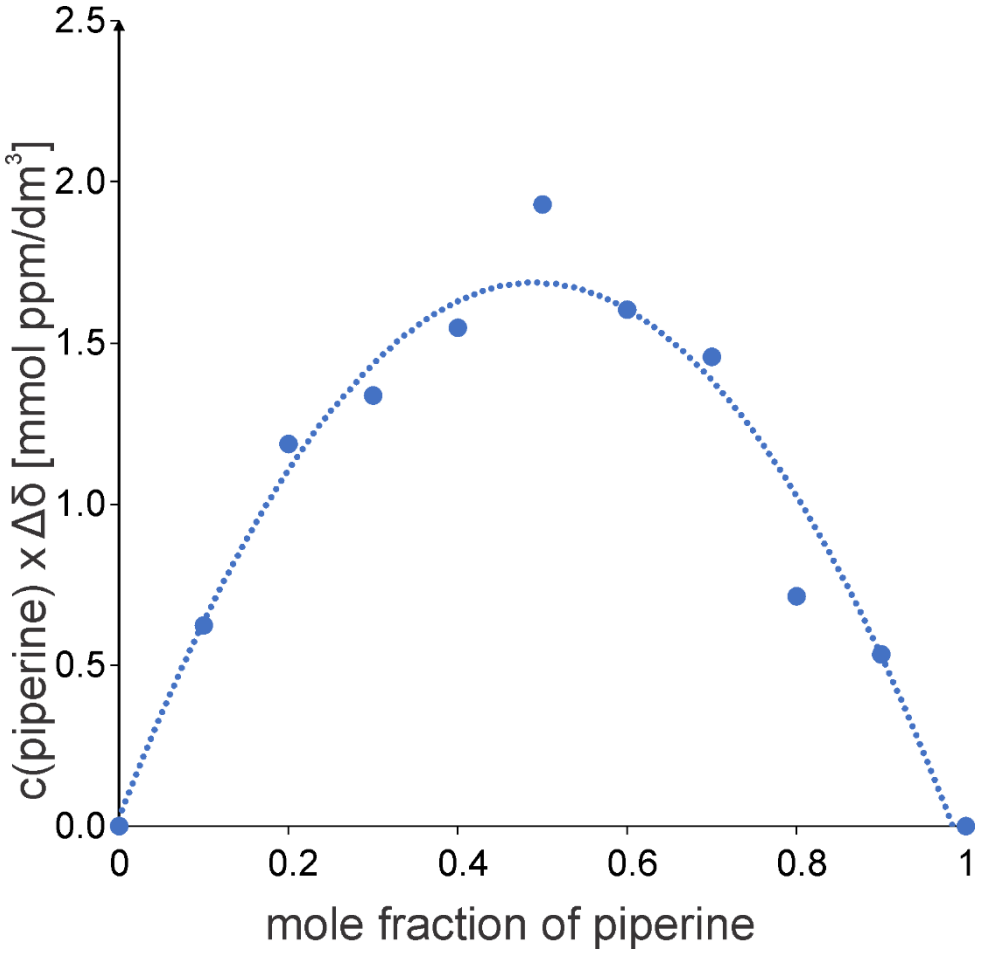

Fig. S1 Job's Plot of curcumin (**1**) and piperine (**2**) determined by chemical shift changes of the signal from protons in position 3 of piperine (**2**), recorded in methanol-d_4.

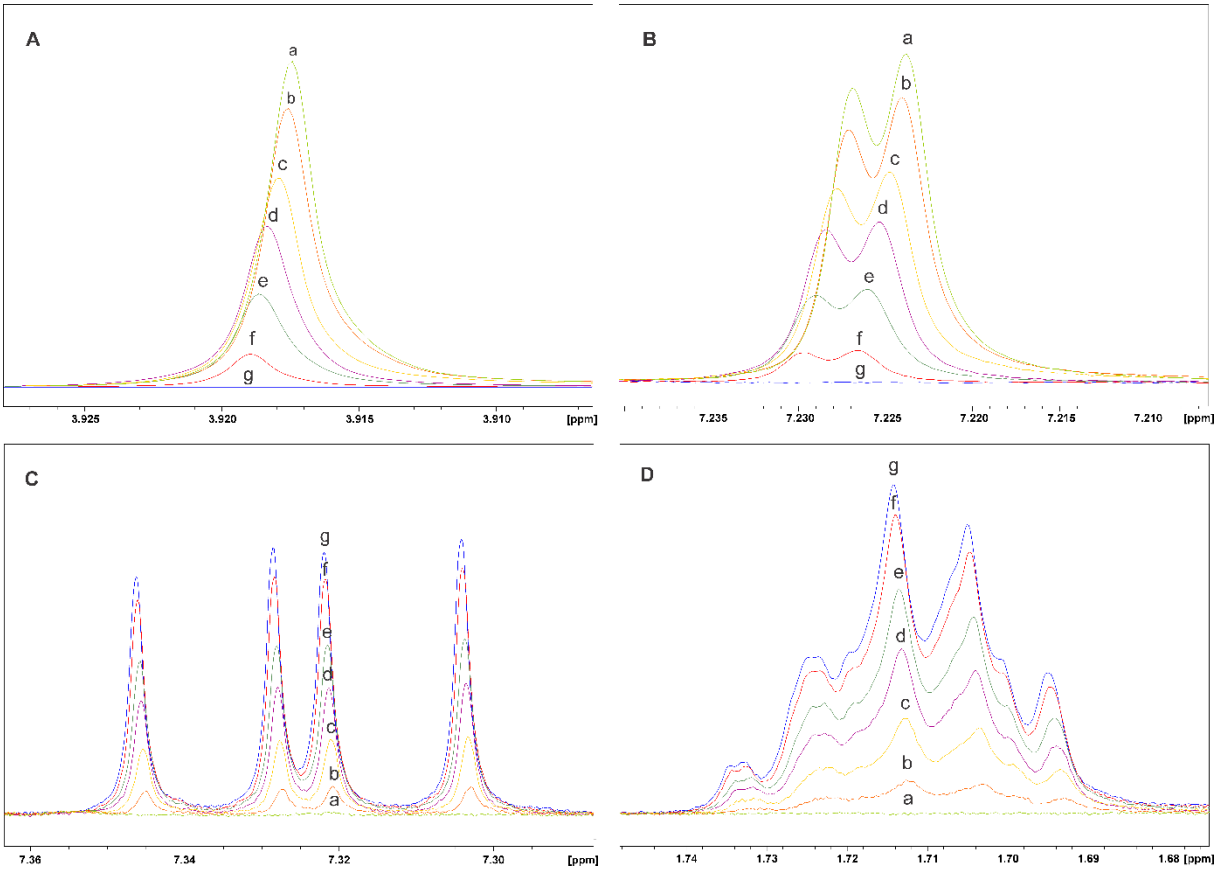

Fig. S2 ^{1}H NMR signals of protons in the two methoxy groups of curcumin (**1**) (A), position 9 and 15 of curcumin (**1**) (B), position 3 of piperine (**2**) (C) and position 3' of piperine (**2**) (D) from representative spectra of the Job's Plot in methanol-d_4. Molar ratio of (**1**)/(**2**): a: 10/0; b 9/1; c: 7/3; d: 5/5; e: 3/7; f: 1/9; g: 0/10.

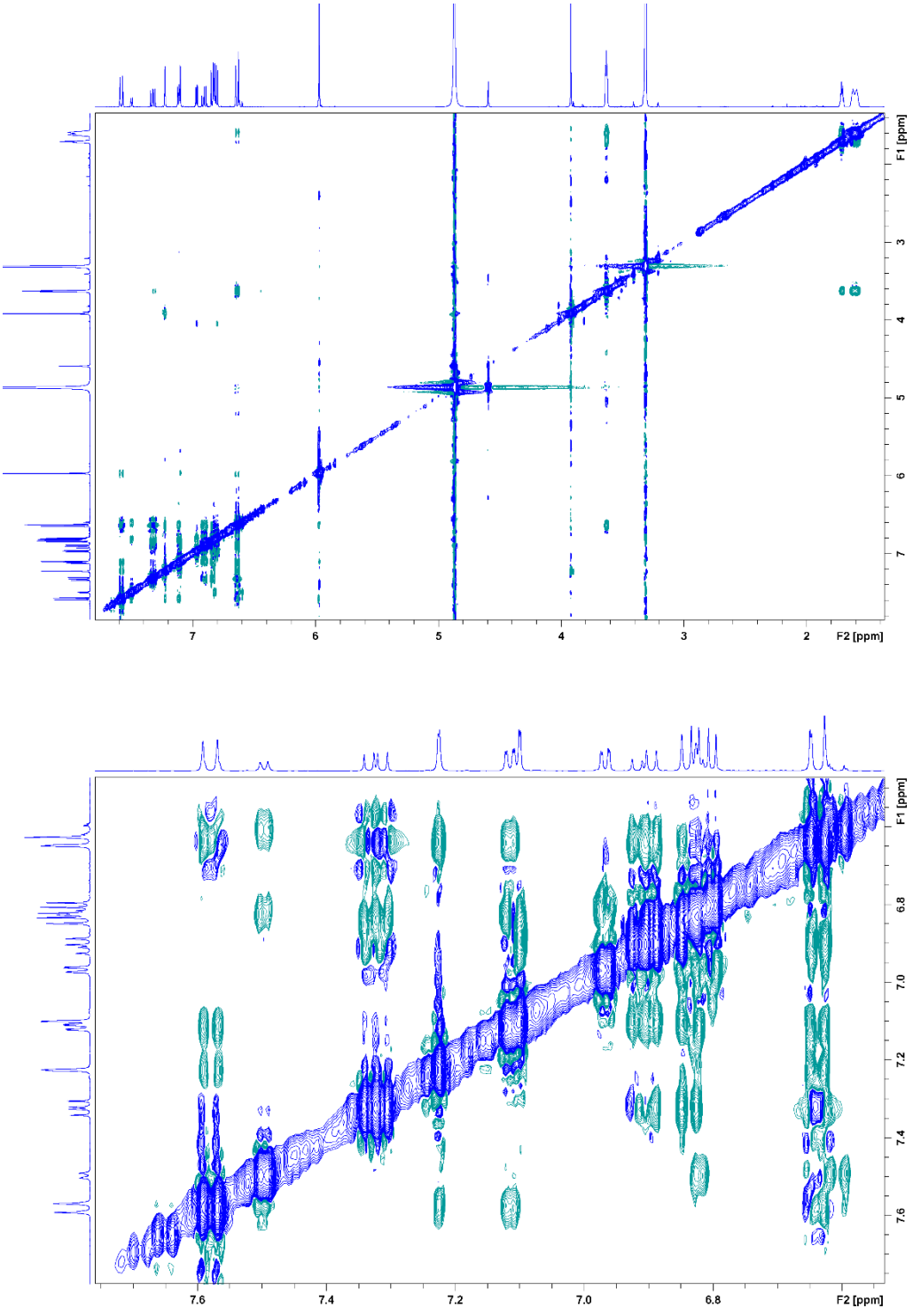

Fig. S3 NOESY spectrum of 1:1 mixture of curcumin (**1**) and piperine (**2**) in methanol-d_4 measured at 700 MHz and at 300 K.

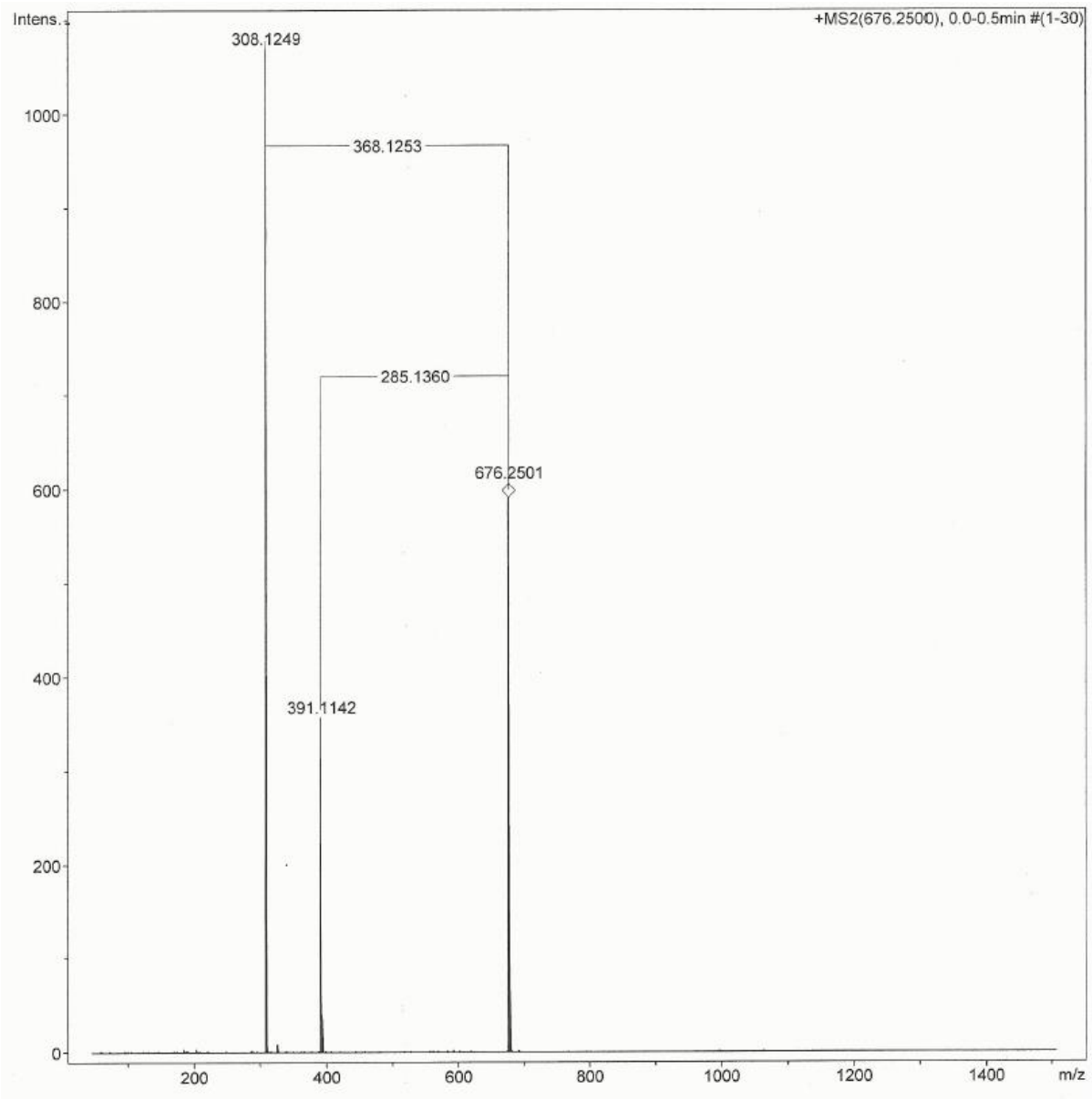

Fig. S4 Unmodified MS-MS spectrum of Fig. 4.

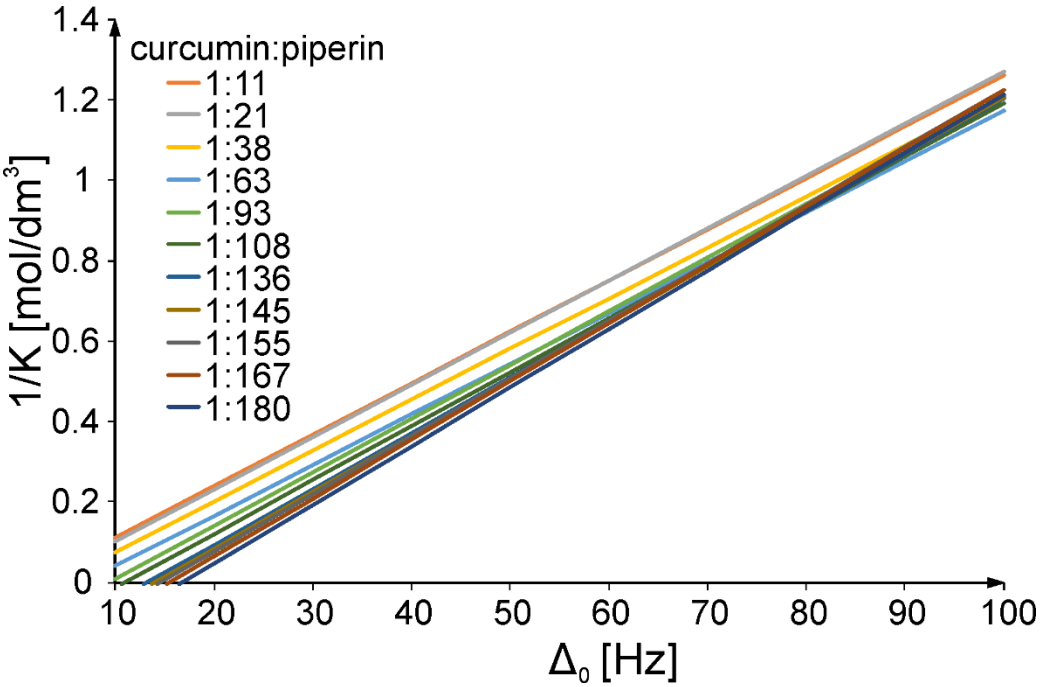

Fig. S5 Rose-Drago Plot to determine the binding constant K of the curcumin-piperine complex in methanol-d_4 – evaluated for the two methoxy-groups of curcumin (**1**). 1/K can be determined at the meeting point of all lines, Δ_0 represents the shift difference between bound and free host molecules. As this is unknown it is varied arbitrarily.

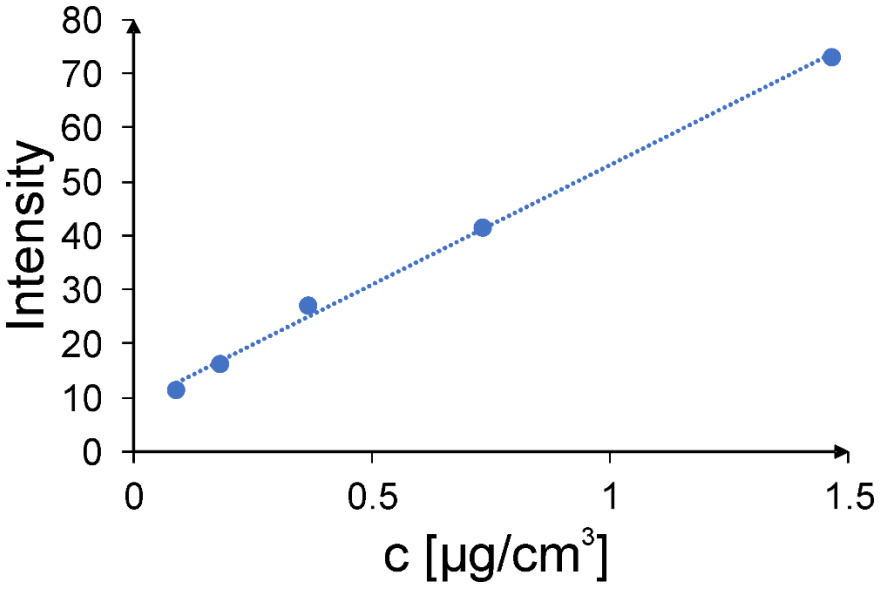

Fig. S6 Calibration curve for curcumin (**1**) concentration in DMSO/water 1:1. Best fit linear equation parameters: y = 44.305x + 8.66. Determination coefficient r^2 = 0.9972.