Electronic Supplementary Information

A novel drug-drug cocrystal of Carbamazepine with *para*-Aminosalicylic acid: Screening, crystal structure and comparative study of Carbamazepine cocrystals formation thermodynamics

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Table of Contents

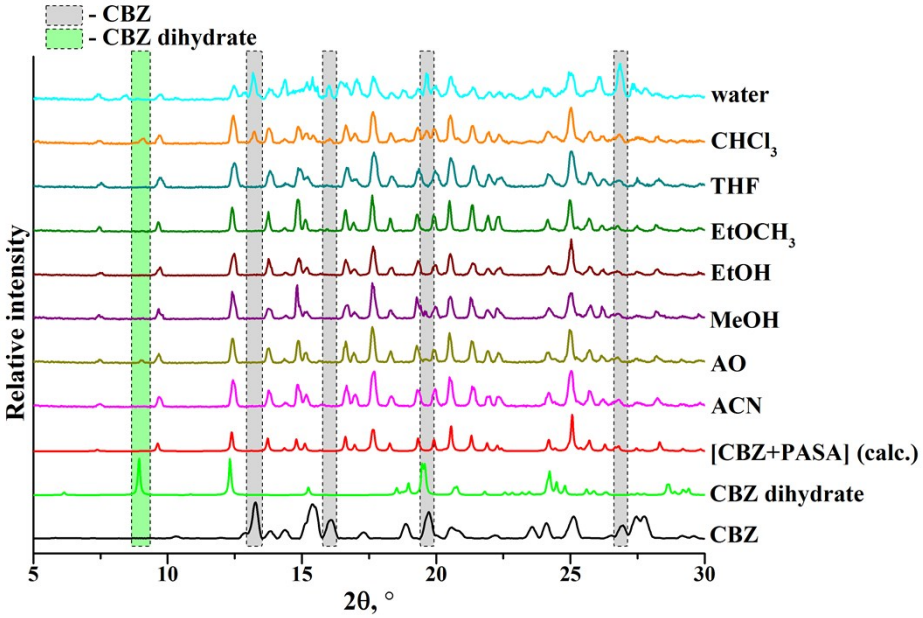


Figure S1. Experimental XRPD patterns of CBZ and PASA mixtures in a 1:1 molar ratio obtained by slurrying.

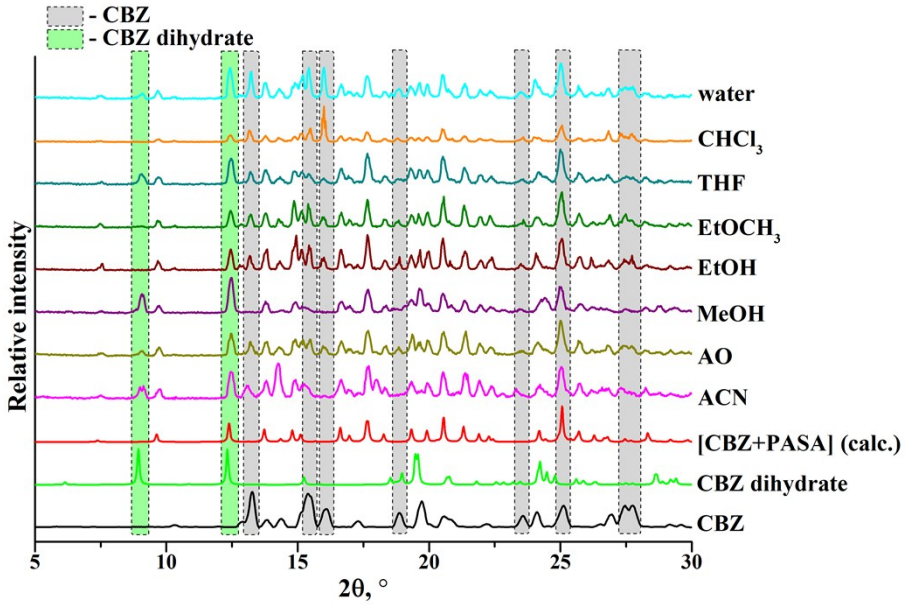


Figure S2. Experimental XRPD patterns of CBZ and PASA mixtures in a 2:1 molar ratio obtained by slurrying.

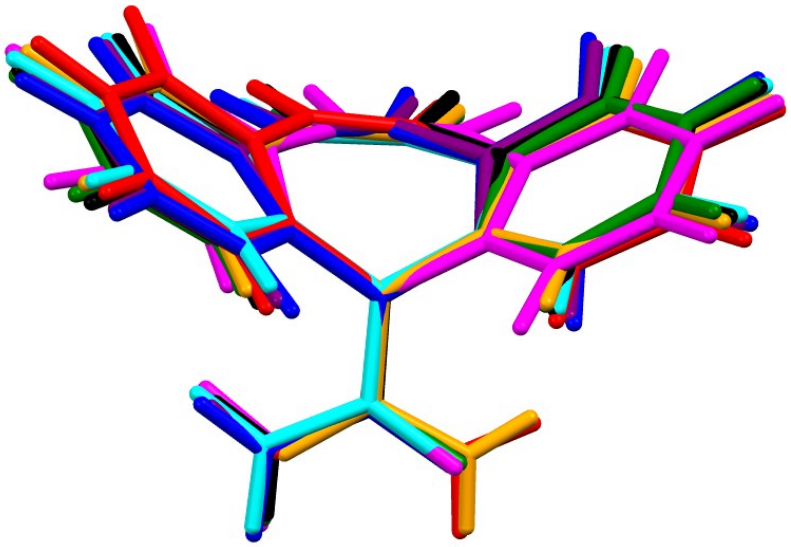


Figure S3. Overlay of carbamazepine conformations for form III.

CSD refcode	Colour	Ref.
CBMZPN01	black	[1]
CBMZPN02	red	[2]
CBMZPN10	orange	[3]
CBMZPN14	green	[4]
CBMZPN18	cyan	[5]
CBMZPN21	blue	[6]
CBMZPN22	purple	
CBMZPN23	magenta	

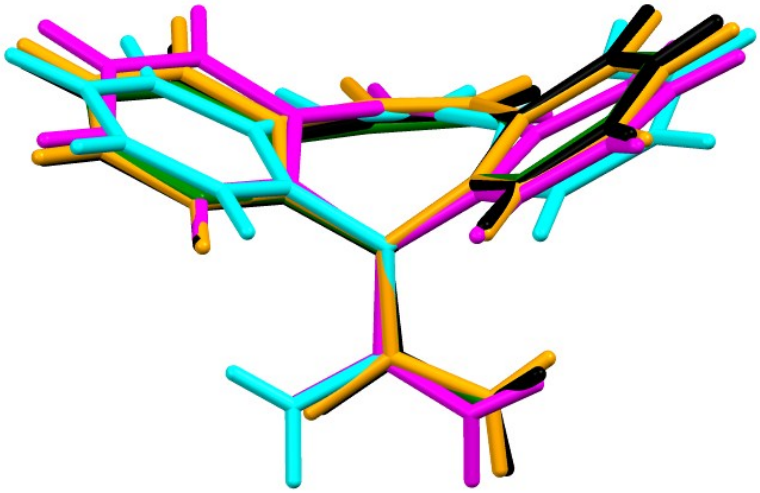
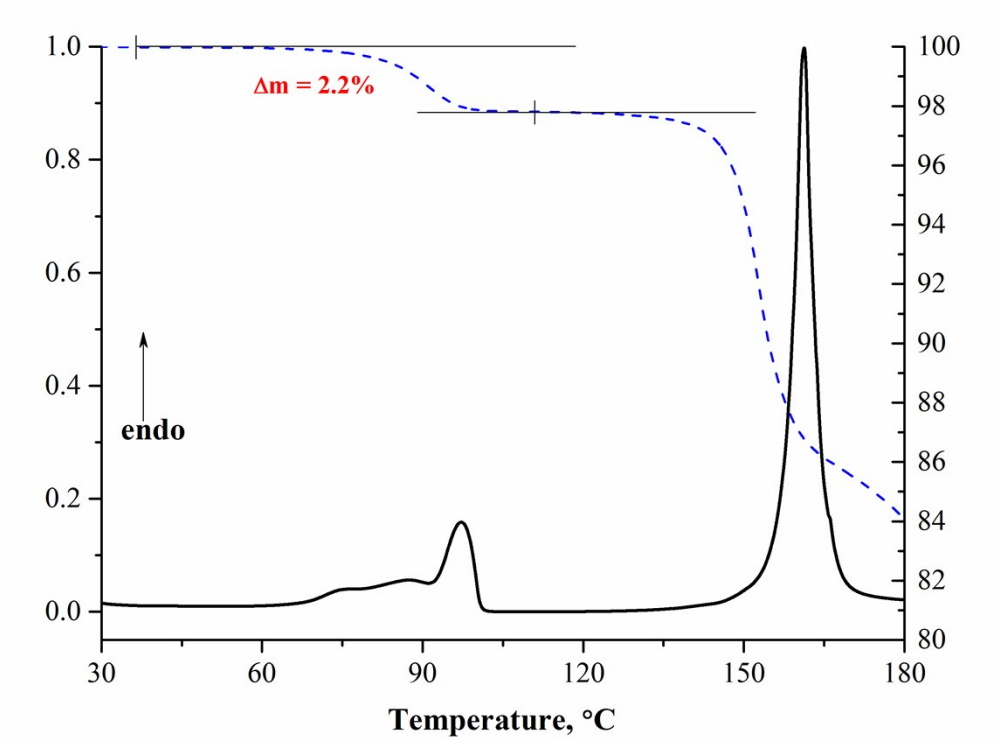
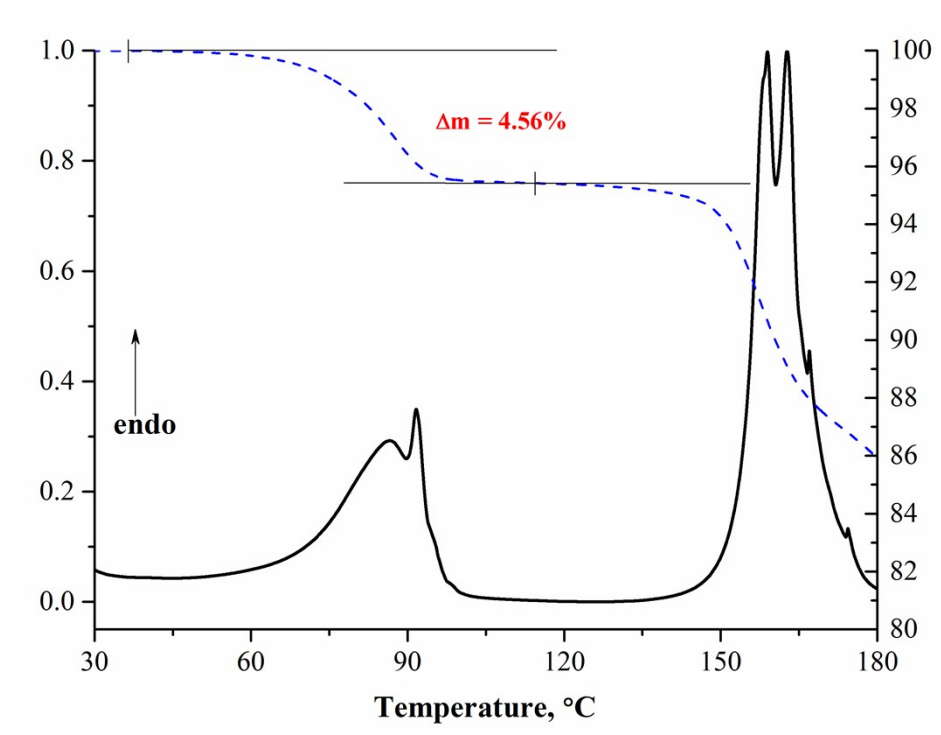


Figure S4. Overlay of carbamazepine conformations in the known polymorph crystal forms.

CSD refcode	Colour	Polymorph	Ref.
CBMZPN11	black	I	[7]
CBMZPN03	green	II	[8]
CBMZPN10	orange	III	[3]
CBMZPN12	cyan	IV	[9]
CBMZPN16	magenta	V	[10]



a



b

Figure S5. DSC thermograms and TG analysis of [CBZ+PASA+H_2O] (2:1:1) (a), and [CBZ+PASA+MeOH] (2:1:1) (b)

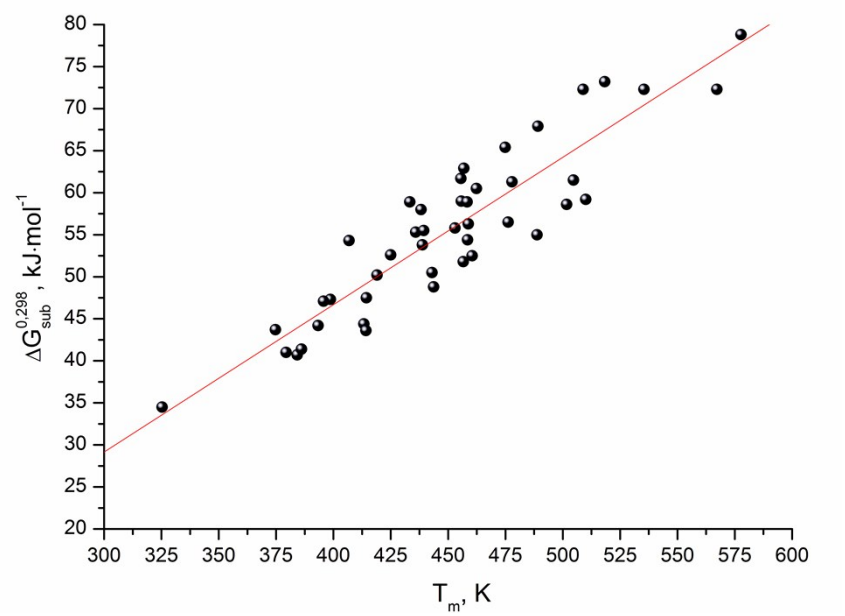


Figure S6. Dependence of experimental sublimation Gibbs energies ($\Delta G_{sub}^{0,298}$) versus melting points (T_m) for the structurally similar compounds with PASA.

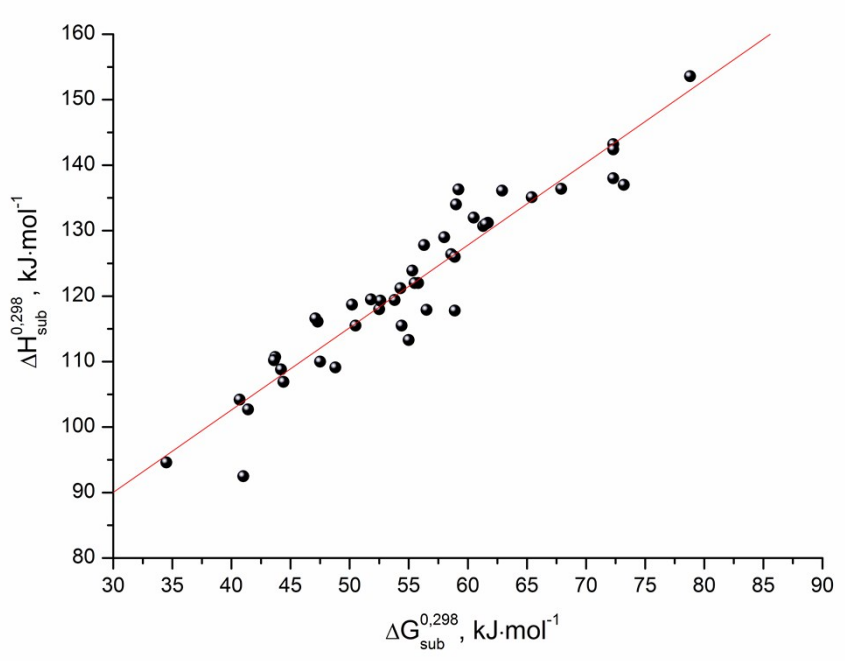


Figure S7. Dependence of experimental sublimation enthalpies ($\Delta H_{sub}^{0,298}$) versus Gibbs energies ($\Delta G_{sub}^{0,298}$) for the structurally similar compounds with PASA

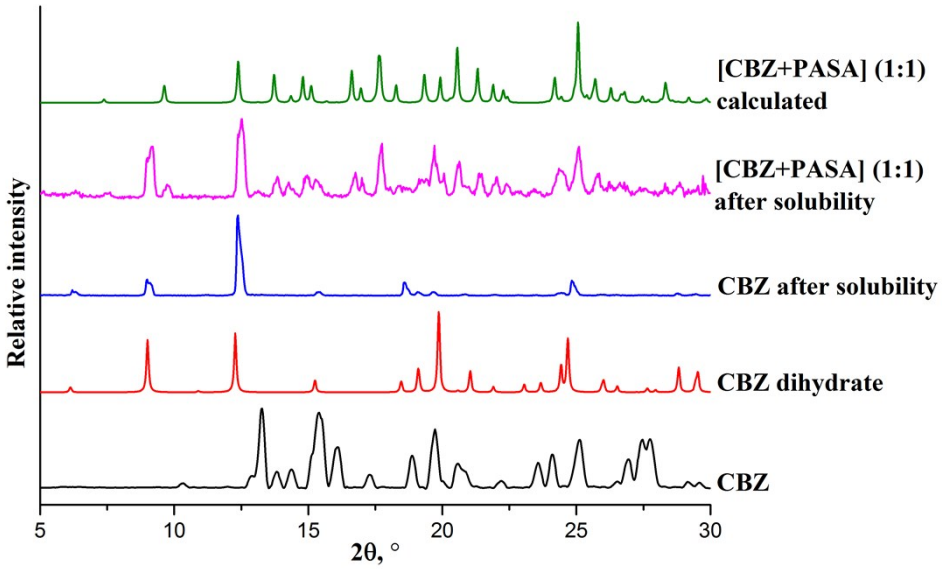


Figure S8. Comparison of the XRPD patterns of the product obtained from dissolution experiments in buffer pH 7.4 using [CBZ+PASA] cocrystal with XRPD patterns of pure CBZ, dihydrate CBZ form and simulated XRPD pattern of [CBZ+PASA] cocrystal.

Table S1. Geometry of intermolecular interactions in the crystal structure of CBZ cocrystals

D–H…A[a]	d(H…A)/Å	d(D…A)/Å	D–H…A/°	Symmetry code
Carbamazepine/*para*-Aminosalicylic Acid 1:1 Cocrystal, (1)				
N11-H12…O1	2.006(18)	2.8970(13)	164.9(16)	x, y, z
O2-H2…O11	1.60(2)	2.5481(11)	167.4(18)	x, y, z
O3-H3…O1	1.698(18)	2.5740(11)	152.0(16)	x, y, z
N1-H1…O3	2.221(18)	3.0600(14)	163.4(15)	1.5-x, -1/2+y, 1.5-z
Carbamazepine/*para*-Aminosalicylic Acid 2:1 Cocrystal Hydrate, (2)				
O5-H51…O11	1.91(2)	2.7991(12)	170.1(16)	-1/2+x, 1.5-y,-1/2+z
O5-H52…O21	1.783(18)	2.6583(12)	165.0(16)	1/2-x, 1/2+y, 1/2-z
N1-H10…O11	2.157(18)	3.0542(15)	170.8(15)	1.5-x, -1/2+y, 1.5-z
N11-H12…O21	2.019(17)	2.9022(14)	174.4(14)	1-x, 1-y, 1-z
N21-H22…O1	2.046(17)	2.9252(13)	167.5(15)	1/2-x, 1/2+y, 1/2-z
O2-H2…O5	1.66(2)	2.5699(12)	174(2)	x, y, z
O3-H3…O1	1.77(2)	2.6113(13)	151.3(17)	x, y, z
Carbamazepine/*para*-Aminosalicylic acid 2:1 Cocrystal Solvate, (3)				
O2-H2…O4	1.66(2)	2.5982(16)	176.7(19)	x, -1+y, z
O3-H3…O1	1.71(2)	2.5673(16)	153.9(19)	x, y, z
N1-H1…O11	2.17(2)	2.9849(19)	156.0(16)	x, y, z
N1-H10…O3	2.430(19)	3.2692(19)	165.7(15)	x, -1+y, z
N11-H11…O2	2.583	3.187	126.51	1+x, y, z
N11-H12…O21	2.077(19)	2.9843(17)	175.2(15)	x, -1+y, z
N21-H22…O1	2.07(2)	2.9408(17)	174.7(17)	x, -1+y, z
O4-H41…O21	1.78(2)	2.6434(16)	161(2)	1+x, y, z

Table S2. Values of selected torsion and dihedral angles for the CBZ molecule in all polymorphic forms and cocrystals (a search of the CSD: v 5.36, May 2015 update).

API	CF	Stoich.	CSD refcode	Ref.	Torsion angle, τ	Dihedral angle, β
Polymorphs						
CBZ I			CBMZPN11	[7]	161.52 -163.66 168.15 163.66	124.98 125.83 124.42 124.81
CBZ II			CBMZPN03	[8]	-166.60	124.77
CBZ III			CBMZPN10	[3]	178.04	126.62
CBZ IV			CBMZPN12	[9]	173.15	130.23
CBZ V			CBMZPN16	[10]	-173.89	125.91
Cocrystals						
CBZ	Indomethacin	1:1	LEZKEI	[11]	178.19	126.58
CBZ	Isonicotinamide	1:1	LOFKIB	[12]	177.72	119.57
			LOFKIB01	[13]	174.00	125.63
CBZ	Benzoic Acid	1:1	MOXVAX	[14]	-163.91	130.31
CBZ	Adipic Acid	1:0.5	MOXVEB	[14]	-176.95 176.95	127.45 129.98
CBZ	4-OH-Benzoic Acid	1:1	MOXVIF	[14]	170.50	126.88
			MOXVIF01	[14]	170.08	126.44
CBZ	Glutaric Acid	1:1	MOXVOL	[14]	-173.23	129.74
CBZ	Malonic Acid	1:1	MOXVUR	[14]	172.97	129.14
CBZ	Salicylic Acid	1:1	MOXWAY	[14]	-169.97	126.52
CBZ	L-1-Hydroxy-2-naphthoic acid	1:1	MOXWEC	[14]	172.88	127.71
CBZ	DL-Tartaric Acid	1:1	MOXWIG	[14]	173.96	127.57

CBZ	Maleic Acid	1:1	MOXWOM	[14]	170.85	130.42
CBZ	(+)-Camphoric acid	1:1	MOXXAZ	[14]	169.88 -174.65	127.65 130.75
CBZ	Aspirin	1:1	TAZRAO	[15]	173.84	126.16
CBZ	Saccharin	1:1	UNEZAO	[16]	-166.48	131.71
			UNEZAO01	[17]	173.49	127.99
CBZ	Nicotinamide	1:1	UNEZES	[16]	166.75	126.50
CBZ	Adamantane-1,3,5,7-tetracarboxylic Acid	1:0.5	UNIBIC	[16]	-161.18	125.06
CBZ	Quinoxaline-N,N'-dioxide	1:1	VIGGOI	[18]	-174.59	127.89
CBZ	Fumaric Acid	2:1	WEYFEN	[19]	-176.16	122.97
CBZ	4,4'-Bipyridine	2:1	XAQQUC	[20]	173.45 -176.77	123.58 133.58
CBZ	4-NH_2-Benzoic Acid	2:1	XAQRAJ	[20]	175.34 -169.83	127.08 122.27
CBZ	2,6-Pyridinedicarboxylic Acid	1:1	XAQRIR	[20]	176.50	126.18
CBZ	Malonic Acid	1:0.5	XOBCEX	[21]	-177.52	122.26
CBZ	Succinic Acid	1:0.5	XOBCIB	[21]	-173.45	123.82
CBZ	4-NH_2-Benzoic Acid	1:1	XOXHEY	[22]	163.61	125.42
CBZ	Pterostilbene	1:1	YABHIU	[23]	-169.60	128.79
CBZ	4-NH_2-Benzoic Acid	1:0.25		[24]	-168.63	130.57
CBZ	4- NH_2-Salicylic Acid	1:1		[tw]	174.92	125.99
Cocrystal solvates/hydrates						
CBZ	5-Nitroisophthalic acid (methanol solvate)	1:1:0.5	UNIBEY	[16]	-165.52	134.16
CBZ	4-NH_2-Benzoic	2:1:1	XAQREN	[20]	-172.72	118.00

	Acid (H2O)				-173.79	125.43
CBZ	4-NH_2-Salicylic Acid (H2O)	2:1:1		[tw]	-173.41 176.19	117.83 123.83
CBZ	4-NH_2-Salicylic Acid (methanol solvate)	2:1:1		[tw]	-166.20 179.12	125.53 123.72

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