Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting information

Insightful vibrational imaging study on the hydration mechanism of carbamazepine

Sara Fateixa*[a], Helena I. S. Nogueira[a], José A. Paixão[b], Rui Fausto[c], Tito Trindade*[a]

[a]*Department of Chemistry and CICECO-Aveiro Institute of Materials, University of Aveiro, 3810-193 Aveiro, Portugal*

[b]*CFisUC, Department of Physics, University of Coimbra, P-3004-516 Coimbra, Portugal*

[c]*CQC-IMS, Department of Chemistry, University of Coimbra, P-3004-535 Coimbra, Portugal*

** sarafateixa@ua.pt; tito@ua.pt*

Table S1: Experimental Raman data and respective band assignments of CBZ III and CBZ DH.[1,2]

CBZ III	CBZ DH	Assignments
1624	1626	ν(C=C) non-aromatic
1601	1501	δ(N-H)
1590	----	ν(C=C) aromatic
1566	1568	ν(C=C) aromatic
1490	1495	νsym(C=C), aromatic/ν(N-H)
1413	1407	ν(C=C)/δ(CH)
1309	1309	δ(CH) non-aromatic, in-plane
----	1259	ν(C=C)
1250	-----	ν(N-H)
1222	1220	ν(N-H) amide
1208	1205	ν(C-C) ring
1161	1160	νasym(C-C) ring/(C-N-C)
1120	1117	ρ (NH2)
1042	1044	δ(C-H) aromatic, in-plane
1026	1024	δ(C-H) aromatic, in-plane
988	----	ν(C-N)
950	-----	δ(C-H) aromatic, out-plane
875	891	νsym(C-N-C) ring
803	808	δ(N-H), out of plane
793	791	δ(N-H), out of plane
769	772	δ(N-H), out of plane
724	719	ν(C-N-C)
700	702	δ aromatic, in-plane/C-H wag cis
648	650	δ(O-C-N) ring/δ(C=O)
621	618	δ(O-C-N) ring
583	-----	δ(O-C-N)
546	548	δ aromatic, out-plane
539	---	δ aromatic, out-plane
414	414	Lattice vibration
391	393	Lattice vibration
375	383	Lattice vibration
331	332	Lattice vibration
272	----	Lattice vibration
253	259	Lattice vibration
181	----	Lattice vibration
170	171	Torsion
----	142	Lattice vibration
138	136	Lattice vibration
120	---	Lattice vibration
----	110	Lattice vibration
104	----	Lattice vibration
89	----	Lattice vibration
74	76	Lattice vibration

Table S2: Experimental infrared data and respective band assignment of CBZ III and CBZ DH.[3–6]

CBZ III	CBZ DH	Assignments
3463	3427	$\nu(NH_2)$
-----	3371	$\nu(NH_2)$
3279	3328	ν(O-H)
3155	3180	ν(C-N-C) ring
1670	1678	ν_{sym}(C=O)
1597	1592	$\delta(NH_2)$
1488	1492	ν_{sym}(C=C) ring
-----	1404	δ(OH) crystalline water
1376	-----	δ(CH)
1307	1313	ν_{sym}(C-N)
1039	1042	δ(N-H)

Table S3: Table S3: Percentage of CBZ III and CBZ DH in two tablet samples in function of time kept at 89% RH, as estimated by IR and Raman imaging.

	Sample I_MCR analysis		Sample II_ CRM	
Time (h)	**% of CBZ III**	**% of CBZ DH**	**% of CBZ III**	**% of CBZ DH**
24	>99	<1	100	0
48	95	5	>99	<1
72	58	42	91	9
96	44	56	2	98
120	23	77	0	100

Table S4: Estimated percentages of CBZ III and CBZ DH in tablets, by using the Raman maps, in comparison to the nominal amounts used in their preparation: 50%, 10% and 1% in CBZ DH.

CBZ DH Nominal amount	CBZ III (CRM)	CBZ DH (CRM)
50%	59%	41%
10%	94%	6%
1%	99%	1%

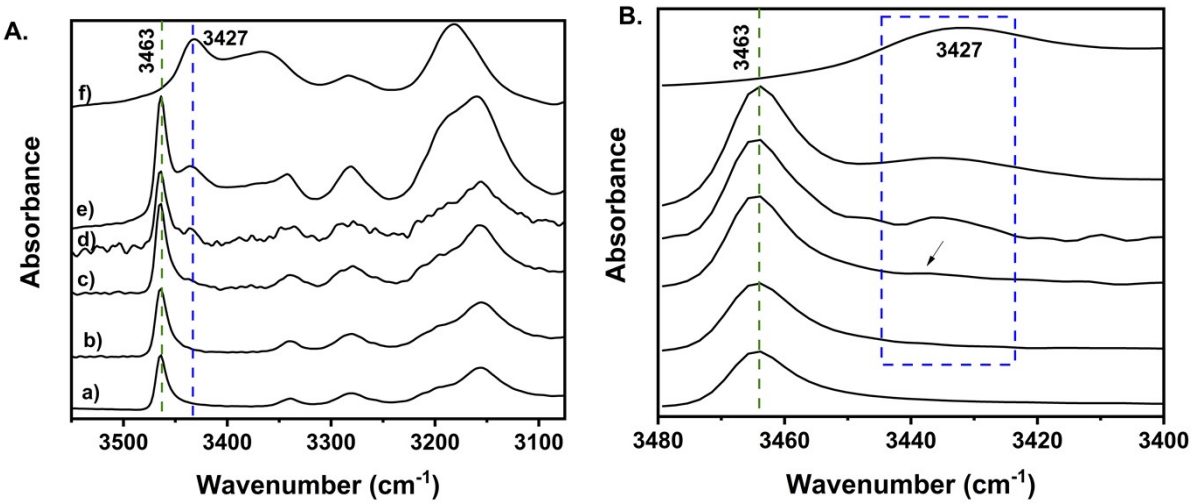

Figure S1: A) FTIR spectra of CBZ III tablet (a), CBZ III tablets with variable amount of CBZ DH: 0.5% (b), 1% (c), 10% (d) and 50% (e); CBZ DH (f). B) Magnification of the region 3480-3400 cm^{-1}.

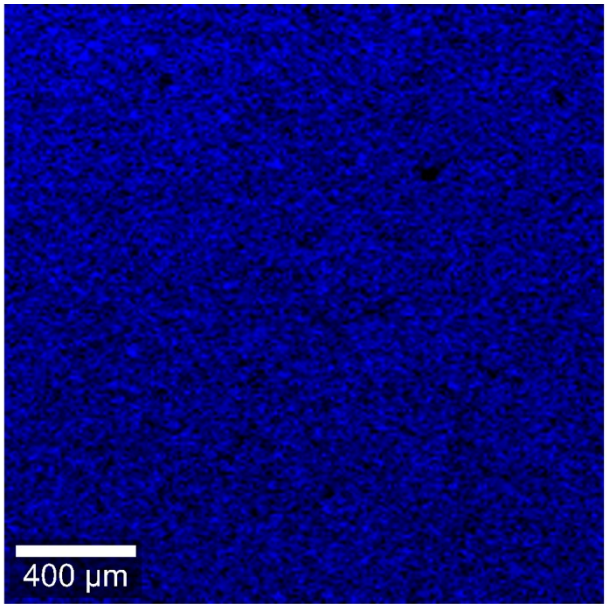

Figure S2: Combined Raman images of CBZ III tablet after 9 months exposed to RH 6% at room temperature.

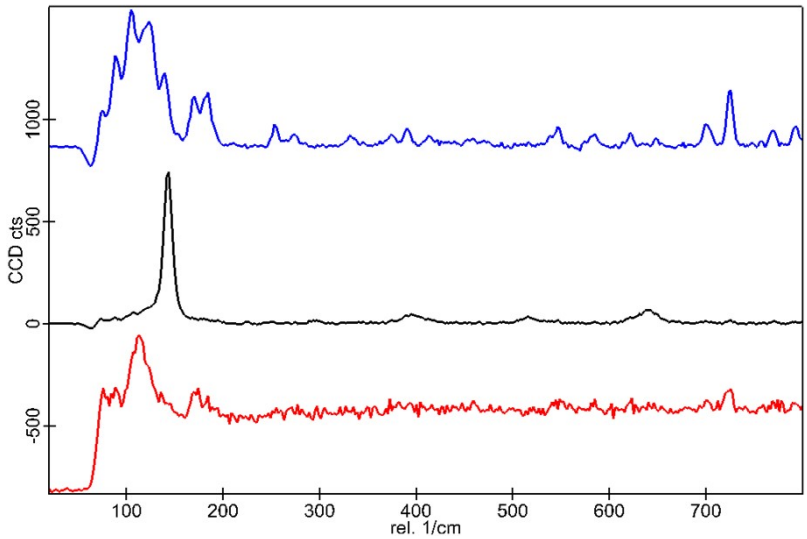

Figure S3: Average Raman spectra (range 20-800 cm^{-1}) of distinct regions mapped in the tablets (blue: CBZ III; black: TiO_2; red: CBZ DH).

References

1 L. E. O'Brien, P. Timmins, A. C. Williams and P. York, Use of in situ FT-Raman spectroscopy to study the kinetics of the transformation of carbamazepine polymorphs, *J. Pharm. Biomed. Anal.*, 2004, **36**, 335–340.

2 R. Prasad, K. Panwar, J. Katla and S. V. Dalvi, Polymorphism and Particle Formation Pathway of Carbamazepine during Sonoprecipitation from Ionic Liquid Solutions, *Cryst. Growth Des.*, 2020, **20**, 5169–5183.

3 C. J. Strachan, S. L. Howell, T. Rades and K. C. Gordon, A theoretical and spectroscopic study of carbamazepine polymorphs, *J. Raman Spectrosc.*, 2004, **35**, 401–408.

4 S. F. Barakh Ali, Z. Rahman, S. Dharani, H. Afrooz and M. A. Khan, Chemometric Models for Quantification of Carbamazepine Anhydrous and Dihydrate Forms in the Formulation, *J. Pharm. Sci.*, 2019, **108**, 1211–1219.

5 M. Krstić, M. Popović, V. Dobričić and S. Ibrić, Influence of Solid Drug Delivery System Formulation on Poorly Water-Soluble Drug Dissolution and Permeability, *Molecules*, 2015, **20**, 14684–14698.

6 Y. Otsuka, A. Ito, S. Matsumura, M. Takeuchi and H. Tanaka, Effect of hydroxypropyl cellulose and hydroxypropyl methylcellulose on carbamazepine polymorphic transformation, , DOI:10.1007/s00396-015-3698-1.