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Supplementary information

Liquid-Liquid Phase Separation and Crystallization of Aspirin Polymorphs from Water-Acetonitrile Mixed Solvent medium through Swift Cooling Process

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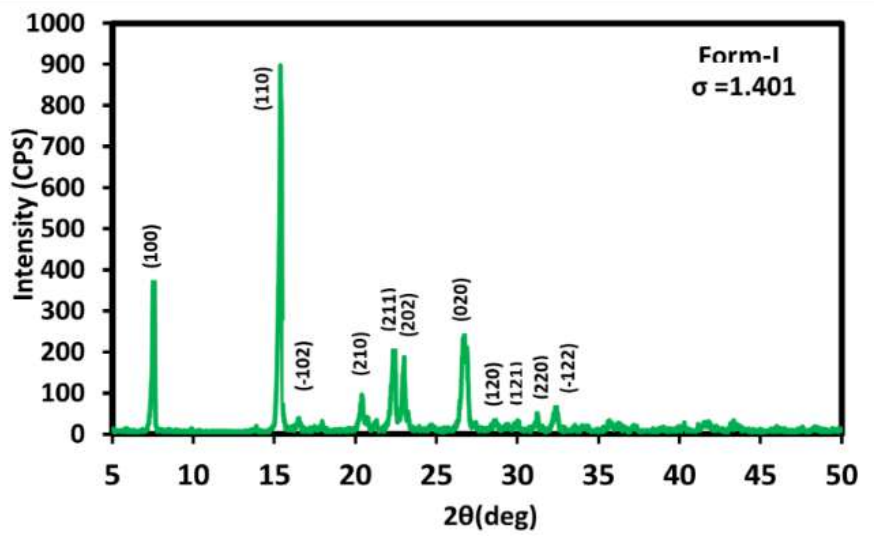

Fig S1. PXRD pattern of the grown aspirin polymorphic Form-I by swift cooling crystallization process from acetonitrile-rich mixing composition (0.24W:0.76A).

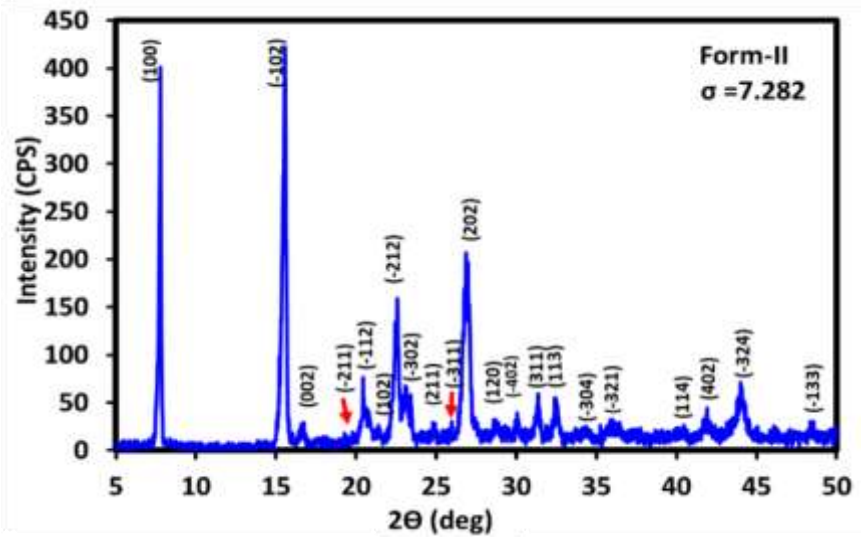

Fig S2. PXRD pattern of the grown aspirin polymorphic Form-II by swift cooling crystallization process from acetonitrile-rich mixing composition (0.24W:0.76A).

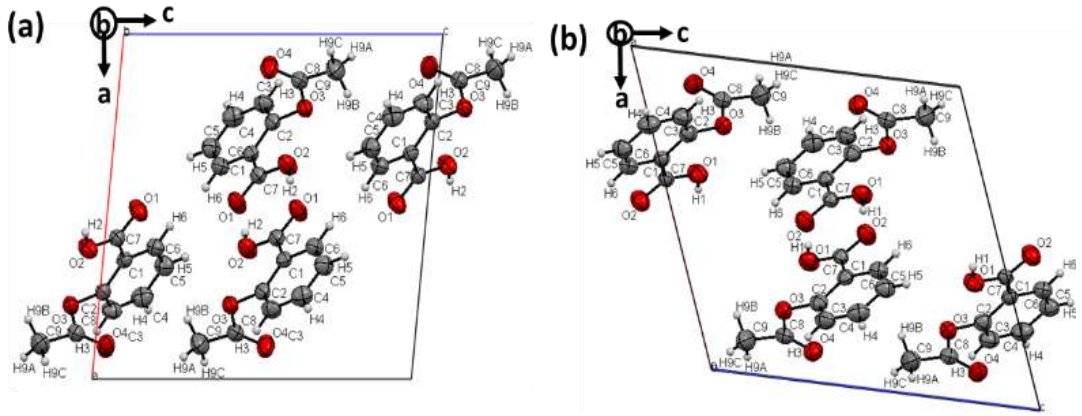

Fig S3. Unit cell packing diagram of aspirin polymorphic forms refined through SCXRD analysis, (a) Form-I, and (b) Form-II.

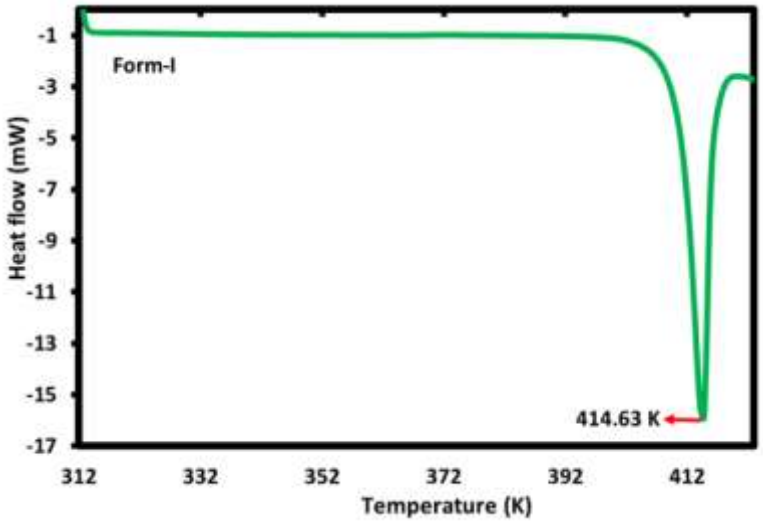

Fig S4. Recorded DSC thermogram of the grown aspirin polymorphic Form-I from acetonitrile-rich (0.24W:0.76A) solvent mixing composition through a swift cooling process.

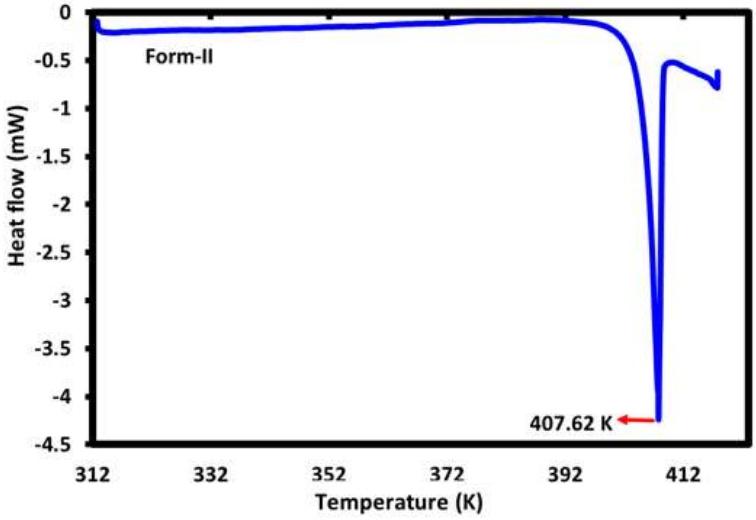

Fig S5. Recorded DSC thermogram of the grown aspirin polymorphic Form-II from water-rich (0.96W:0.04A) solvent mixing composition through a swift cooling process.

Table S1.Lattice parameter values of the grown aspirin polymorphs.

Lattice Parameters	Form-I		Form-II	
	Present work	Literature value	Present work	Literature value
a (Å)	11.441	11.233	12.103	12.095
b (Å)	6.481	6.544	6.408	6.491
c (Å)	11.161	11.231	11.319	11.323
β (°)	95.34	95.89	111.59	111.50
Volume $(Å)^3$	816.38	821.21	824.11	827.18

Table S2. Data collection details and refined crystallographic information of Form-I and Form-II polymorphs of aspirin through SCXRD analysis

Parameters	**Form-I**	**Form-II**
Chemical formula	$C_9H_8O_4$	$C_9H_8O_4$
Formula weight	180.15 g/mol	180.15 g/mol
Temperature	296(2) K	296(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal habit	Clear intense white prismatic	Clear intense white platy
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$
Unit cell dimensions	a=11.429(4) Å, α= 90°	a=12.2633(15) Å, α=90°
	b=6.597(2) Å, β= 95.750(9)°	b=6.5624(8)Å, β=111.627(3)°
	c=11.395(4) Å, γ= 90°	c=11.4726(14)Å, γ=90°
Volume	854.8(5) $Å^3$	858.2(18) $Å^3$
Z	4	4
Reflection Collected/Unique	45382/1946 [R(int) = 0.1422]	51801/1915 [R(int) = 0.1492]
Density	1.400 g/cm^3	1.394 g/cm^3
Absorption Coefficient	0.112 mm^{-1}	0.111 mm^{-1}
F(000)	376	376
Theta range for data collection	3.57 to 27.44°	3.57 to 27.25°
Completeness of data	99.3%	99.8%
Refinement Method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
Goodness-of-fit of F2	1.037	1.012
Data/restraints/parameters	1946 / 0 / 120	1915 / 0 / 120
Final R indices	R1 = 0.0524, wR2 = 0.1074	R1 = 0.0748, wR2 = 0.1681
R indices (all data)	R1 = 0.1119, wR2 = 0.1246	R1 = 0.1545, wR2 = 0.2056
Largest diff. Peak and hole	0.170 and -0.194e$Å^{-3}$	0. 1514 and -0.238 e$Å^{-3}$
Reference Number	2164673	2161484

Form-I (CCDC No:2164673)

Table S3. Atomic coordinates and equivalent isotropic atomic displacement parameters ($Å^2$)

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O3	0.21473(12)	0.5887(2)	0.58794(11)	0.0410(4)
O1	0.37983(13)	0.8598(2)	0.55085(14)	0.0513(5)
O2	0.48955(14)	0.8120(2)	0.40343(13)	0.0528(5)
O4	0.09651(15)	0.7795(3)	0.46551(13)	0.0614(5)
C7	0.40975(17)	0.7571(3)	0.46213(16)	0.0355(5)
C1	0.34702(17)	0.5643(3)	0.43238(17)	0.0349(5)
C2	0.25423(18)	0.4878(3)	0.49045(16)	0.0369(5)
C8	0.13424(19)	0.7383(3)	0.56368(18)	0.0411(5)
C6	0.38307(18)	0.4499(3)	0.34026(18)	0.0414(5)
C3	0.20213(19)	0.3060(3)	0.4584(2)	0.0473(6)
C5	0.3300(2)	0.2688(3)	0.3068(2)	0.0486(6)
C4	0.2402(2)	0.1977(4)	0.3665(2)	0.0507(6)
C9	0.1029(2)	0.8366(4)	0.6731(2)	0.0603(7)

Table S4. Bond lengths (Å)

O3-C8	1.359(3)	O3-C2	1.408(2)
O1-C7	1.292(2)	O1-H1	0.82
O2-C7	1.238(2)	O4-C8	1.189(2)
C7-C1	1.483(3)	C1-C6	1.388(3)
C1-C2	1.399(3)	C2-C3	1.372(3)
C8-C9	1.480(3)	C6-C5	1.377(3)

C6-H6	0.93	C3-C4	1.374(3)
C3-H3	0.93	C5-C4	1.369(3)
C5-H5	0.93	C4-H4	0.93
C9-H9A	0.96	C9-H9B	0.96
C9-H9C	0.96		

Table S5. Bond angles (°)

C8-O3-C2	116.55(15)	C7-O1-H1	109.5
O2-C7-O1	122.44(19)	O2-C7-C1	119.55(18)
O1-C7-C1	118.00(17)	C6-C1-C2	117.27(19)
C6-C1-C7	117.75(17)	C2-C1-C7	124.98(18)
C3-C2-C1	121.23(19)	C3-C2-O3	117.27(18)
C1-C2-O3	121.41(18)	O4-C8-O3	122.11(19)
O4-C8-C9	126.6(2)	O3-C8-C9	111.27(18)
C5-C6-C1	121.66(19)	C5-C6-H6	119.2
C1-C6-H6	119.2	C2-C3-C4	119.7(2)
C2-C3-H3	120.2	C4-C3-H3	120.2
C4-C5-C6	119.4(2)	C4-C5-H5	120.3
C6-C5-H5	120.3	C5-C4-C3	120.7(2)
C5-C4-H4	119.6	C3-C4-H4	119.6
C8-C9-H9A	109.5	C8-C9-H9B	109.5
H9A-C9-H9B	109.5	C8-C9-H9C	109.5
H9A-C9-H9C	109.5	H9B-C9-H9C	109.5

Table S6. Torsion angles (°)

O2-C7-C1-C6	1.5(3)	O1-C7-C1-C6	-177.19(19)
O2-C7-C1-C2	-178.78(19)	O1-C7-C1-C2	2.5(3)
C6-C1-C2-C3	0.8(3)	C7-C1-C2-C3	-178.96(19)
C6-C1-C2-O3	177.37(17)	C7-C1-C2-O3	-2.4(3)
C8-O3-C2-C3	-97.9(2)	C8-O3-C2-C1	85.4(2)
C2-O3-C8-O4	1.8(3)	C2-O3-C8-C9	-178.11(18)
C2-C1-C6-C5	0.1(3)	C7-C1-C6-C5	179.85(19)
C1-C2-C3-C4	-1.0(3)	O3-C2-C3-C4	-177.7(2)
C1-C6-C5-C4	-0.8(3)	C6-C5-C4-C3	0.6(4)
C2-C3-C4-C5	0.3(3)		

Table S7. Anisotropic atomic displacement parameters (Å^2)

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O3	0.0447(9)	0.0479(9)	0.0310(8)	0.0054(7)	0.0075(6)	0.0039(7)
O1	0.0546(10)	0.0505(10)	0.0513(10)	-0.0166(8)	0.0167(8)	-0.0133(8)
O2	0.0597(10)	0.0534(10)	0.0486(9)	-0.0089(8)	0.0221(8)	-0.0174(8)
O4	0.0654(11)	0.0806(13)	0.0379(9)	0.0051(9)	0.0032(8)	0.0268(9)
C7	0.0365(12)	0.0400(12)	0.0304(11)	0.0022(10)	0.0056(9)	0.0028(9)
C1	0.0338(11)	0.0373(11)	0.0336(11)	0.0030(10)	0.0030(9)	0.0026(9)
C2	0.0403(12)	0.0393(12)	0.0311(11)	0.0048(10)	0.0038(9)	0.0038(10)
C8	0.0391(12)	0.0485(13)	0.0367(12)	0.0019(11)	0.0078(10)	-0.0010(11)
C6	0.0382(12)	0.0448(13)	0.0418(12)	0.0003(10)	0.0075(10)	0.0001(10)

C3	0.0440(13)	0.0445(13)	0.0543(14)	0.0076(12)	0.0098(11)	-0.0060(11)
C5	0.0505(14)	0.0454(14)	0.0505(14)	-0.0099(11)	0.0091(11)	0.0013(11)
C4	0.0533(15)	0.0379(13)	0.0601(15)	-0.0035(12)	0.0019(12)	-0.0042(11)
C9	0.0589(15)	0.0774(18)	0.0455(14)	-0.0111(13)	0.0100(12)	0.0093(14)

Table S8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2)

	x/a	**y/b**	**z/c**	**U(eq)**
H1	0.4243	0.9568	0.5630	0.077
H6	0.4446	0.4969	0.3001	0.05
H3	0.1413	0.2563	0.4987	0.057
H5	0.3549	0.1953	0.2442	0.058
H4	0.2047	0.0748	0.3446	0.061
H9A	0.0477	0.9439	0.6532	0.09
H9B	0.1725	0.8914	0.7157	0.09
H9C	0.0683	0.7383	0.7212	0.09

Form-II (CCDC-2161484)

Table S9. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2)

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O3	0.78414(19)	0.5882(4)	0.72717(18)	0.0494(7)
O2	0.6191(2)	0.8595(4)	0.6088(2)	0.0569(7)
O1	0.5101(2)	0.8103(4)	0.4082(2)	0.0593(7)

	x/a	y/b	z/c	U(eq)
O4	0.9040(2)	0.7804(4)	0.6661(2)	0.0618(8)
C7	0.5902(3)	0.7557(5)	0.5058(3)	0.0363(8)
C1	0.6534(3)	0.5644(5)	0.5073(3)	0.0389(8)
C8	0.8650(3)	0.7404(5)	0.7439(3)	0.0448(8)
C2	0.7452(3)	0.4867(5)	0.6110(3)	0.0441(8)
C6	0.6182(3)	0.4494(5)	0.3979(3)	0.0468(9)
C5	0.6714(3)	0.2669(5)	0.3912(3)	0.0518(9)
C3	0.7978(3)	0.3031(6)	0.6048(3)	0.0539(10)
C4	0.7604(3)	0.1984(6)	0.4946(4)	0.0576(10)
C9	0.8958(4)	0.8347(8)	0.8687(3)	0.0741(13)

Table S10. Bond lengths (Å)

O3-C8	1.370(4)	O3-C2	1.407(4)
O2-C7	1.295(4)	O2-H2	0.82
O1-C7	1.240(4)	O4-C8	1.187(4)
C7-C1	1.472(4)	C1-C6	1.390(4)
C1-C2	1.399(4)	C8-C9	1.477(5)
C2-C3	1.381(5)	C6-C5	1.380(5)
C6-H6	0.93	C5-C4	1.359(5)
C5-H5	0.93	C3-C4	1.361(5)
C3-H3	0.93	C4-H4	0.93
C9-H9A	0.96	C9-H9B	0.96
C9-H9C	0.96		

Table S11. Bond angles (°)

C8-O3-C2	116.9(2)	C7-O2-H2	109.5
O1-C7-O2	122.1(3)	O1-C7-C1	119.7(3)
O2-C7-C1	118.2(3)	C6-C1-C2	117.0(3)
C6-C1-C7	117.8(3)	C2-C1-C7	125.2(3)
O4-C8-O3	121.8(3)	O4-C8-C9	127.4(3)
O3-C8-C9	110.7(3)	C3-C2-C1	121.3(3)
C3-C2-O3	117.4(3)	C1-C2-O3	121.2(3)
C5-C6-C1	121.7(3)	C5-C6-H6	119.1
C1-C6-H6	119.1	C4-C5-C6	118.9(3)
C4-C5-H5	120.6	C6-C5-H5	120.6
C4-C3-C2	119.0(3)	C4-C3-H3	120.5
C2-C3-H3	120.5	C5-C4-C3	122.1(4)
C5-C4-H4	119.0	C3-C4-H4	119.0
C8-C9-H9A	109.5	C8-C9-H9B	109.5
H9A-C9-H9B	109.5	C8-C9-H9C	109.5
H9A-C9-H9C	109.5	H9B-C9-H9C	109.5

Table S12. Torsion angles (°)

O1-C7-C1-C6	-1.3(4)	O2-C7-C1-C6	177.1(3)
O1-C7-C1-C2	179.8(3)	O2-C7-C1-C2	-1.7(4)
C2-O3-C8-O4	-2.7(5)	C2-O3-C8-C9	179.0(3)
C6-C1-C2-C3	-0.4(4)	C7-C1-C2-C3	178.5(3)
C6-C1-C2-O3	-177.6(3)	C7-C1-C2-O3	1.3(5)
C8-O3-C2-C3	97.8(3)	C8-O3-C2-C1	-84.9(3)

C2-C1-C6-C5	-0.2(5)	C7-C1-C6-C5	-179.2(3)
C1-C6-C5-C4	0.2(5)	C1-C2-C3-C4	1.1(5)
O3-C2-C3-C4	178.4(3)	C6-C5-C4-C3	0.6(6)
C2-C3-C4-C5	-1.2(6)		

Table S13. Anisotropic atomic displacement parameters ($Å^2$)

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O3	0.0540(14)	0.0602(16)	0.0308(12)	0.0010(11)	0.0121(10)	-0.0029(12)
O2	0.0595(16)	0.0580(17)	0.0471(14)	-0.0113(12)	0.0125(12)	0.0119(12)
O1	0.0666(16)	0.0628(17)	0.0395(14)	-0.0012(12)	0.0089(13)	0.0136(13)
O4	0.0642(16)	0.079(2)	0.0453(14)	-0.0075(13)	0.0238(13)	-0.0165(14)
C7	0.0375(17)	0.0375(19)	0.0316(17)	-0.0004(15)	0.0100(14)	-0.0040(14)
C1	0.0399(17)	0.0416(19)	0.0363(17)	-0.0001(15)	0.0151(14)	-0.0047(15)
C8	0.0403(19)	0.054(2)	0.0366(19)	0.0002(16)	0.0096(15)	0.0017(16)
C2	0.0472(19)	0.045(2)	0.0399(18)	0.0051(16)	0.0155(15)	-0.0042(16)
C6	0.0459(19)	0.051(2)	0.0410(19)	-0.0011(16)	0.0132(15)	-0.0019(17)
C5	0.054(2)	0.049(2)	0.050(2)	-0.0081(18)	0.0171(18)	-0.0037(17)
C3	0.048(2)	0.060(2)	0.050(2)	0.0095(19)	0.0139(17)	0.0056(18)
C4	0.058(2)	0.052(2)	0.065(3)	-0.001(2)	0.024(2)	0.0039(19)
C9	0.068(3)	0.106(4)	0.048(2)	-0.024(2)	0.022(2)	-0.012(2)

Table S14. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2)

	x/a	y/b	z/c	U(eq)
H2	0.5704	0.9492	0.6009	0.085
H6	0.5571	0.4967	0.3273	0.056
H5	0.6469	0.1921	0.3172	0.062
H3	0.8579	0.2518	0.6748	0.065
H4	0.7968	0.0760	0.4900	0.069
H9A	0.9439	0.9524	0.8744	0.111
H9B	0.9379	0.7382	0.9322	0.111
H9C	0.8254	0.8749	0.8808	0.111