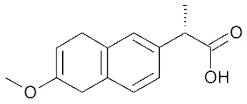
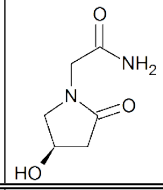
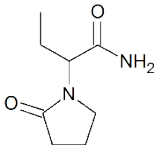
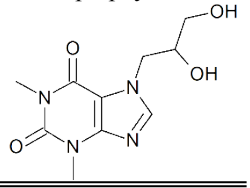
Table 1. Screening of APIs with amino acids (liquid-assisted grinding, ~100 mg of mixture, 10 μL of methanol, 90 min at 30 Hz)

Amino acid	S-Naproxen 	S-oxiracetam 	Levetiracetam 	Diprophylline 
L-asparagine	—	—	—	—
D-asparagine	—	—	—	—
L-cysteine	—	—	—	—
L-glutamine	—	—	—	—
D-glutamine	—	—	—	—
L-histidine	—	—	—	—
D-histidine	—	—	—	—
DL-serine	—	—	—	—
L-serine	—	—	—	—
D-serine	—	—	—	—
D-threonine	—	—	—	—
L-threonine	—	—	—	—
D-tryptophan	+†	—	—	—
L-tryptophan	+	—	—	—
L-tyrosine	—	—	—	—
D-tyrosine	+*	—	—	—
L-proline	known	—	—	—
D-proline	known	—	—	—
L-valine	—	—	—	—
D-valine	—	—	—	—
L-alanine	+*	—	—	—
D-alanine	+*	—	—	—
L-leucine	—	—	—	—
D-leucine	—	—	—	—
L-phenyalanine	—	—	—	—
D-phenylalanine	—	—	—	—
L-isoleucine	—	—	—	—
DL-isoleucine	—	—	—	—
L-methionine	—	—	—	—
D-methionine	—	—	—	—
L-aspartic acid	—	—	—	—
D-aspartic acid	—	—	—	—
L-glutamic acid	—	—	—	—
D-glutamic acid	—	—	—	—

(—) no new phases detected; (+) new phases detected; (+*) structures solved; (+†) cocrystal hydrate identified

Table 2. Cocrystals/salts with amino acid co-formers found in the Cambridge Structural Database (CSD) for compounds with a hydroxyl group ("salt/cocrystal" means that the compound contain both ionized and non-ionized molecules)

No.	*refcode*	*name*	*nature*
1	CAPKEL	L-alaninium L-alanine picrate monohydrate	salt
2	ABEHOF	L-Valinium picrate	salt
3	FOGYEG	L-Leucine L-leucinium picrate	salt
4	HAGBOG	L-Tryptophan picric acid	cocrystal
5	ATONAZ	L-Threonine picrate	salt
6	PAHCIL	DL-valine DL-valinium picrate	salt/cocrystal
7	QQQBTG02	glycinium glycine picrate	salt/cocrystal
8	TPTPCM	DL-Tryptophan picrate methanol solvate	salt
9	WAMPOQ	L-Asparaginium picrate	salt
10	XAZNAO	DL-methionine DL-methioninium picrate	salt/cocrystal
11	YAMVIS	DL-Phenylalanine DL-phenylalaninium picrate	salt/cocrystal
12	CONVAD	L-lysinium monohydrogen squarate monohydrate	salt
13	CONVEH	bis(L-lysinium) bis(monohydrogen squarate) squarate dihydrogen squarate dihydrate	salt
14	NUYFUI	(L)-(-)-Asparaginium hydrogen squarate hemihydrate	salt
15	PAZCUO	L-(+)-Serinium hydrogensquarate	salt
16	NAZGAY	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol bis(L-phenylalanine) monohydrate	cocrystal
17	NAZGEC	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol L-phenylalanine monohydrate	cocrystal
18	NAZGIG	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol bis(L-proline) tetrahydrate	cocrystal
19	NAZGOM	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol bis(L-proline) ethanol solvate monohydrate	cocrystal
20	NAZGUS	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol L-proline	cocrystal
21	NAZHAZ	(2S,3R,4R,5S,6R)-2-(3-(4-Ethylbenzyl)-phenyl)-6-hydroxymethyltetrahydro-2H-pyran-3,4,5-triol bis(L-proline)	cocrystal

Table 3. Cocrystals/salts with amino acid co-formers found in the Cambridge Structural Database (CSD) for compounds with a carboxyl group ("salt/cocrystal" means that the compound contain both ionized and non-ionized molecules)

No.	*refcode*	*name*	*nature*
1	ADAVOQ	L-Histidinium hydrogen glutarate monohydrate	salt
2	ADAVUV	L-Histidinium L-histidine hydrogen glutarate	salt/cocrystal
3	AHERAG	L-Alaninium tartrate	salt
4	AWIHIY	Glycinium hydrogen malonate	salt
5	AWIHOE	Glycine glutaric acid	cocrystal
6	BEYVAD	(R)-2-(Phenoxy)propionic acid (S)-alanine	cocrystal
7	BOQTEG	L-Alaninium maleate	salt
8	BOWKOO	DL-Cysteinium semioxalate	salt
9	CAMWOD	DL-Histidine malonic acid	cocrystal
10	CAMWUJ	L-Histidine malonic acid	cocrystal
11	CAVCUY	L-Lysinium L-tartrate	salt
12	EDAXIQ	L-Phenylalaninium maleate	salt
13	ETEYOR	DL-Threoninium hydrogen maleate	salt
14	EWOZIZ	bis(DL-Valine) succinic acid	cocrystal
15	FONJAU	(R)-Methioninium(R)-mandelate (R)-mandelate (R)-mandelic acid	salt/cocrystal
16	GALPIT	(R)-2-Phenoxypropionic acid (S)-valine	cocrystal
17	GINGEK	L-Argininium maleate dihydrate	salt
18	GOLZIR	Glycinium hydrogen fumarate glycine solvate monohydrate	salt/cocrystal
19	GOMDAO	(S)-2-Amino-3-(1H-indol-3-yl)propanoic acid acetic acid monohydrate	cocrystal
20	HAGYEU	bis(DL-Valine) fumaric acid	cocrystal
21	HAGZUL	L-Leucinium oxalate	salt
22	HIDGOQ	L-Cysteine L-tartrate monohydrate	cocrystal
23	IMEGIR	DL-Alaninium semioxalate monohydrate	salt
24	IREKAR	(R)-Phenylalanine (R)-mandelic acid	cocrystal
25	IROVAM	(S)-Alanine (S)-mandelic acid	cocrystal
26	IXAVEI	DL-Histidinium DL-tartrate	salt
27	IZAJUO	D-Histidinium (2S,3S)-tartrate	salt
28	JAXZIS	L-Phenylalanine benzoic acid solvate	cocrystal
29	JOTKIM	L-Phenylalanine L-phenylalaninium formate	salt/cocrystal
30	KOHPOM	DL-Lysine hemisuccinate hemisuccinic acid	salt/cocrystal
31	KOHPUS	L-Lysine hemisuccinate	salt
32	LAWKIE	L-(R)-cysteine L-(S)-mandelic acid	cocrystal
33	LERXUD	Glycine D-tartaric acid	cocrystal
34	LGPYRG	L-Glutamic acid L-pyroglutamic acid monohydrate	cocrystal
35	LHISTM	L-Histidinium dihydrogen-trimesate acetone solvate	salt
36	LOCJET	DL-Cysteinium hemikis(oxalate)	salt
37	LOCLOF	L-Cysteinium hydrogen oxalate	salt
38	LYSASP	L-Lysine L-aspartate	salt
39	MIFQUN	bis(DL-Serinium)oxalate dihydrate	salt
40	MOCXUX	DL-Methioninium maleate	salt
41	MOHDIX	L-lysine bis(hydrogen oxalate) monohydrate	salt
42	MUGKAA	L-Tryptophan formic acid solvate	cocrystal
43	MUPNUG	DL-arginine semimalonate monohydrate	salt
44	MUPPAO	L-arginine semimalonate	salt
45	MUVXAC	bis(DL-Aspartic acid) oxalate	salt
46	NELPUP	DL-Alaninium oxalate	salt
47	NEPXIR	Glycine phthalic acid	cocrystal
48	NOBYAE	L-Histidine 4,5-imidazoledicarboxylic acid	cocrystal
49	NOBYEI	L-Lysine 4,5-imidazoledicarboxylic acid	cocrystal
50	NONZOF	(S)-Phenylalanine (S)-mandelic acid	cocrystal
51	NONZUL	(R)-Phenylalanine (S)-mandelic acid	cocrystal
52	NOSXAU	DL-Arginine hydrogen oxalate	salt
53	NOSXEY	L-Arginine hydrogen oxalate	salt
54	NUQHIR	L-Tryptophan pyridine-2,4-dicarboxylic acid ethanol solvate	cocrystal
55	OJEPEY	L-Phenylalanine fumaric acid	cocrystal
56	PAVYIW	(S)-Alanine (S)-2-phenoxypropionic acid	cocrystal
57	QOYJUJ	DL-Lysinium semi-glutarate	salt
58	QOYKAQ	L-Lysinium semi-glutarate	salt
59	QURSUR	DL-Valinium hydrogen maleate	salt
60	RALRUS	L-phenylalanine L-phenylalaninium malonate	salt
61	RARXOX01	L-Histidine oxalate	salt
62	RAZPUE	L-(R)-cysteine D-(R)-mandelic acid	cocrystal

63	REHTII	L-Arginine dioxalate	salt
64	REJZUC	L-Histidinium hydrogen L-malate	salt
65	RENBAN	Glycinium hydrogen maleate	salt
66	REPFEX	DL-Threoninium oxalate	salt
67	RIFXAG	bis(DL-Arginine) hydrogen bis(DL-tartaric acid)	cocrystal
68	RIHMEB	L-Lysine hydrogen D-tartrate	salt
69	SITCUU	Pyridine-2,4-dicarboxylic acid serine	cocrystal
70	SUYWEP	L-Asparaginium L-tartrate	salt
71	TENVUF	L-histidinium maleate monohydrate	salt
72	TENZOV	L-histidinium bis(hydrogen maleate)	salt
73	TRYPTB	D-Tryptophan hydrogen oxalate	salt
74	TUWBOD	diglycinium oxalate methanol solvate	salt
75	UCEMEV	Glycine 3,5-dihydroxybenzoic acid monohydrate	cocrystal
76	UGITAG	L-(S)-Tryptophane D-(R)-mandelate sesquihydrate	salt
77	UKORUH	L-Histidinium L-tartrate hemihydrate	salt
78	VAGVIJ	DL-Phenylalaninium hydrogen maleate	salt
79	VAZJUD	L-Histidinium maleate sesquihydrate	salt
80	VIKLOR	DL-Phenylalanine fumaric acid	cocrystal
81	VIKLUX	bis(L-Valine) fumaric acid	cocrystal
82	WEHZAL	bis(Glycinium) oxalate	salt
83	WOVYOV	Glycinium oxalate	salt
84	XADTIF	L-Histidine semi-maleate	salt
85	XADTOL	L-lysine semi-maleate	salt
86	XENXOF	L-serinium hydrogen oxalate	salt
87	XENXUL	bis(L-serinium) oxalate dihydrate	salt
88	XOXGUM	DL-Lysinium hydrogen oxalate dihydrate	salt
89	XOXHAT	bis(L-Lysinium) oxalate bis(hydrogen oxalate)	salt
90	XUGMER	(S)-Alanine (R)-mandelic acid hemihydrate	cocrystal
91	YAGKAT	(R)-Histidinium (2R,3R)-tartrate	salt
92	YEFXOX	L-lysine hydrogen adipate	salt
93	YEJYIV	L-Alaninium oxalate	salt
94	YIFLOP	Glycinium 3-nitrophthalate	salt
95	YOWDET	L-Arginine hemisuccinate hemisuccinic acid monohydrate	salt/cocrystal

Table 4. Cocrystals/salts with amino acid co-formers found in the Cambridge Structural Database (CSD) for compounds with an amide group

No.	*refcode*	*name*	*nature*
1	MUYTEG	5-Hydroxy-L-tryptophan barbituric acid	cocrystal
2	MUYVAE	5-Hydroxy-L-tryptophan 1,3-dimethylbarbituric acid monohydrate	cocrystal

Table 5. Selected hydrogen-bond parameters in the S-naproxen/L-alanine cocrystal

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
N1—H1A···O1	0.85 (3)	2.00 (3)	2.834 (2)	168 (3)
N1—H1B···O5^{i}	0.95 (3)	1.90 (3)	2.838 (2)	167 (3)
N1—H1C···O4^{ii}	0.88 (3)	2.44 (3)	2.8211 (19)	107 (2)
N1—H1C···O5^{iii}	0.88 (3)	1.95 (3)	2.794 (2)	161 (3)
O2—H2···O4^{ii}	0.97 (4)	1.57 (4)	2.5277 (19)	172 (4)

Symmetry code(s): (i) *x*+1, *y*, *z*; (ii) -*x*+1, *y*+1/2, -*z*+1/2; (iii) -*x*, *y*+1/2, -*z*+1/2.

Table 6. Selected hydrogen-bond parameters in the S-naproxen/D-alanine cocrystal

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
N1—H1A···O1	0.91	1.90	2.810 (7)	177
N1—H1B···O5^{i}	0.91	1.89	2.790 (7)	168
N1—H1C···O5^{ii}	0.91	2.05	2.933 (7)	164
O2—H2···O4^{iii}	0.84	1.68	2.513 (7)	171

Symmetry code(s): (i) -*x*, *y*+1/2, -*z*+1/2; (ii) *x*+1, *y*, *z*; (iii) -*x*+1, *y*+1/2, -*z*+1/2.

Table 7. Selected hydrogen-bond parameters in S-naproxen/D-tryptophan monohydrate

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
N2—H2D···O1^{i}	0.89 (4)	2.29 (3)	2.956 (4)	132 (3)
N1—H1A···O1	0.99	2.00	2.906 (4)	149.8
N1—H1B···O6	0.99	1.79	2.779 (4)	174.5
N1—H1C···O5^{ii}	0.99	1.77	2.742 (4)	164.9
O2—H2···O4^{ii}	0.94 (4)	1.67 (4)	2.562 (4)	156 (4)
O6—H6B···O5^{iii}	0.85 (4)	1.86 (4)	2.703 (4)	172 (5)

Symmetry code(s): (i) -*x*, *y*-1/2, -*z*+3/2; (ii) *x*-1, *y*, *z*; (iii) -*x*+1, *y*-1/2, -*z*+3/2.

Table 8. Selected hydrogen-bond parameters in S-naproxen/D-tyrosine

D—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
N1—H1A···O5^{i}	0.916 (3)	2.081 (3)	2.940 (3)	155.6 (3)
N1—H1B···O6^{ii}	0.915 (3)	2.082 (3)	2.709 (3)	124.7 (2)
N1—H1C···O4^{iii}	0.908 (3)	1.935 (3)	2.825 (3)	165.9 (3)
O2—H2···O4	0.853 (3)	1.761 (3)	2.613 (3)	177.0 (2)
O6—H6A···O5^{ii}	0.815 (3)	2.045 (3)	2.859 (3)	176.4 (3)

Symmetry code(s): (i) -*x*+1, *y*-1/2, -*z*+2; (ii) -*x*+2, *y*-1/2, -*z*+2; (iii) *x*, *y*-1, *z*.

Figure 1. Experimental diffraction patter for S-naproxen ground with D-alanine (*1*) (10 μL of methanol, 90 min at 30 Hz); simulated diffraction pattern of the S-naproxen/D-alanine cocrystal (*2*); reference diffraction patterns for S-naproxen (*3*) and D-alanine (*4*). Cu*K*α radiation. Simulated diffraction pattern for S-naproxen/D-alanine (*2*) coincides with the diffraction pattern of ground material (*1*).

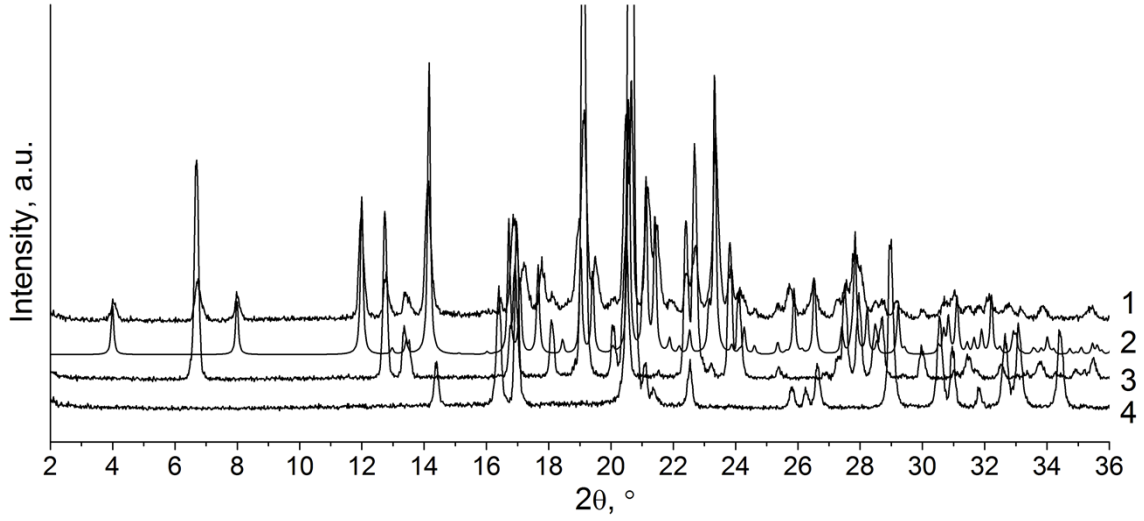


Figure 2. Experimental diffraction patter for S-naproxen ground with L-alanine (*1*) (10 μL of methanol, 90 min at 30 Hz); simulated diffraction pattern of the S-naproxen/L-alanine cocrystal (*2*); reference diffraction patterns for S-naproxen (*3*) and L-alanine (*4*). Cu*K*α radiation. Simulated diffraction pattern for S-naproxen/L-alanine (*2*) coincides with the diffraction pattern of ground material (*1*).

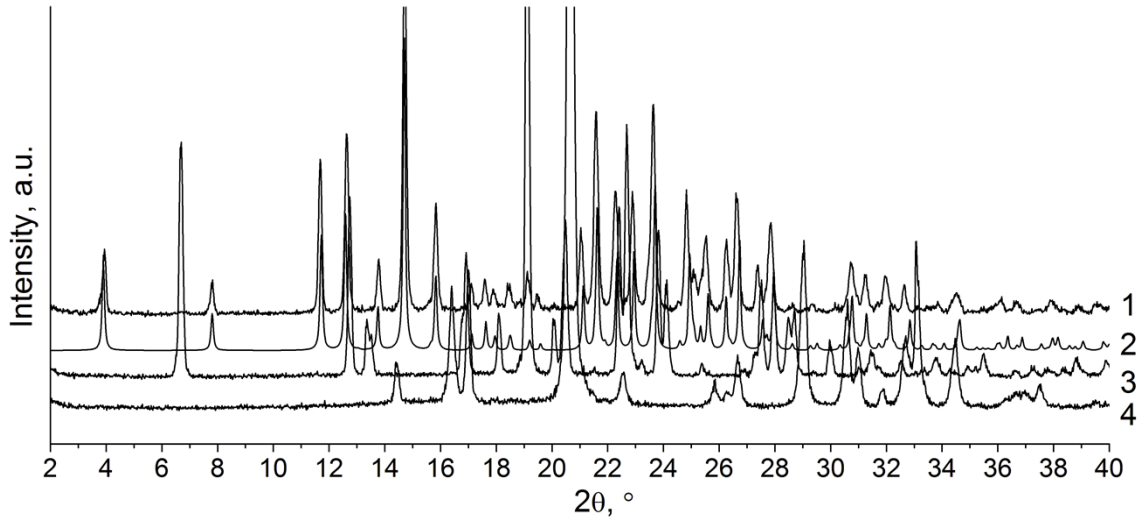


Figure 3. Comparison of the diffraction patterns (Cu*K*α radiation) of ground S-naproxen/L-tryptophan powder (*1*) (10 μL of methanol, 90 min at 30 Hz) and powder obtained from solution (60/40 % ethanol/water solution, slow evaporation, room temperature) (*2*). Both patterns show the presence of the same phase. Along with this new phase, the powder from solution (*2*) contains some amount of S-naproxen (*3*).

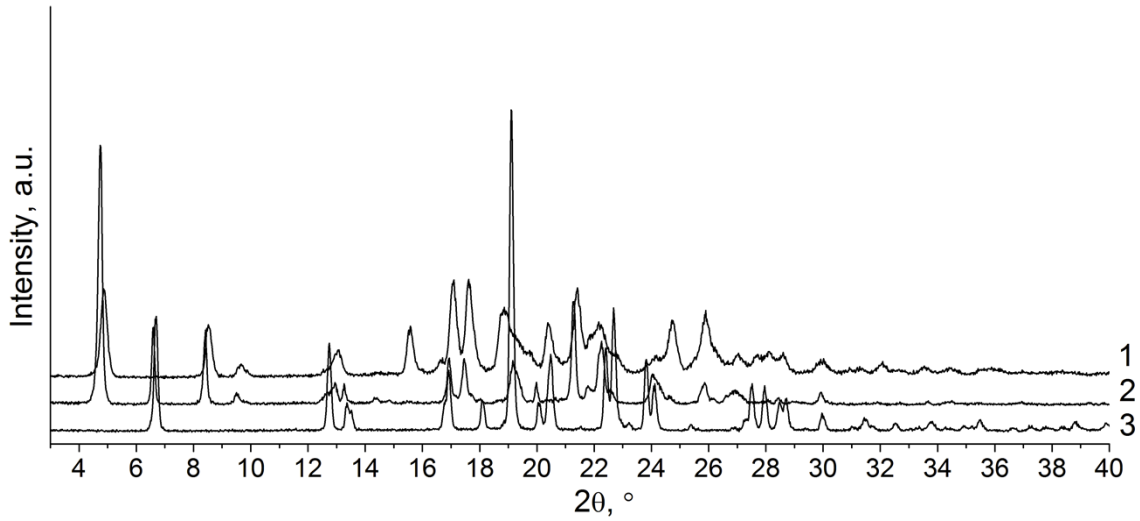


Figure 4. Experimental diffraction pattern (Cu*K*α radiation) of ground S-naproxen/D-tryptophan powder (*1*) (10 μL of methanol, 90 min at 30 Hz); simulated diffraction pattern for S-naproxen/D-tryptophan monohydrate; reference diffraction patterns for S-naproxen (*3*) and D-tryptophan (*4*). Cu*K*α radiation. Grinding of S-naproxen with D-tryptophan (*1*) yields a new phase, however different from S-naproxen/D-tryptophan monohydrate obtained from solution (arrows indicate some of the new peaks)

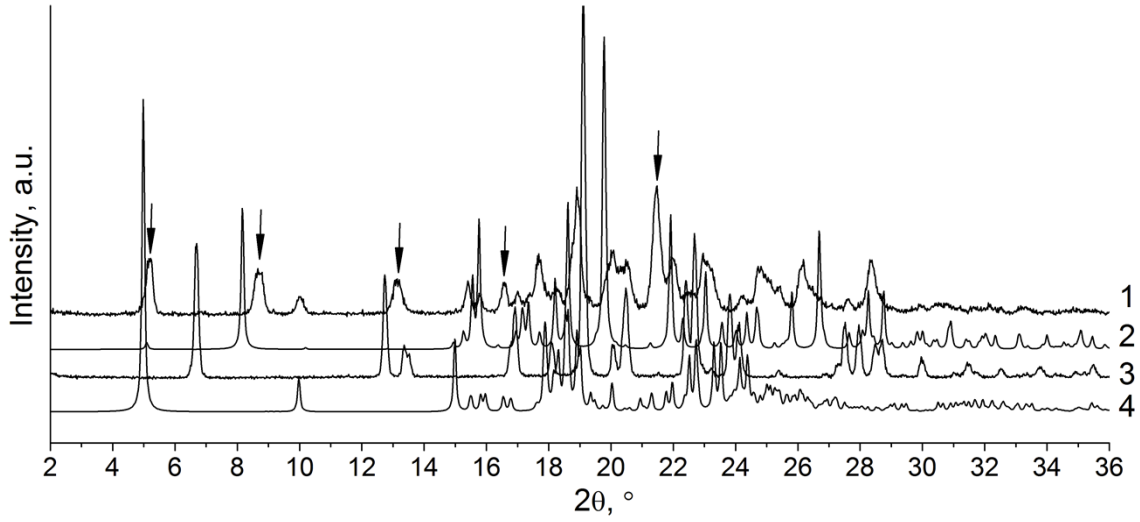


Figure 5. Rietveld refinement plot for S-naproxen/D-tryptophan at 100 K (λ = 0.775045(1), zeroshift = –0.0079). Red crosses and black line show experimental and calculated data, respectively; blue line is the difference profile; green marks indicate Bragg positions. The corresponding unit cell parameters are a = 20.6445(2), b = 11.77119(18), c = 40.7116(6), β = 118.2805(9) (V = 8712.5(2), Z' = 8 in $P21$). Due to the large unit cell volume, no crystal structure was determined

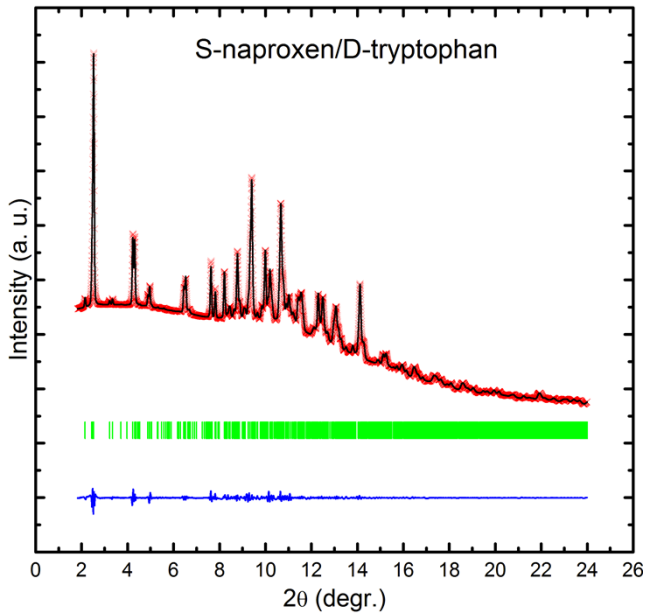


Figure 6. Rietveld refinement plot for S-naproxen/L-tryptophan at room temperature (λ = 0.775045(1), zeroshift = –0.0079). Red crosses and black line show experimental and calculated data, respectively; blue line is the difference profile; green marks indicate Bragg positions. The corresponding unit cell parameters are a = 22.2064(4), b = 10.49608(14), c = 45.2843(10), β = 124.3265(15) (V = 8716.6(3), Z' = 8 in $P21$). Due to the large unit cell volume, no crystal structure was determined

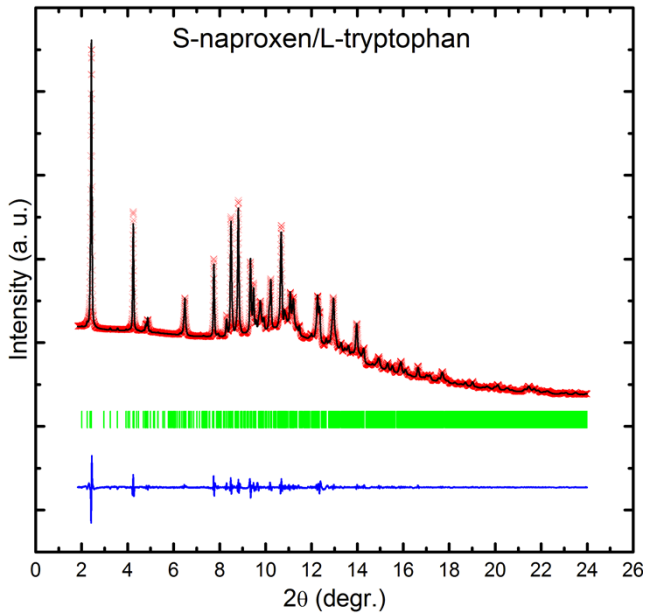


Figure 7. DSC data for S-naproxen/D-tryptophan monohydrate crystals and S-naproxen/L-tryptophan powder obtained from 60/40 % ethanol/water solution by slow evaporation. S/naproxen/L-tryptophan is in an unhydrated form

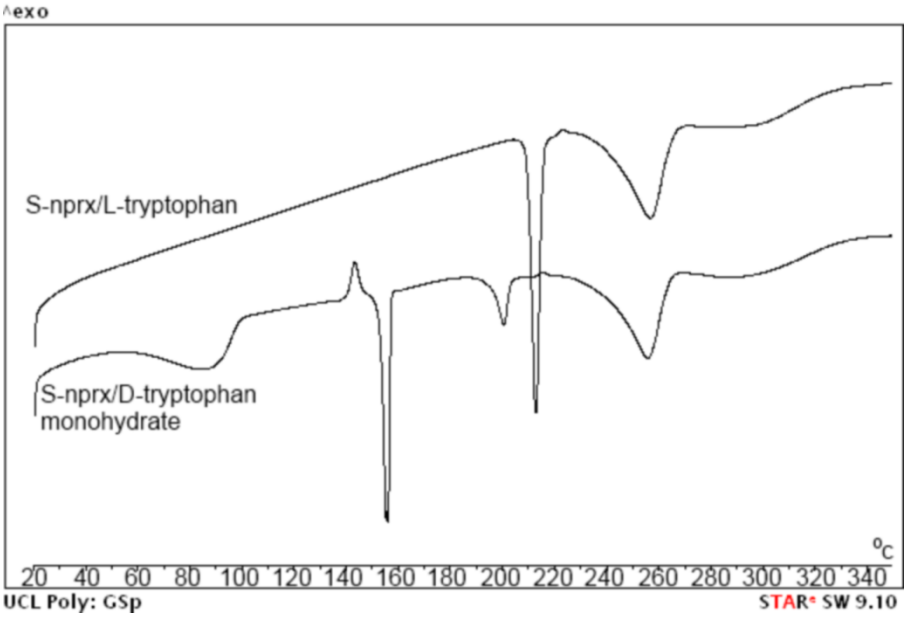


Figure 8. TGA data for S-naproxen/D-tryptophan monohydrate crystals and S-naproxen/L-tryptophan powder obtained from 60/40 % ethanol/water solution by slow evaporation S/naproxen/L-tryptophan is in an unhydrated form