Supporting Information

Computational screening and experimental validation on multicomponent crystals of a new class of Janus Kinase (JAK) inhibitor drug with improved solubility

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Table S1. Preparation of Multicomponent Crystal Forms

Complex	Experimental details
SHR0302-SAL	**Slurry method**
	SHR0302:41.4mg; SAL: 13.8mg; isopropyl acetate:2mL
	SHR0302:41.4mg; SAL: 13.8mg; isopropanol:2mL
	SHR0302:41.4mg; SAL: 13.8mg; acetonitrile:2mL
	SHR0302:41.4mg; SAL: 13.8mg; dichloromethane-ethanol (volume ratio 12:1):2mL
	SHR0302:41.4mg; SAL: 13.8mg; dichloromethane:2mL
	Solvent-assisted grinding method
	SHR0302:414mg; SAL:138mg; ethanol/methanol/acetonitrile/acetone/dichloromethane: 50μL
SHR0302-CA	**Slurry method**
	SHR0302:41.4mg; SAL: 19.2mg; isobutanol:2mL
	SHR0302:41.4mg; SAL: 19.2mg; dichloromethane-methanol (volume ratio 12:3) :2mL
	SHR0302:41.4mg; SAL: 19.2mg; acetonitrile:2mL
	SHR0302:41.4mg; SAL: 19.2mg; dichloromethane-ethanol (volume ratio 12:1):2mL
	SHR0302:41.4mg; SAL: 19.2mg; methyl tert-butyl ether:2mL
	SHR0302:41.4mg; SAL: 19.2mg; dichloromethane-isopropyl alcohol (volume ratio 8:2):2mL
	Solvent-assisted grinding method
	SHR0302:414mg; SAL:138mg; ethanol/methanol/acetonitrile/acetone/dichloromethane: 50μL
SHR0302-26DHBA	**Slurry method**
	SHR0302:41.4mg; 26DHBA:15.4mg; isobutanol:2mL
	SHR0302:41.4mg; 26DHBA:15.4mg; dichloromethane:2mL
	Solvent-assisted grinding method
	SHR0302:414mg;26DHBA:154mg; ethanol/methanol/acetonitrile/acetone/dichloromethane: 50μL

Table S2. COSMO-RS Calculation and MC Analysis Results of SHR0302 with Coformers

	Coformer	ΔH_{ex}(kcal/mol)	Hit Rate(%)	New form
1	oxalic acid	-10.00	0	Yes
2	phloroglucinol	-9.24	0	
3	gallic acid	-8.82	0	
4	fumaric acid	-8.56	100	
5	2,4-dihydroxybenzoic acid	-8.38	0	
6	**citric acid**	-8.05	0	Yes
7	tartaric acid	-7.87	100	Yes
8	2,5-dihydroxybenzoic acid	-7.78	0	Yes
9	2,7-dihydroxynaphthalene	-7.20	0	
10	2,6-dihydroxynaphthalene	-7.15	0	
11	p-toluenesulfonic acid	-7.11	100	
12	pyrogallol	-7.05	0	
13	resorcinol	-6.90	0	
14	3-hydroxybenzoic acid	-6.50	0	
15	catechol	-6.47	0	
16	maleic acid	-6.24	100	
17	4-hydroxybenzoic acid	-6.14	100	
18	vanillic acid	-6.00	0	
19	hydroquinone	-5.76	0	
20	**2,6-dihydroxybenzoic acid**	-5.35	0	Yes
21	**salicylic acid**	-5.11	0	Yes
22	succinic acid	-4.97	100	
23	L-hydroxybutanedioic acid	-4.87	100	
24	malonic acid	-4.53	100	
25	glutaric acid	-4.46	100	
26	ferulic acid	-4.18	100	
27	4-aminosalicylic acid	-3.69	0	
28	m-aminobenzoic acid	-3.67	0	
29	benzoic acid	-3.57	100	
30	acetylsalicylic acid	-3.52	0	
31	p-aminobenzoic acid	-2.58	100	
32	nicotinic acid	-2.48	100	

33	acetaminophen	-2.12	100
34	glycine	-1.18	0
35	saccharin	-0.73	0
36	histidine	-0.68	100
37	piperazine	-0.49	0
38	proline	-0.39	0
39	theophylline	-0.17	0
40	isoniazid	-0.04	0
41	adipic acid	0.04	100
42	caffeine	0.09	0

Table S3. Data of TPR, FPR and Youden Index Used in Prediction Performance Evaluation

	Coformer	ΔH_{ex}(kcal/mol)	TPR	FPR	Youden index
1	Oxalic acid	-10.00	0.17	0.00	0.17
2	Phloroglucinol	-9.24	0.17	0.03	0.14
3	Gallic acid	-8.82	0.17	0.06	0.11
4	Fumaric acid	-8.56	0.17	0.08	0.09
5	2,4-Dihydroxybenzoic acid	-8.38	0.17	0.11	0.06
6	**citric acid**	-8.05	0.33	0.11	0.22
7	tartaric acid	-7.87	0.50	0.11	0.39
8	2,5-Dihydroxybenzoic acid	-7.78	0.67	0.11	0.56
9	2,7-Dihydroxynaphthalene	-7.20	0.67	0.14	0.53
10	2,6-Dihydroxynaphthalene	-7.15	0.67	0.17	0.50
11	p-toluenesulfonic acid	-7.11	0.67	0.19	0.48
12	pyrogallol	-7.05	0.67	0.22	0.45
13	resorcinol	-6.90	0.67	0.25	0.42
14	3-hydroxybenzoic acid	-6.50	0.67	0.28	0.39
15	catechol	-6.47	0.67	0.31	0.36
16	maleic acid	-6.24	0.67	0.33	0.34
17	4-hydroxybenzoic acid	-6.14	0.67	0.36	0.31
18	vanillic acid	-6.00	0.67	0.39	0.28
19	hydroquinone	-5.76	0.67	0.42	0.25
20	**2,6-dihydroxybenzoic acid**	-5.35	0.83	0.42	0.41
21	**salicylic acid**	-5.11	1.00	0.42	0.58
22	succinic acid	-4.97	1.00	0.44	0.56
23	L-hydroxybutanedioic acid	-4.87	1.00	0.47	0.53
24	malonic acid	-4.53	1.00	0.50	0.50
25	glutaric acid	-4.46	1.00	0.53	0.47
26	ferulic acid	-4.18	1.00	0.56	0.44
27	4-aminosalicylic acid	-3.69	1.00	0.58	0.42
28	m-aminobenzoic acid	-3.67	1.00	0.61	0.39
29	benzoic acid	-3.57	1.00	0.64	0.36
30	acetylsalicylic acid	-3.52	1.00	0.67	0.33
31	p-aminobenzoic acid	-2.58	1.00	0.69	0.31
32	nicotinic acid	-2.48	1.00	0.72	0.28

33	acetaminophen	-2.12	1.00	0.75	0.25
34	glycine	-1.18	1.00	0.78	0.22
35	saccharin	-0.73	1.00	0.81	0.19
36	histidine	-0.68	1.00	0.83	0.17
37	piperazine	-0.49	1.00	0.86	0.14
38	proline	-0.39	1.00	0.89	0.11
39	theophylline	-0.17	1.00	0.92	0.08
40	isoniazid	-0.04	1.00	0.94	0.06
41	adipic acid	0.04	1.00	0.97	0.03
42	caffeine	0.09	1.00	1.00	0.00

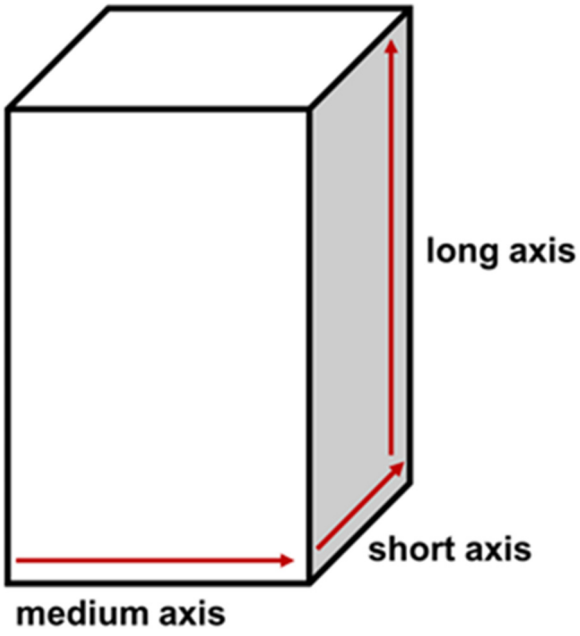

Figure S1. Molecular bounding box model with three unequal dimensions

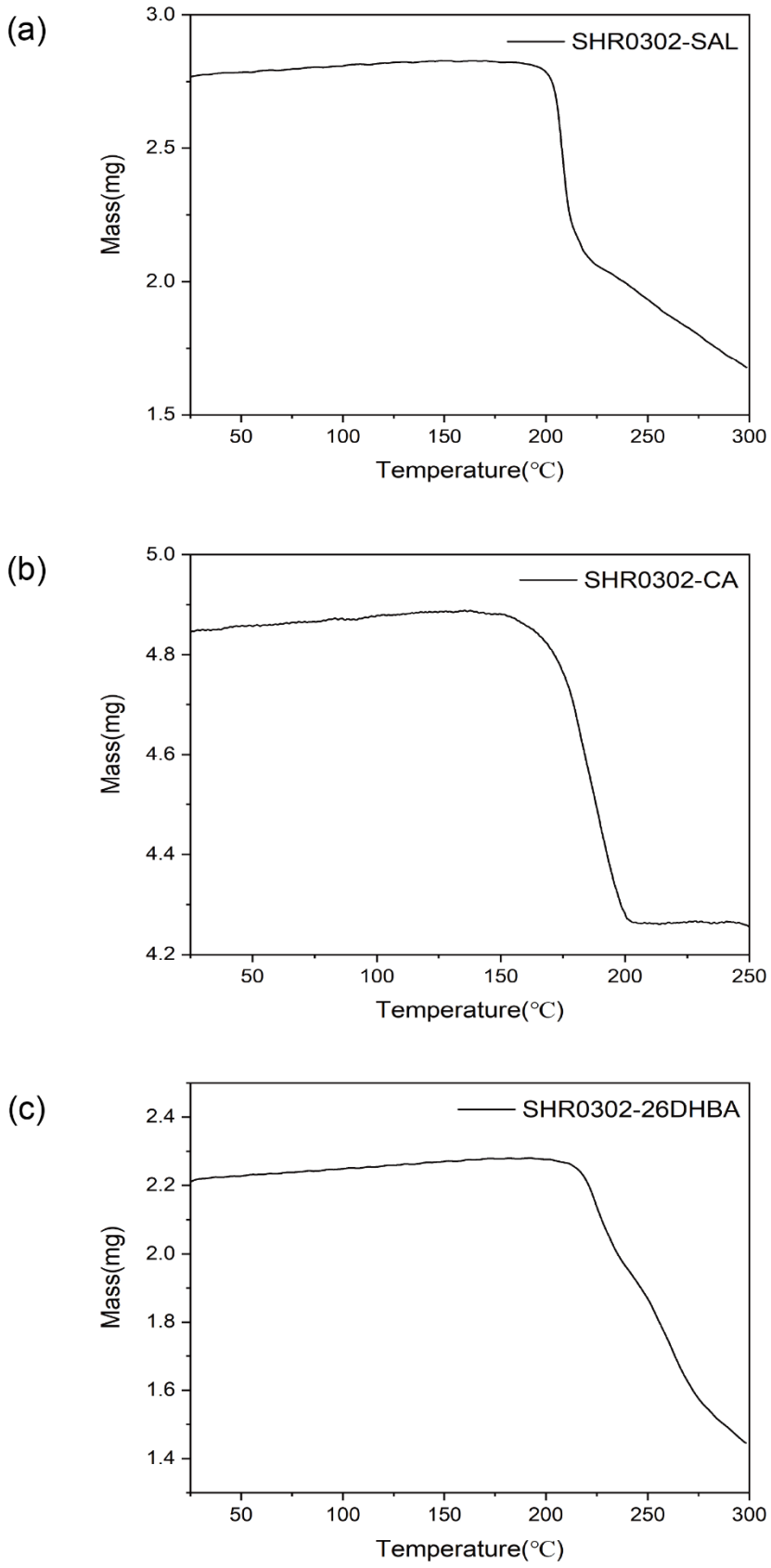

Figure S2. TGA curves of SHR0302-SAL (a), SHR0302-CA (b), and SHR0302-26DHBA (c) multicomponent crystal forms

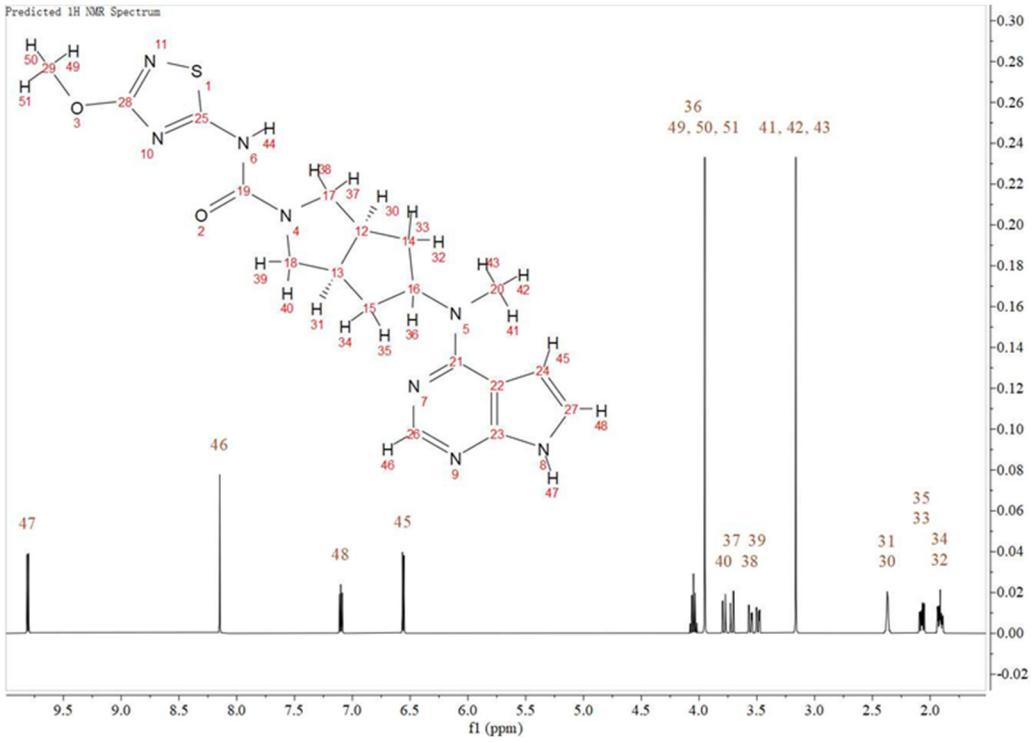

Figure S3. The predicted hydrogen spectrum of SHR0302 with proton assignments

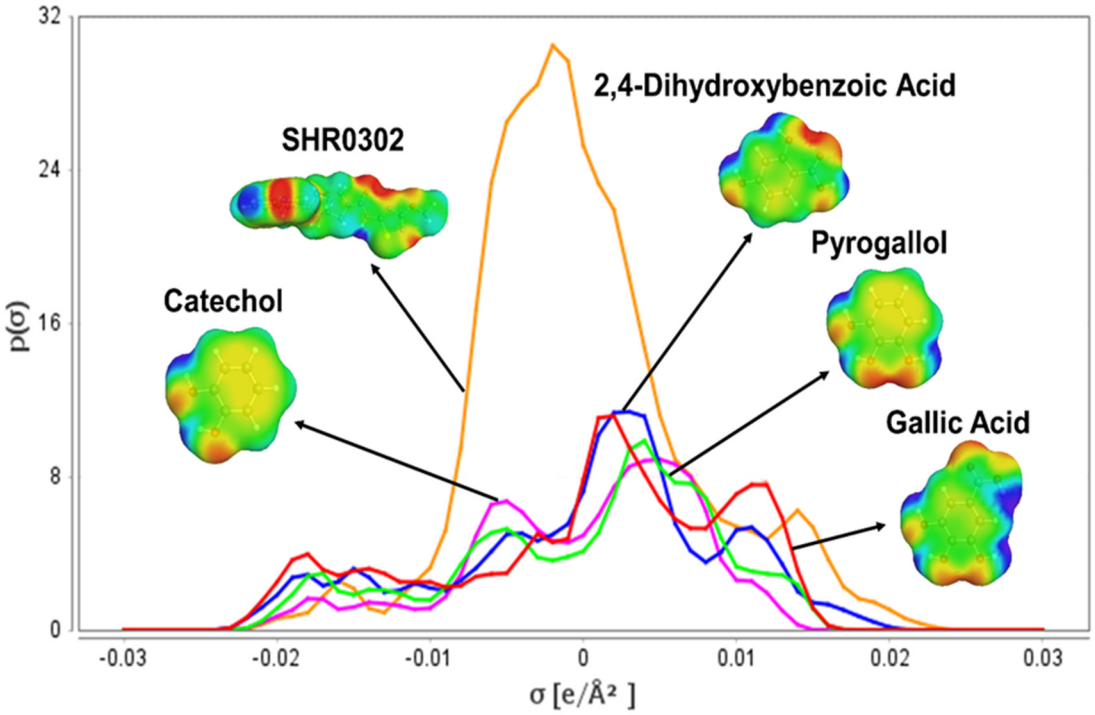

Figure S4. σ-profiles of SHR0302 and representative coformers that cannot form new multicomponent crystal with SHR0302.