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**Supporting information for article:**

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Role of auxiliary interactions in determining a preferred conformation**

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## New multi-component solid forms of an anti-cancer drug Erlotinib: Role of auxiliary interactions in determining a preferred conformation

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**Table S1** Neutron normalized hydrogen bonding parameters of ETB and its binary systems

Crystal forms	Interaction	H...A /Å	D...A/Å	<D-H...A /°	Symmetry code
ETB	N1-H1N...N6	2.03	2.905(4)	165	x,-y,1/2+z
	N4-H4N...N3	2.23	2.910(4)	163	x,1-y,-1/2+z
	C1-H1...O4	2.54	3.050(6)	115	1+x,y,z
	C17-H7B...N5	2.55	3.391(5)	146	x,y,1+z
	C39-H39B...N2	2.50	3.351(5)	146	x,y,z
	C41-H41C...O8	2.60	3.548(5)	172	x,1-y,1/2+z
ETB-URE	N3-H3...O5	1.89	2.838(2)	154	-x,-y,1-z
	N5-H5A...O2	2.46	3.263(2)	136	x,y,1+z
	N5-H5B...O3	2.06	3.047(3)	166	x,y,1+z
	N6-H6A...N1	2.02	3.017(2)	168	1/2-x,y,1/2+z
	N6-H6B...O5	1.96	2.963(2)	177	-x,-y,1-z
	C8-H8B...N2	2.48	3.503(3)	157	-1/2+x,-y,1/2-z
	C9-H9...O5	2.09	3.158(2)	168	-x,-y,1-z
	C16-H16...O5	2.45	3.163(2)	123	-x,-y,1-z
ETB-SUC.	N1-H1A...O7	2.02	3.002(3)	163	1-x,-y,1-z
H <sub>2</sub> O	O6-H6A...O9	1.65	2.604(3)	162	-1+x,y,z
	O8-H8A...N3	1.62	2.602(3)	174	x,y,-1+z
	O9-H9A...O2	1.92	2.807(3)	149	x,y,z
	O9-H9B...O4	1.80	2.761(3)	165	x,y,z

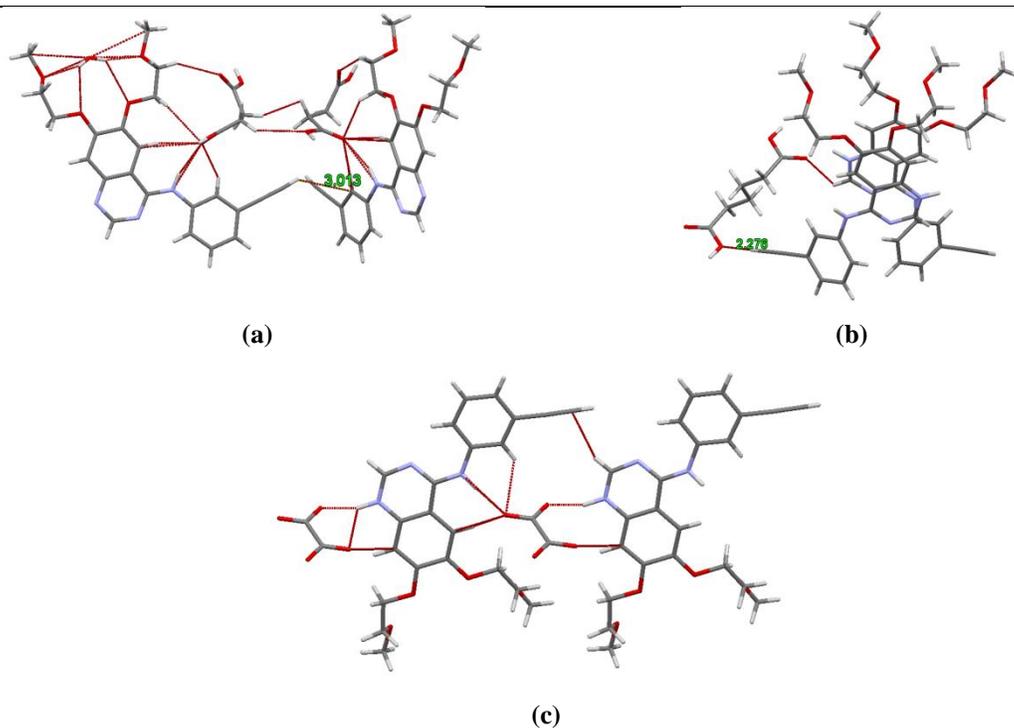
	C13–H13...O7	2.24	3.270(3)	158	1-x,-y,1-z
	C8–H8...O7	2.32	3.190(3)	136	1-x,-y,1-z
	C21–H21B...O5	2.47	3.435(4)	147	1-x,-y,1-z
ETB–GLU.	N1–H1...O8	2.15	3.086(5)	154	1-x,1-y,-z
H <sub>2</sub> O	O5–H5A...O9	1.69	2.613(5)	155	1+x,y,z
	O7–H7...N3	1.63	2.610(4)	172	x,-1+y,z
	O9–H9A...O4	1.88	2.796(5)	154	x,y,z
	O9–H9B...O2	2.07	2.902(5)	141	x,y,z
	C1–H1A...O6	2.12	3.169(6)	162	-1+x,1+y,-1+z
	C8–H8...O8	2.34	3.214(5)	136	1-x,1-y,-z
	C10–H10...O5	2.45	3.490(6)	161	-1+x,1+y,z
	C13–H13...O8	2.36	3.374(5)	155	1-x,1-y,-z
	C21–H21A...O6	2.45	3.452(5)	153	1-x,1-y,-z
ETB <sup>+</sup> ADP <sup>-</sup>	N1–H1N...O5	1.97	2.833(3)	142	1-x,1-y,1-z
.ADP	N3–H3...O7	1.66	2.666(3)	171	x,1/2-y,1/2+z
	N3–H3...O8	2.55	3.254 (3)	126	x,1/2-y,1/2+z
	O6–H6A...O8	1.49	2.474(3)	173	1-x,1-y,1-z
	C6–H6...N2	2.13	2.862(4)	169	1-x,-y,-z
	C10–H10...O5	2.33	3.065(4)	123	x,1/2-y,-1/2+z
	C17–H17...O7	2.42	3.357(4)	143	x,y,1+z

**Table S2** Vibrational frequency ( $\text{cm}^{-1}$ ) of ETBcocrystals/ salts.

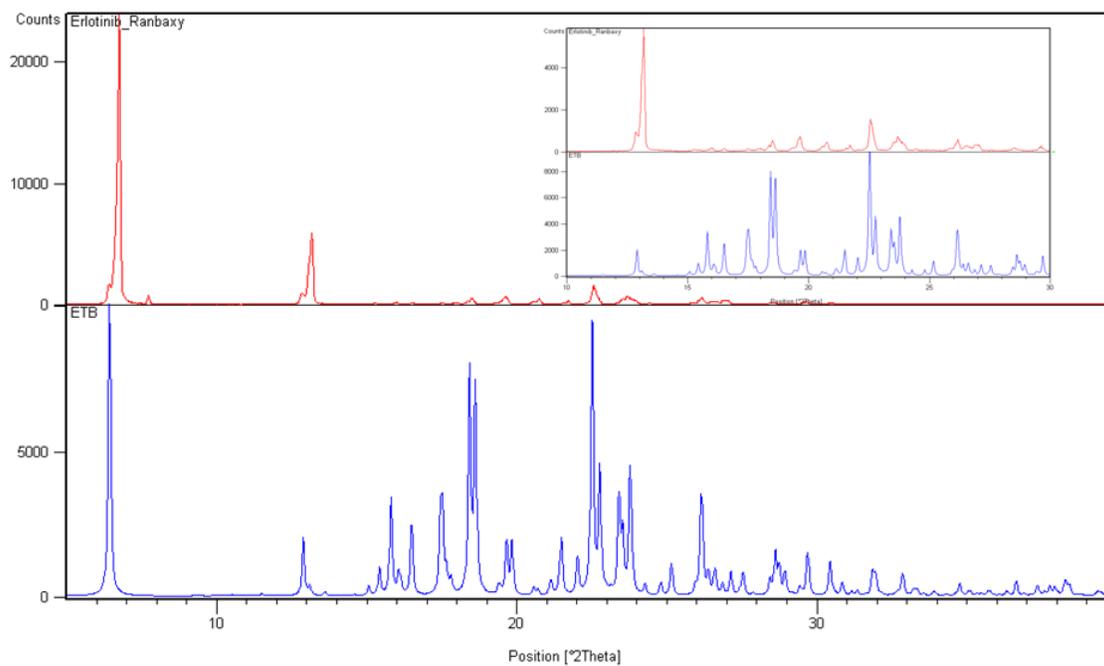
Solid forms	N–H Stretch	C=N Stretch	C=O Stretch	C=O/N–H Stretch (coformer)
ETB	3251.9	1620.1	--	--
ETB HCL	3271.8	1635.2	--	--
ETB–URE	3261.5, 3301.4, 3360.4, 3483.3	1629.7	1718.3	1677.3 3348.2, 3438.3
ETB <sup>+</sup> MLE <sup>-</sup> hydrate	3443.5, 3267.1	1613.5	1644.8	1706.7
ETB–SUC hydrate	3483.3, 3365.2, 3301.4, 3251.9	1629.7	1728.6	1694.4 (broad)
ETB–GLU hydrate	3488.1, 3365.2, 3296.6, 3261.5	1629.7	1723.1	1697.3
ETB <sup>+</sup> ADP <sup>-</sup> ADP	3477.8, 3360.4, 3296.6, 3256.7	1629.7	1723.1, 1693.6	1694.1 (broad)
ETB <sup>+</sup> SCN <sup>-</sup>	3345.3, 3306.2, 3247.1	1620.1	1644.8	1719.4

**Table S3** Melting points ( $^{\circ}\text{C}$ ) of the drug and its binary systems (DSC endotherms)

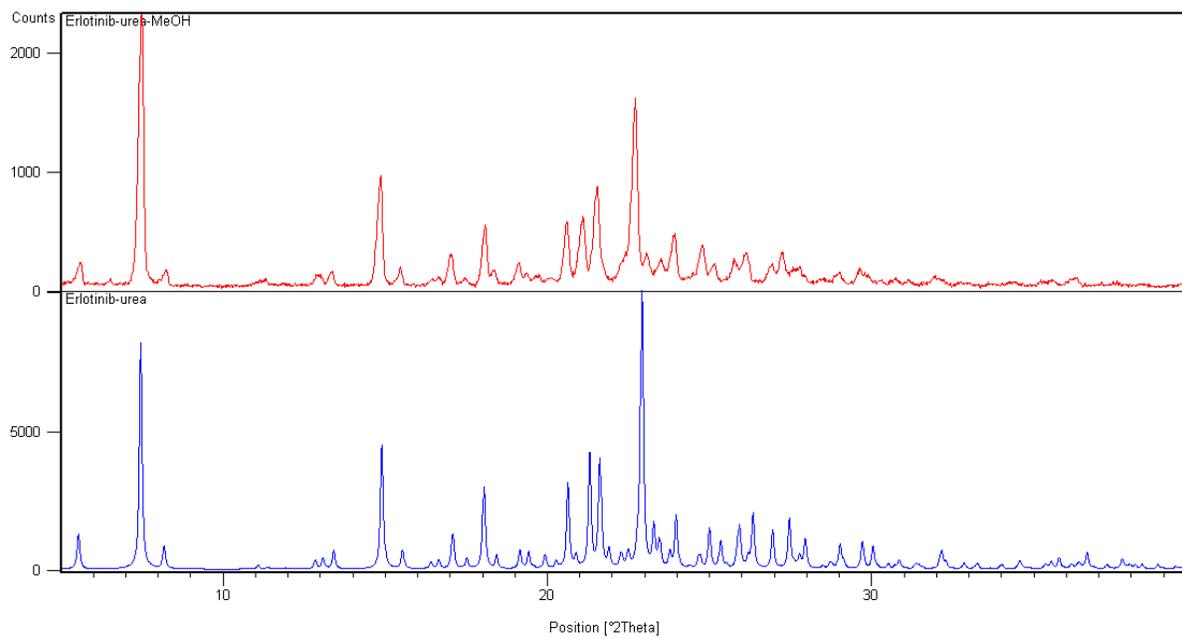
New solid forms	m.p. ( $^{\circ}\text{C}$ )	m.p. ( $^{\circ}\text{C}$ ) of coformers
Erotinib	154.8-155.8	--
Erlotinib–urea	163.6-164.4	133-135
Erlotinib–maleate hydrate	164.2-166.2	135-136
Erlotinib–fumaric acid dihydrate	188-190	285-287
Erlotinib–succinic acid hydrate	136.5-138.4	184-186
Erlotinib–glutaric acid hydrate	125.8-128.3	95-98
Erlotinib–adipic acid adipate	151.9-153.6	152-154
Erlotinibsaccharinate	168.7-170.8	228.8-229.7



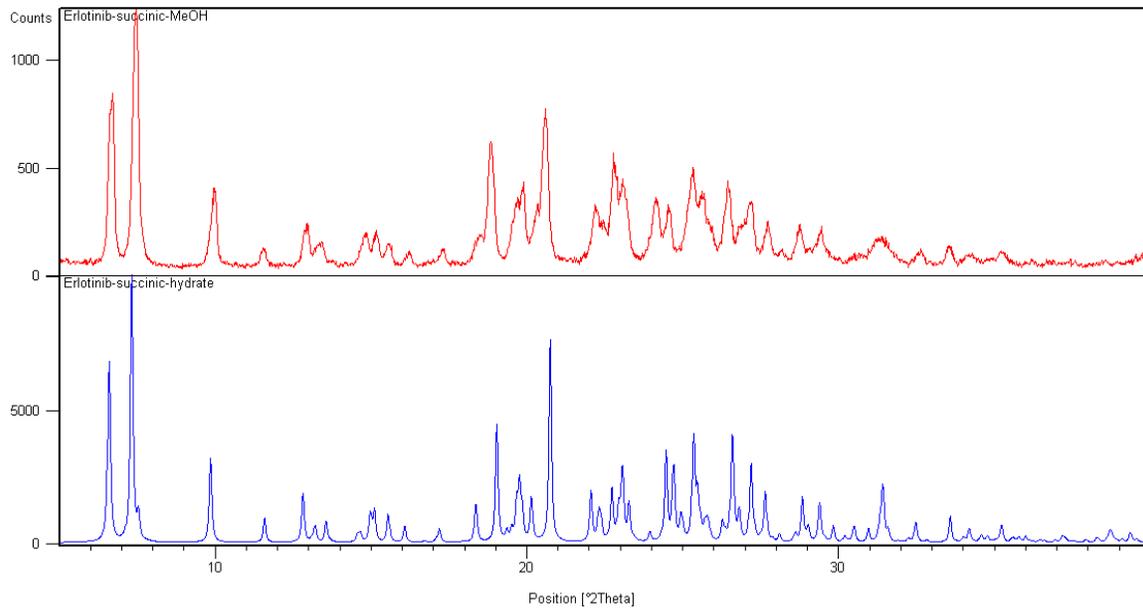
**Figure S1** Auxiliary (C-H...O/ C-H... $\pi$ ) hydrogen bonding between the API and the coformer (a) succinic acid cocrystal, (b) adipate salt and (c) oxalate salt assist to adopt (*syn*) conformation A.



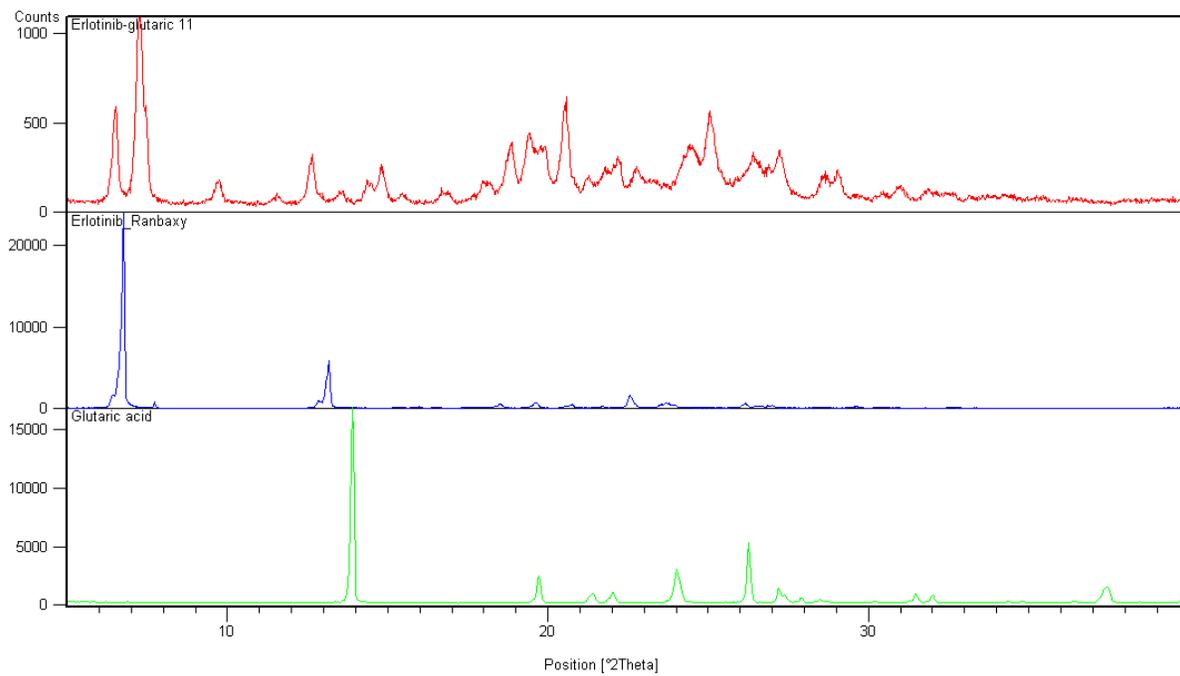
(a)



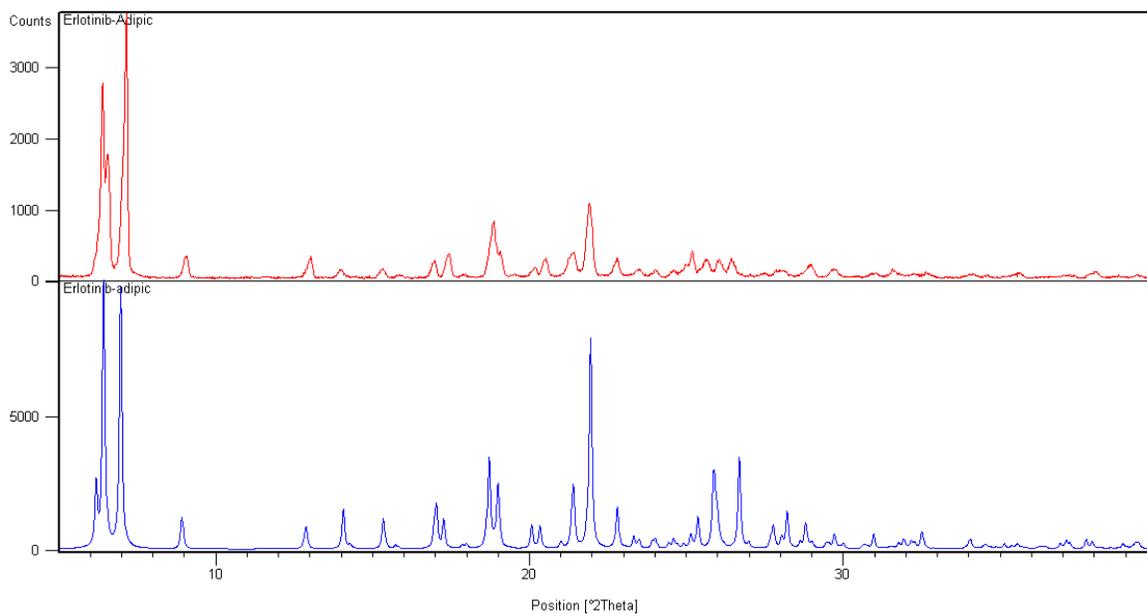
(b)



(c)

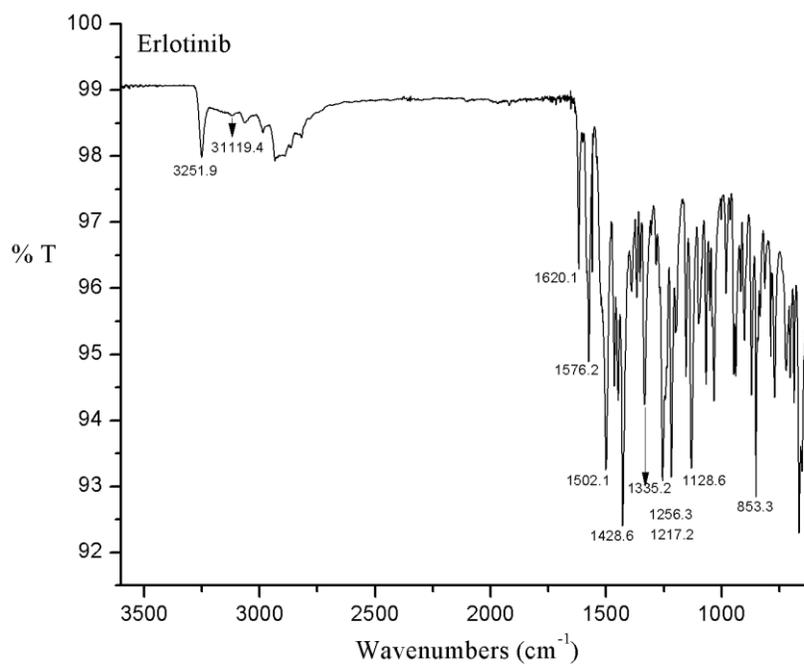


(d)

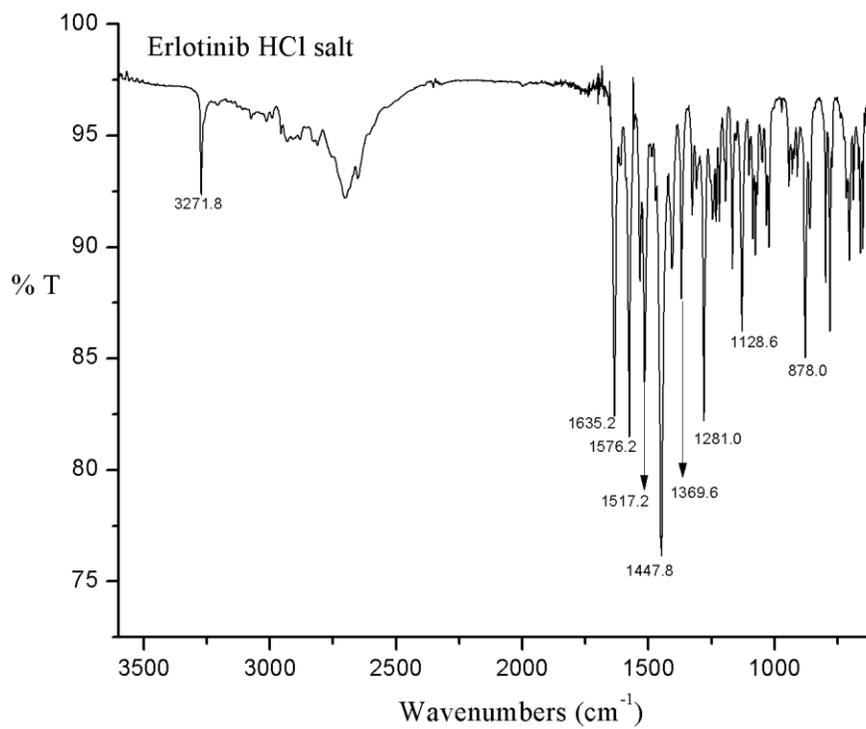


(e) Matched with adipate salt (WO/2013/054147)<sup>12b</sup>

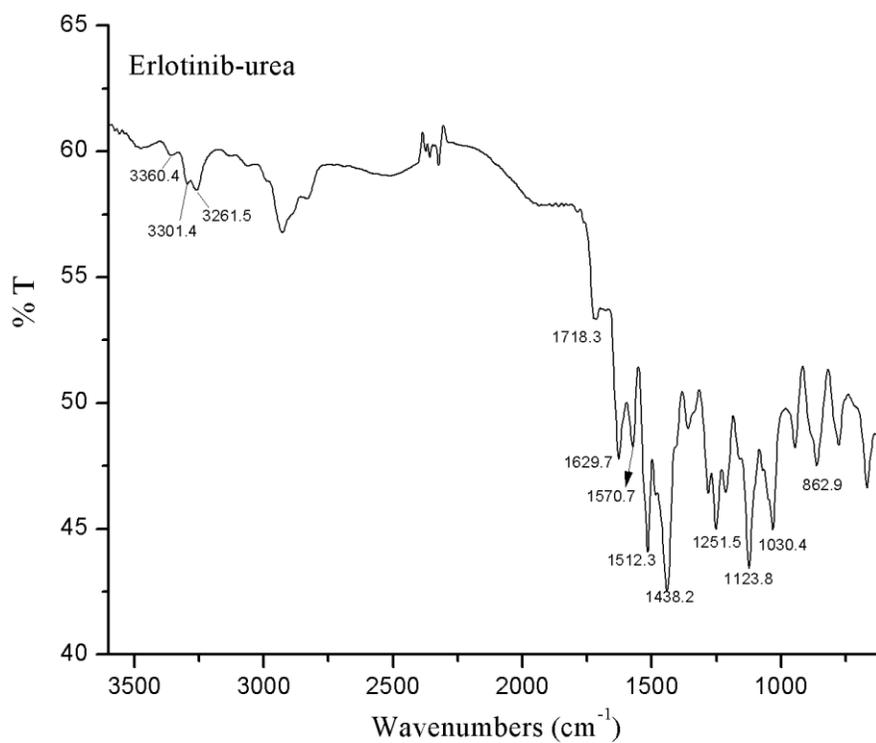
**Figure S2** PXR D (red trace) comparison of ETB and its cocrystals/salts with their calculated X-ray (blue trace) patterns indicate the new solid phases.



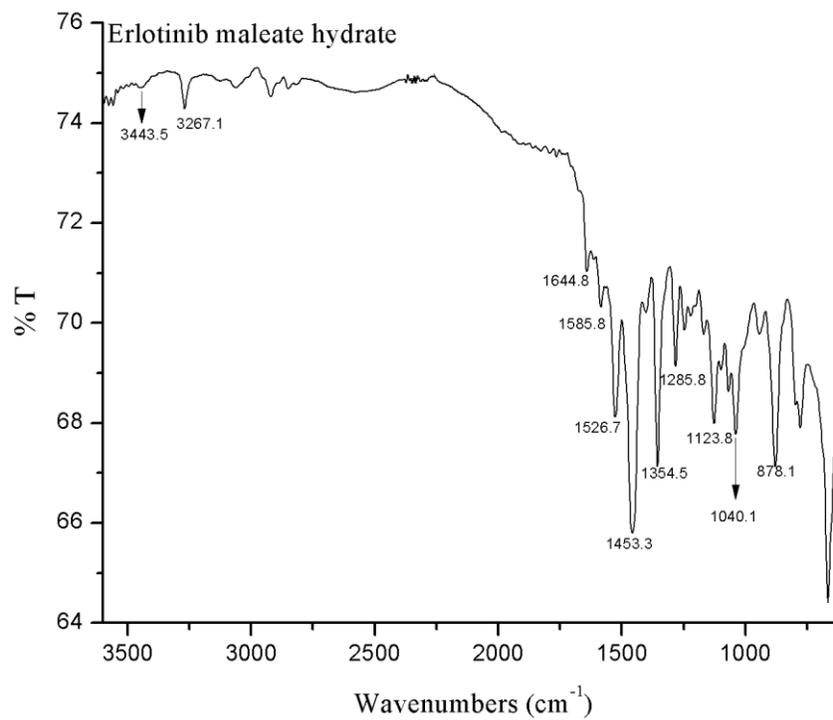
(a)



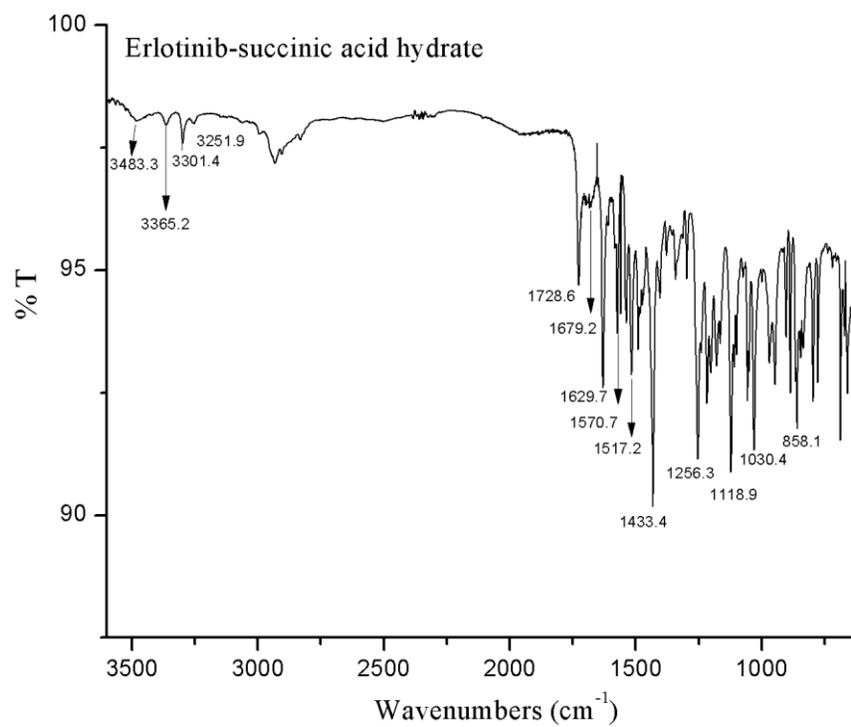
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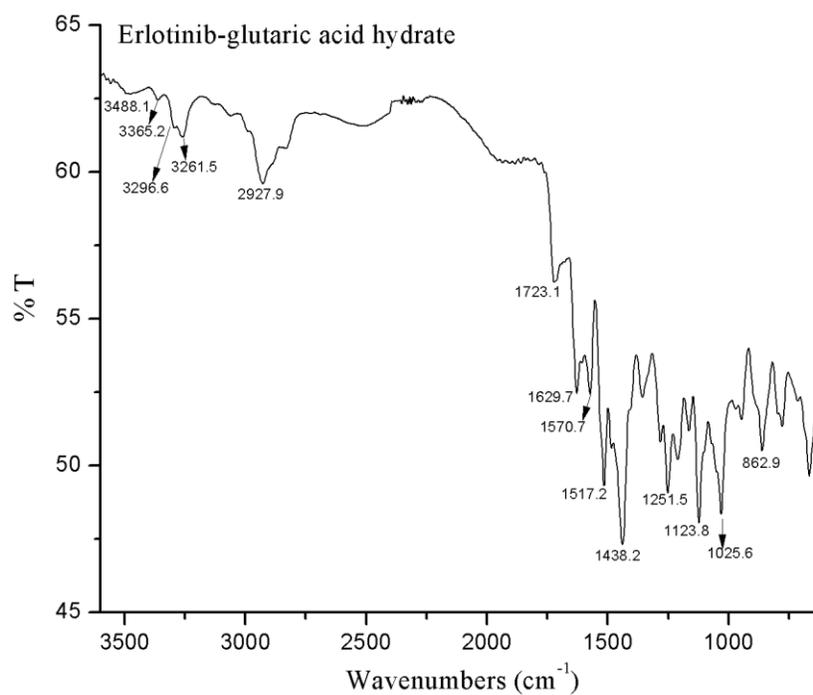
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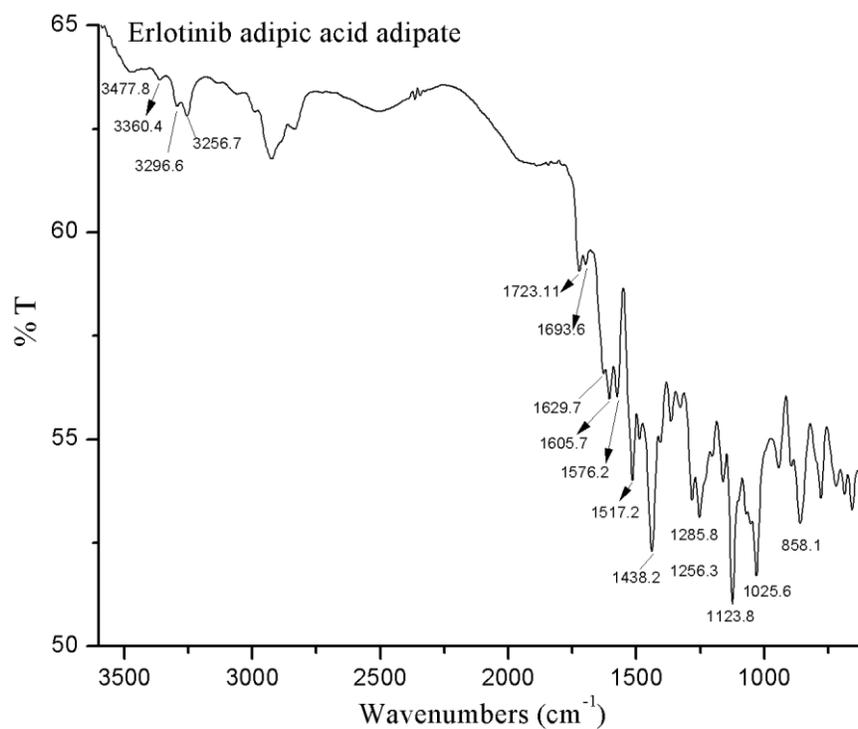
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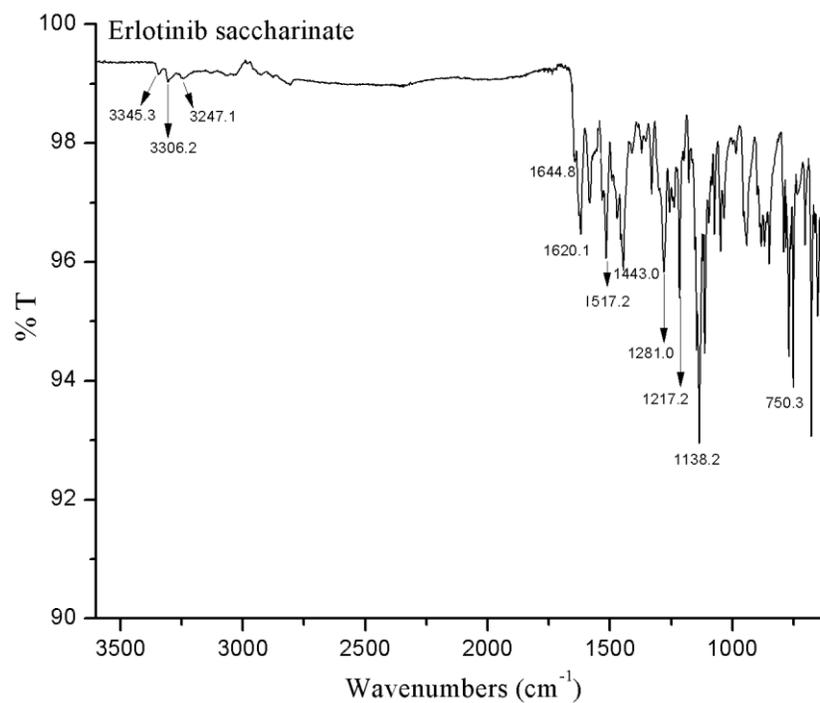
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(f)

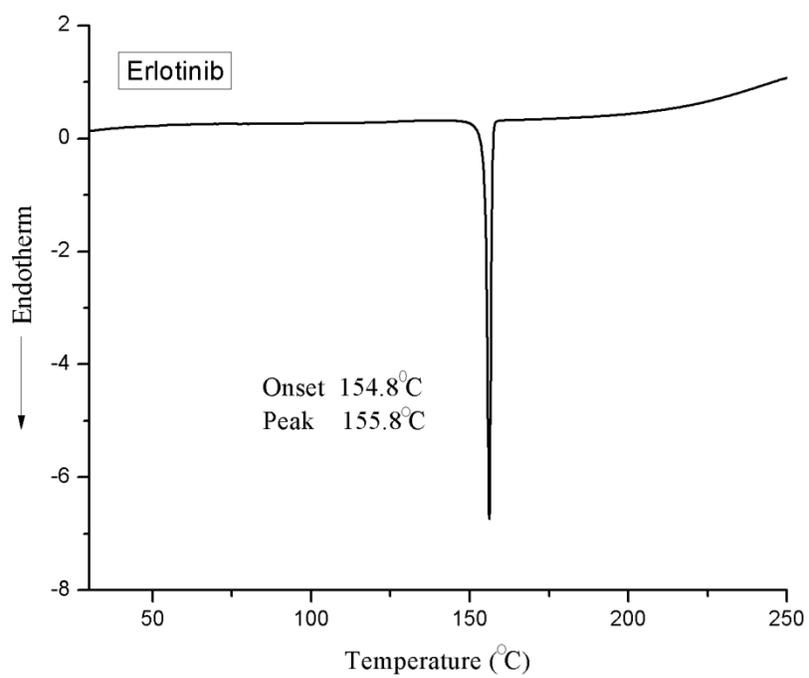


(g)

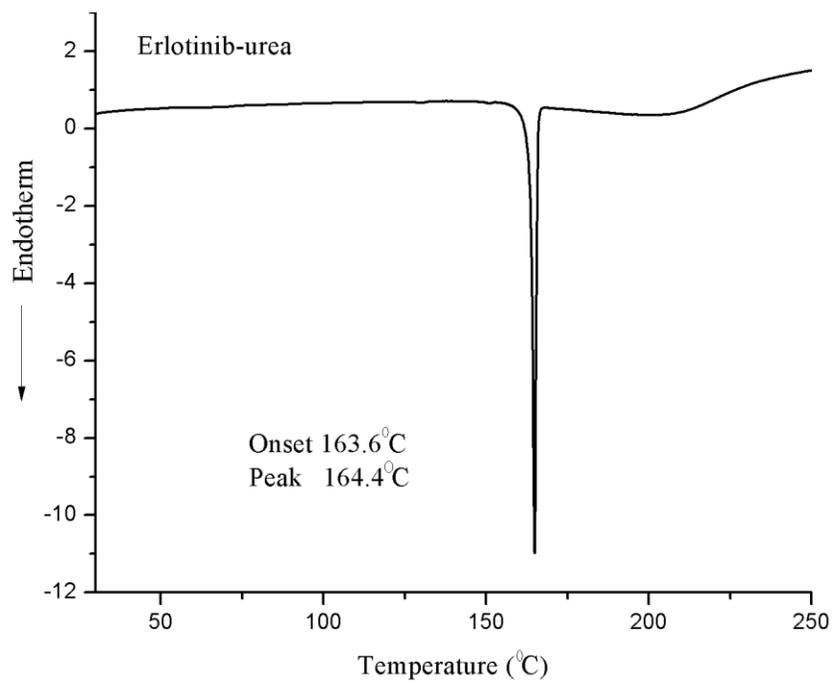


(h)

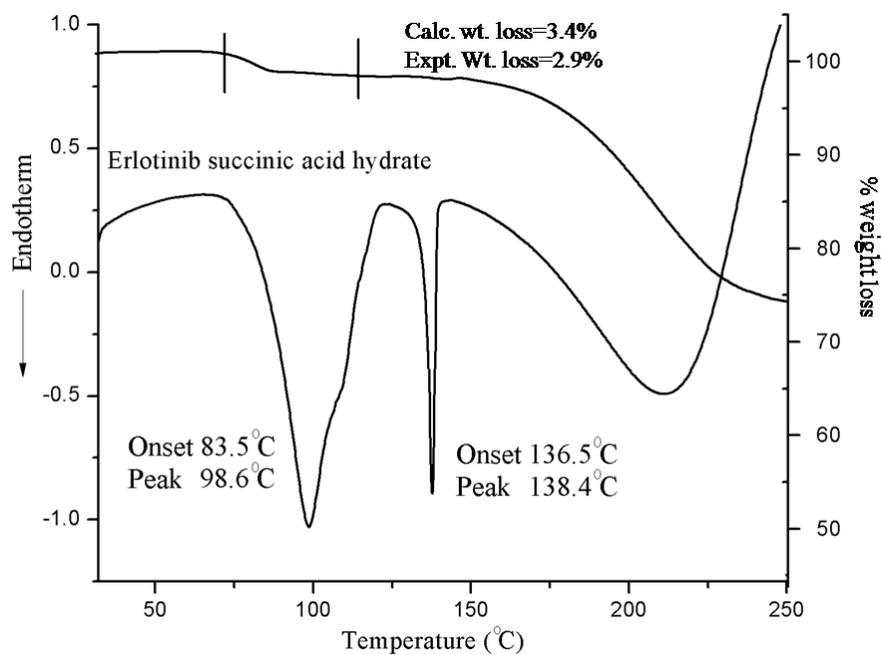
**Figure S3** FT-IR spectra of ETB salts and cocrystals. The IR of the cocrystals (c, e-g) consists of humps at  $\sim 2000$  and  $2500\text{ cm}^{-1}$  indicating the acid-pyridine heterosynthon. However, in the salts (b, d, h), the two broad peaks were not observed.



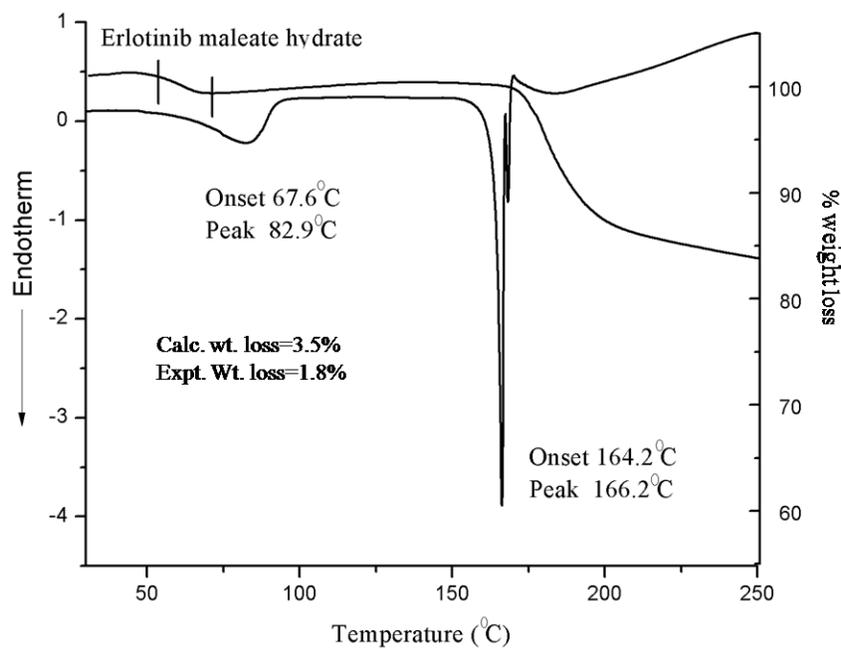
(a)



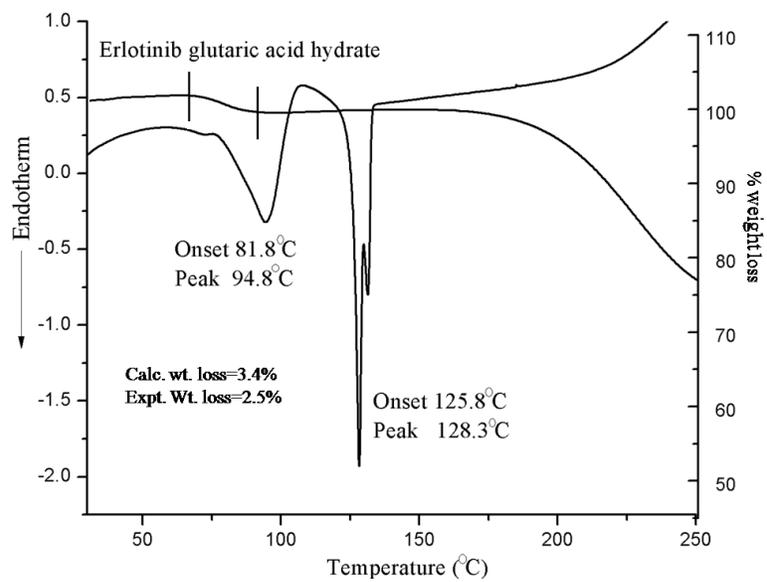
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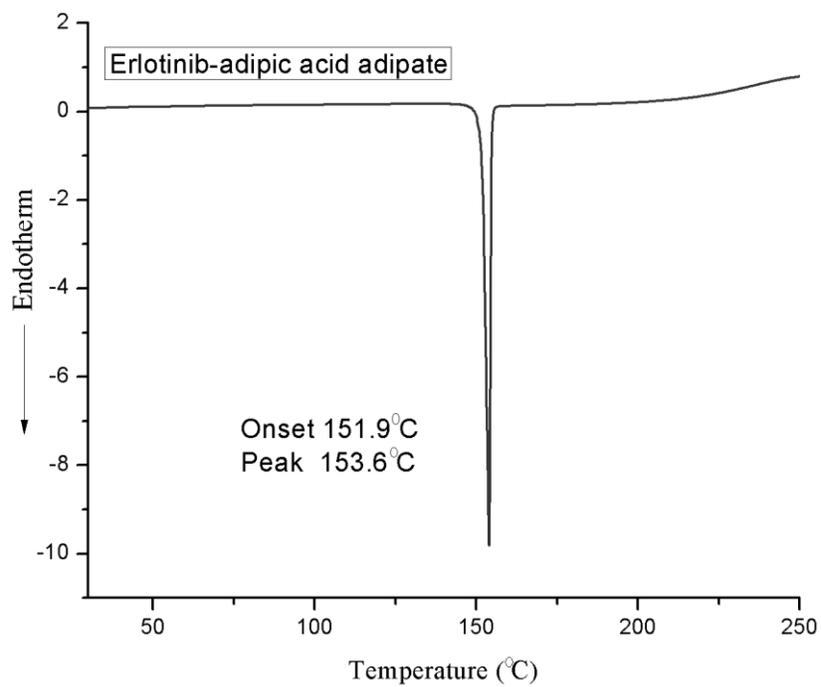
(c)



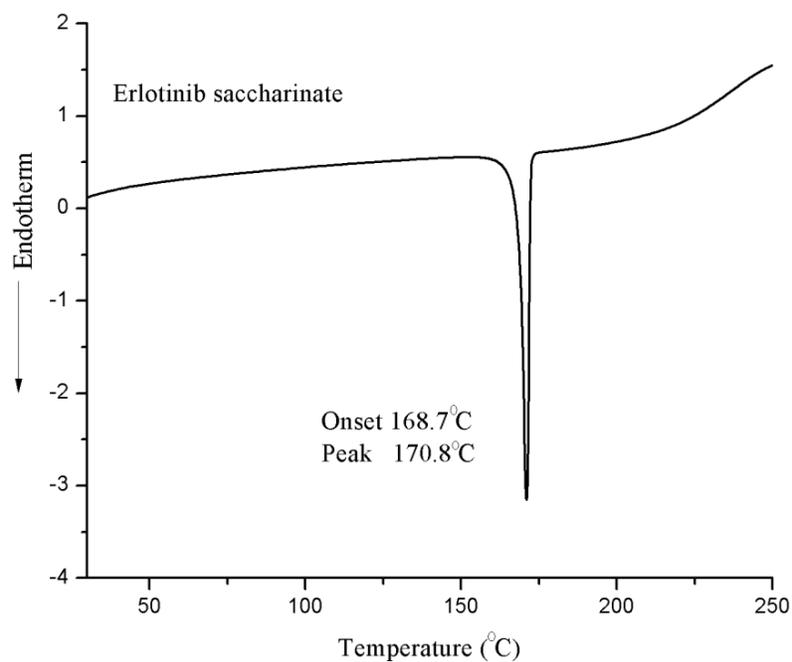
(d)



(e)



(f)



(g)

**Figure S4** DSC endotherms and TGA snaps of erlotinib new multi-component systems. TGA indicates there is a possibility of hemihydrate for the maleate salt.