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Physicochemical and Thermodynamic Evaluation of Ibrutinib Cocrystal Formation with a Long Chain Fatty Acid

Shubhanshu Ranjan Tiwari, Shanmukha Prasad Gopi, Divya Jyothi Kallem, Deepika Chaturvedi, Raja Sekhar Voguri, Srividya Ramakrishnan, Archan Dey, Sharmistha Pal**

IPDO, Dr. Reddys Laboratory, Bachupally, Hyderabad, Telangana, India

Corresponding Author: archan_dey@yahoo.co.in; sharmisthapaldatta@drreddys.com

Supporting Information

Table S1. Crystallographic data of polymorphs and solvates of Ibrutinib

Parameters	Solvates										Anhydrous polymorphs	
Name	4-hydroxy-4-methylpentan -2-one[1]	Dioxolane[1]	Trifluoro toluene[1]	O-Xylene[1]	M-Xylene[1]	P-Xylene[1]	Anisole[1]	Chlorobenzene[1]	Fluorobenzene[2]	Methanol[3]	Ibrutinib polymorph A[3]	Ibrutinib polymorph C[3]
CCDC	HAWLOJ	HAWLID	HAWMIE	HAWMAW	HAWLUP	HAWMEA	HAWLAV	HAWLEZ	LAGVEY	RUYDEW	BETXEG	BETXEG01
Formula	$C_{25}H_{24}N_6O_2$. $C_6H_{12}O_2$	$C_{25}H_{24}N_6O_2 \cdot C_3H_6O_2$	$C_{25}H_{24}N_6O_2$. $C_6H_5CF_3$	$C_{25}H_{24}N_6O_2$. $C_6H_4(CH_3)_2$	$C_{25}H_{24}N_6O_2$. $C_6H_4(CH_3)_2$	$C_{25}H_{24}N_6O_2$. $C_6H_4(CH_3)_2$	$C_{25}H_{24}N_6O_2$. $CH_3OC_6H_5$	$C_{25}H_{24}N_6O_2$. C_6H_5Cl	$C_{25}H_{24}N_6O_2 \cdot C_6H_5F$	$C_{25}H_{24}N_6O_2 \cdot CH_3OH$	$C_{25}H_{24}N_6O_2$	$C_{25}H_{24}N_6O_2$
Formula weight	570.64	514.59	586.61	546.64	546.66	546.68	548.64	553.05	536.6	472.54	440.50	440.50
Crystal system	triclinic	triclinic	triclinic	triclinic	triclinic	triclinic	triclinic	triclinic	triclinic	triclinic	monoclinic	triclinic
Space group	*P*1	*P*1	*P*1	*P*1	*P*1	*P*1	*P*1	*P*1	P1	*P*1	$P2_1$	*P*1
a (Å)	10.7491(2)	9.9709(2)	10.9962(2)	11.3206(2)	10.1055(2)	10.1530(3)	9.9939(2)	11.0598(4)	9.6355 (2)	9.6578(3)	14.2459(10)	9.7764(10)
b (Å)	11.6814(2)	14.8343(2)	11.9991(2)	15.6063(3)	10.4590(2)	10.7810(2)	10.2957(2)	11.8540(4)	11.0547 (2)	9.8034(3)	10.1261(10)	10.0551(11)
c (Å)	13.4100(3)	17.4937(2)	12.0896(2)	16.6997(3)	13.8796(2)	14.5247(3)	13.9251(3)	11.9400(4)	14.2260 (3)	15.0204(5)	30.8586(10)	13.459(2)
α (deg)	75.3769(17)	80.5116(11)	79.7179(16)	87.2953(13)	95.3990(12)	82.5381(19)	94.7775(17)	81.279(3)	73.2323 (18)	105.705(3)	90	90.959(11)
β (deg)	69.4688(17)	78.5650(13)	71.7985(18)	76.7525(15)	100.2221(15)	71.019(2)	100.3620(17)	67.786(3)	82.1198 (15)	95.072(2)	96.908(10)	110.369(12)
γ (deg)	64.9843(17)	74.3710(14)	69.0665(19)	79.8121(15)	116.7545(18)	77.858(2)	116.113(2)	72.096(3)	66.0320 (19)	111.523(3)	90	112.917(10)
V (Å^3)	1418.14(3)	2425.30(7)	1411.29(2)	2826.52(5)	1263.623(18)	1466.54(3)	1243.99(3)	1377.89(5)	1325.44 (5)	1245.28(8)	4419.2(6)	1124.5(3)
Z	2	4	2	4	1	2	1	2	2	1	2	1
CCDC no.	1525561	1525560	1525565	1525563	1525562	1525564	1525558	1525559	1955809	1559243	1559244	1559242

Note: Ibrutinib-nicotinic acid eutectic cocrystal is reported to have has a chiral space group $P2_1$ with cell parameters of: α=90.00°, β=101.19°, γ =90.00° [4]

Table S2. Crystallographic data of palmitic acid[5]

Palmitic acid Form	YEFWEM01
Empirical formula	C16H31O2H
Formula weight	256.4
Crystal system	Orthorhombic
Space group	P21/c
a (Å)	35.72(1)
b (Å)	4.975(1)
c (Å)	9.439(1)
α (deg)	90
β (deg)	90.38
γ (deg)	90
V (Å^3)	1677.2
Z	4
CCDC no.	738619

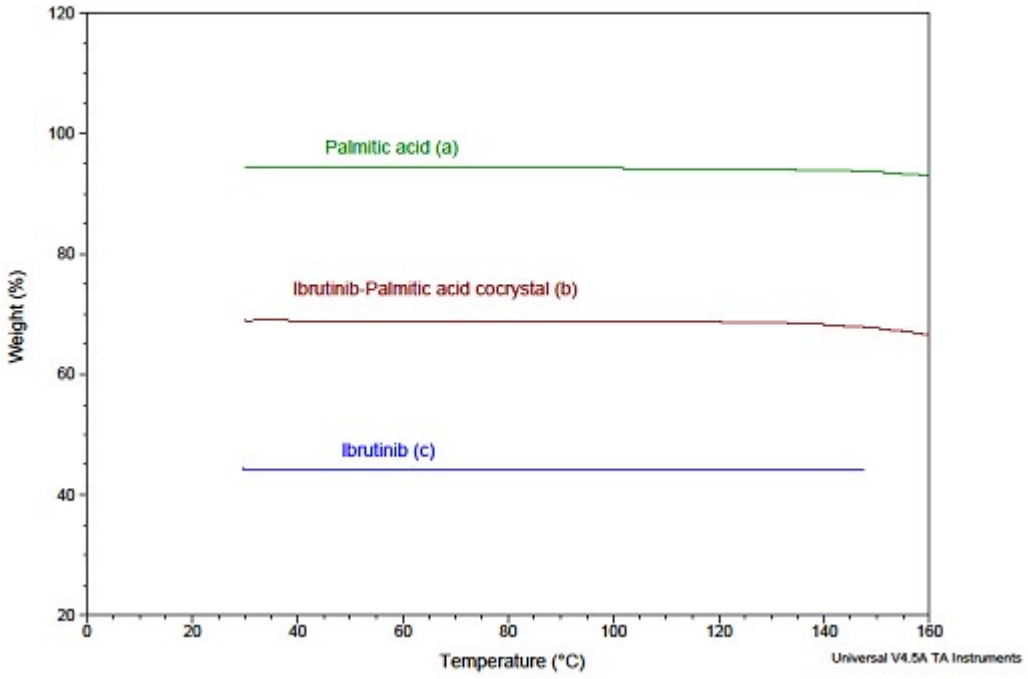

Figure S1. TGA of (a) Palmitic acid, (b) IBT-PAL cocrystal, (c) Ibrutinib

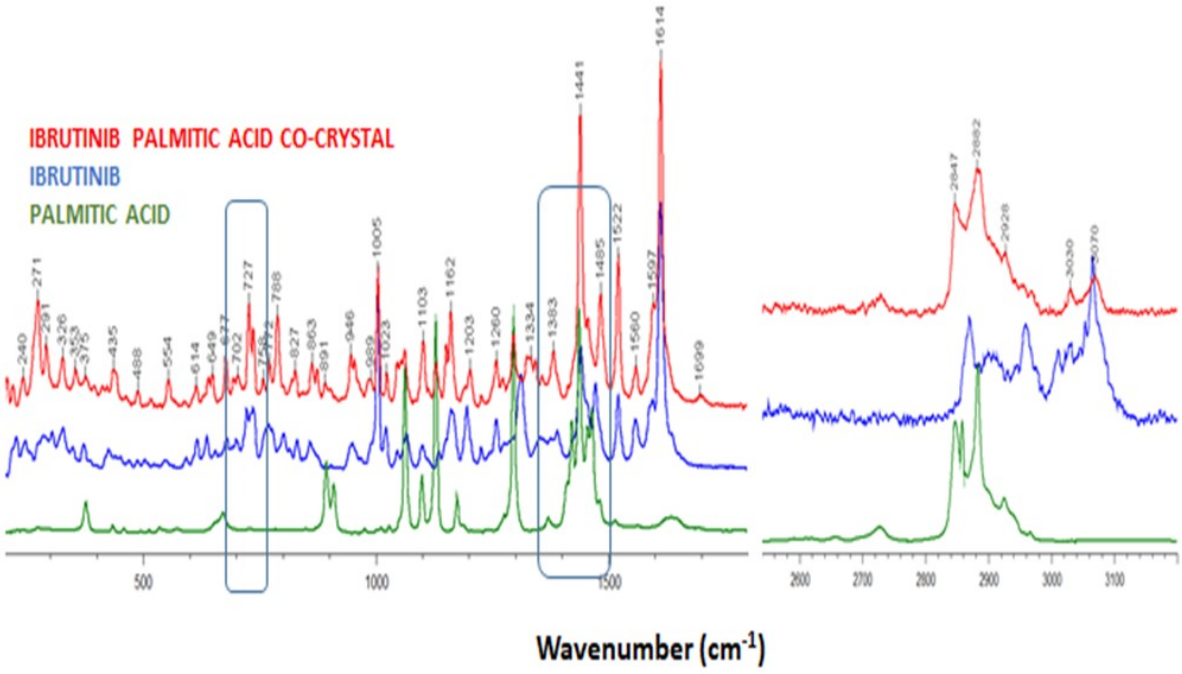

Figure S2. Raman spectra of Ibrutinib, Palmitic acid and IBT-PAL cocrystal

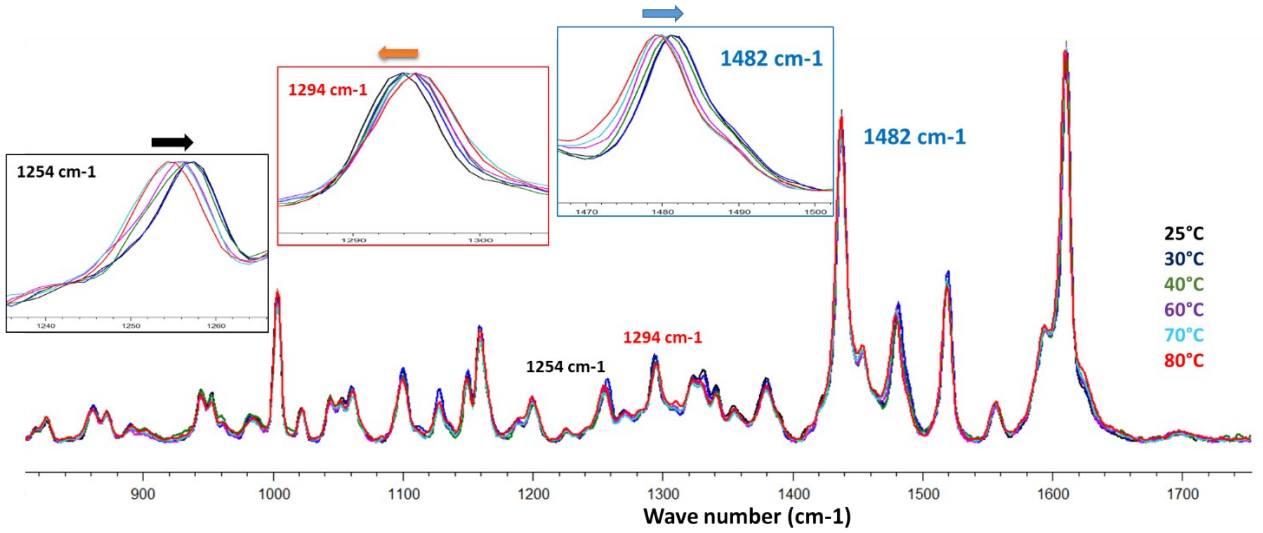

Figure S3. Overlay of variable temperature Raman study of IBT-PAL cocrystal.

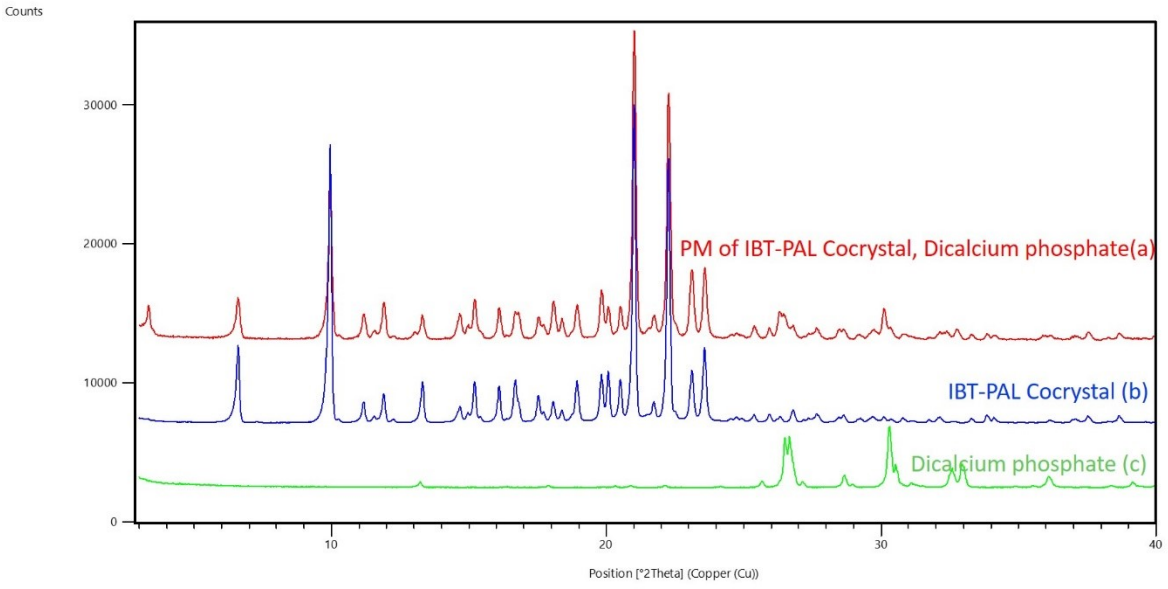

Figure S4. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, dicalcium phosphate

exposed to 30±2 °C/80 % RH for 30 days, b) IBT-PAL cocrystal and c) Dicalcium phosphate

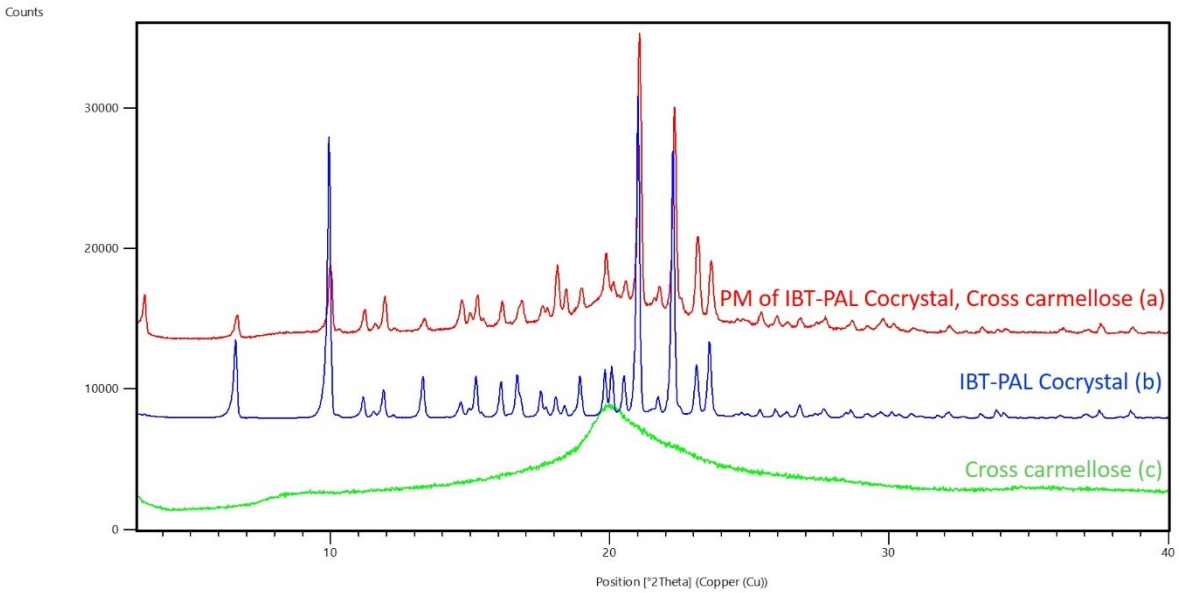

Figure S5. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, cross carmellose exposed to 30±2 °C/80 % RH for 30 days, b) IBT-PAL cocrystal and c) Cross carmellose

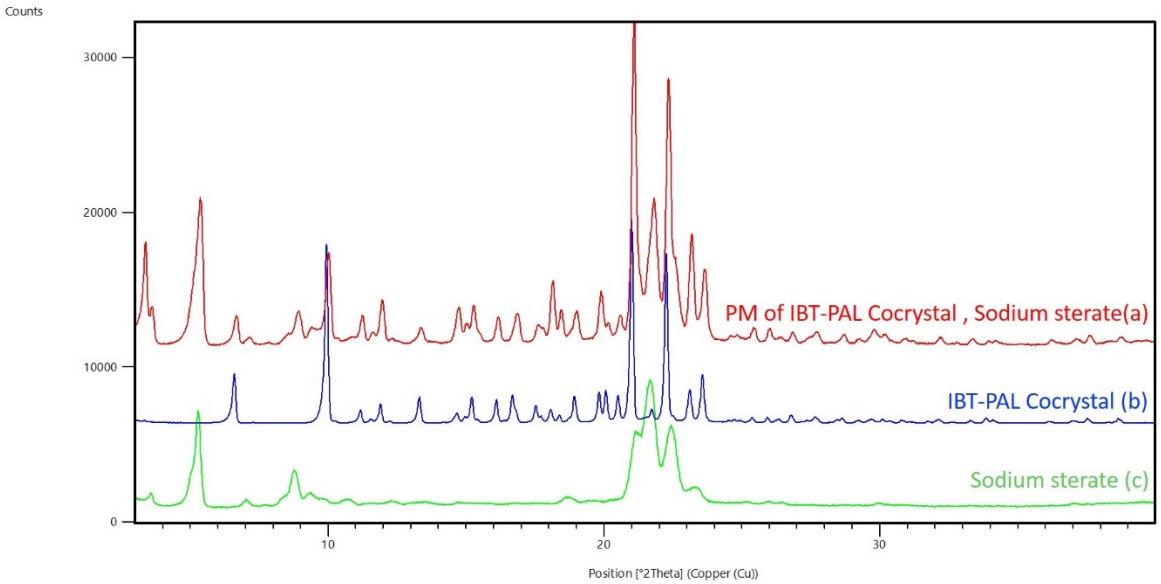

Figure S6. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, sodium sterate exposed to 30±2 °C/80 % RH for 30 days b) IBT-PAL cocrystal and c) Sodium sterate

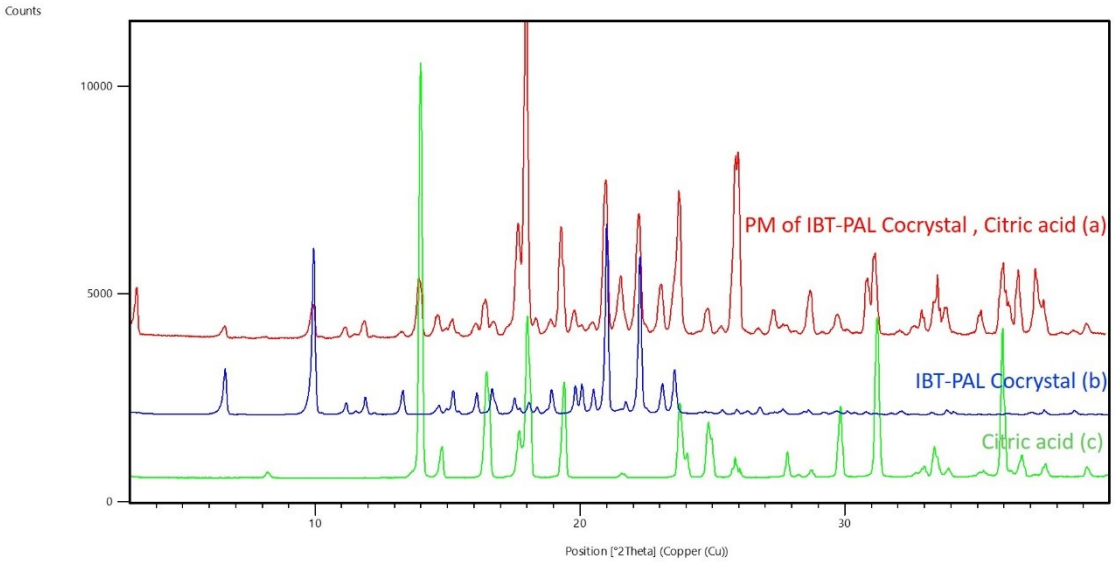

Figure S7. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, citric acid exposed to 30±2 °C/80 % RH for 30 days, b) IBT-PAL cocrystal and c) Citric acid

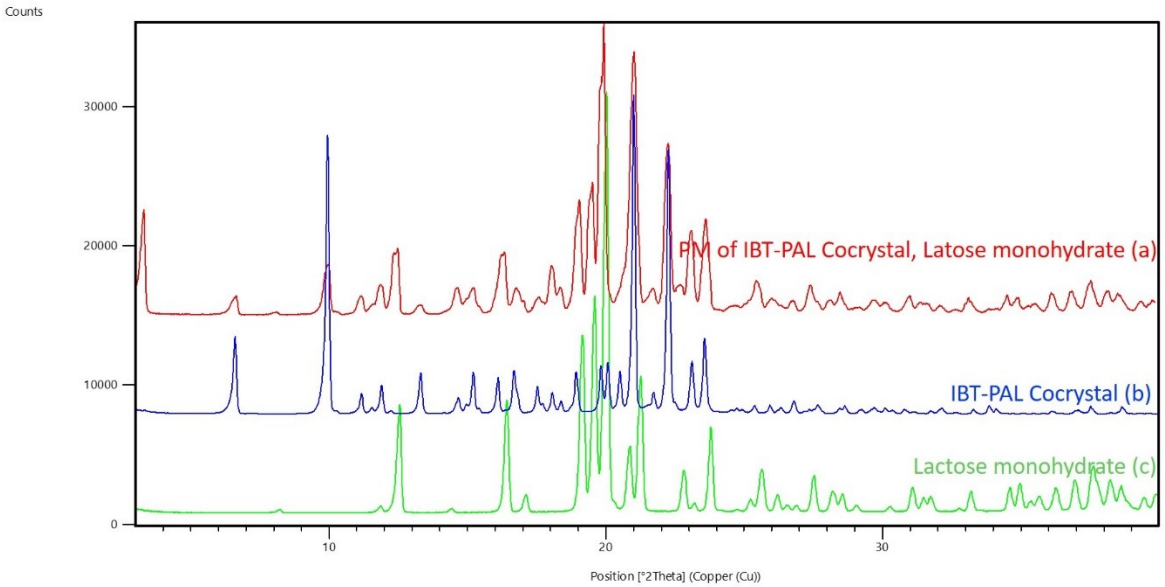

Figure S8. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, lactose monohydrate exposed to 30±2 °C/80 % RH for 30 days, b) IBT-PAL cocrystal and c) Lactose monohydrate

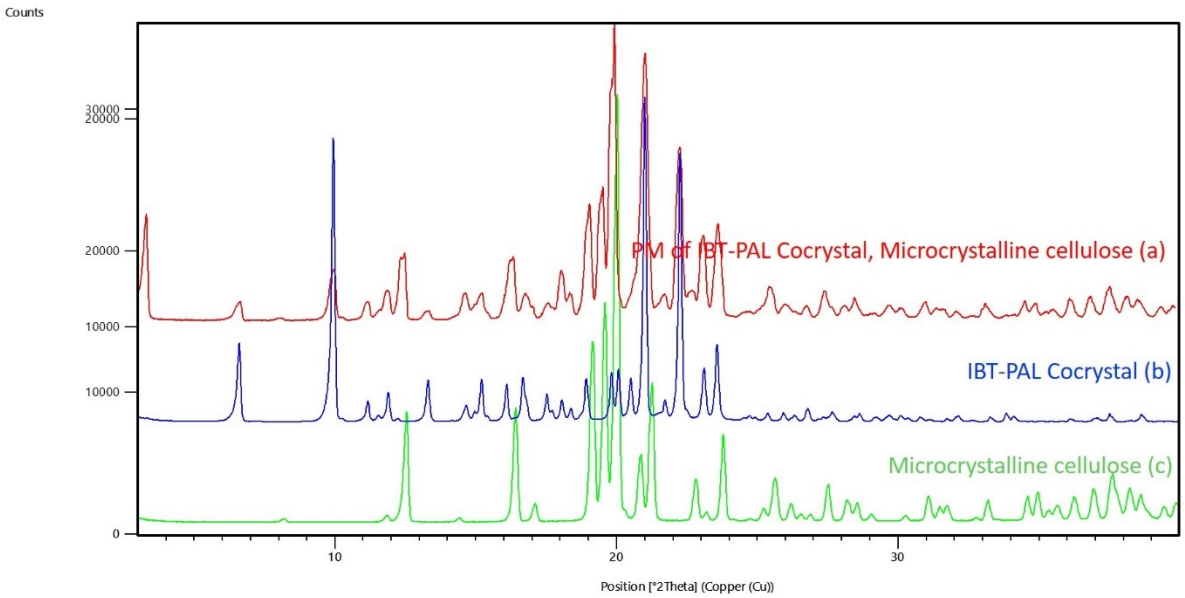

Figure S9. PXRD of a) Physical mixture (PM) of IBT-PAL cocrystal, microcrystalline cellulose exposed to 30±2 °C/80 % RH for 30 days, b) IBT-PAL cocrystal and c) Microcrystalline cellulose

References

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