Electronic Supporting Information (ESI)

Adaptability of aripiprazole towards forming isostructural hydrogen bonding networks in multi-component salts: a rare case of strong O–H···O$^-$ ↔ weak C–H···O mimicry.

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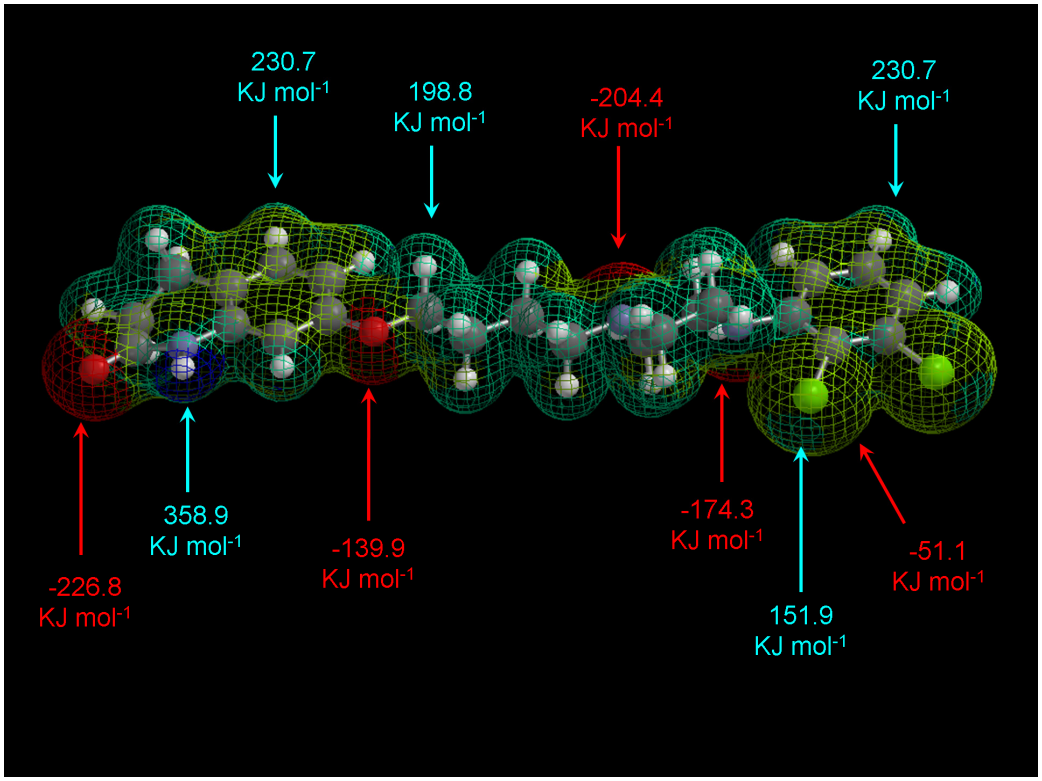
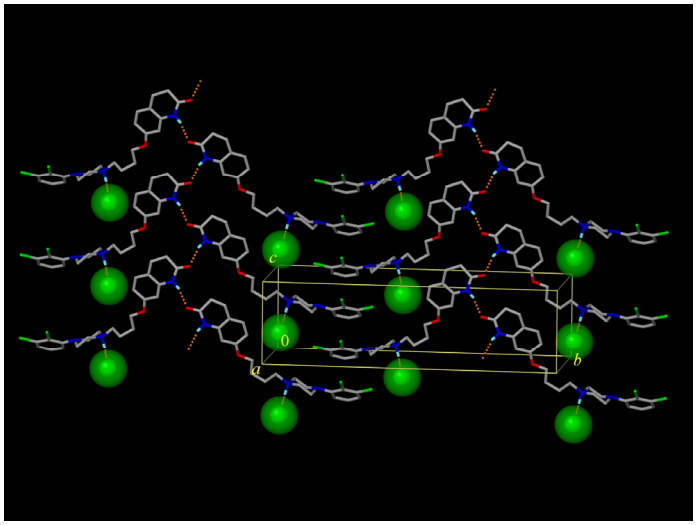


Figure S1. Electrostatic surface potential (ESP) map on the energy minimized aripiprazole. The red regions indicate electron rich and blue region indicates electron deficient and the colors from blue to green forms the continuum. The order of the acceptor groups derived from electrostatic surface potential is, amide O (-226.8 KJ mol^{-1}) > piperazinyl nitrogen attached alkyl group (N-alkyl, -204.4 KJ mol^{-1}) > piperazinyl nitrogen attached to phenyl (N-phenyl, -174.3 KJ mol^{-1}) > alkyl chain O (-139.9 KJ mol^{-1}) > phenyl Cl (-51.1 KJ mol^{-1}), and the order of the donor groups is, amide N-H (+358.9 KJ mol^{-1}) > aromatic C-H (+230.7 KJ mol^{-1}) > alkyl C-H (+198.8 KJ mol^{-1}) > phenyl Cl (+151.9 KJ mol^{-1}). The chlorine atoms play a dual role of both donor and acceptor due to the anisotropy of the electron distribution on the chlorine atom. It has -51.1 KJ mol^{-1} at the periphery and +151.9 KJ mol^{-1} at the centre of the halogen atom.



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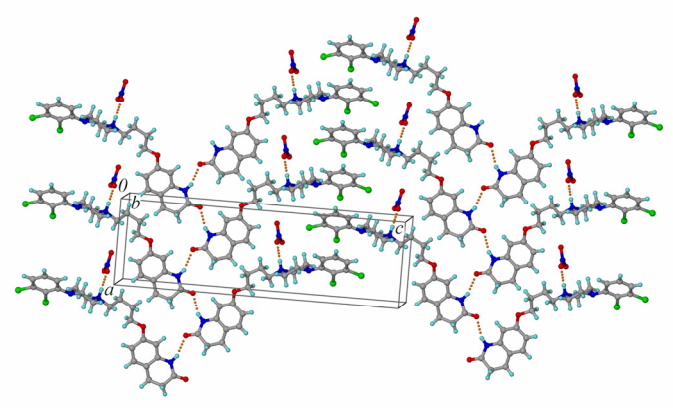

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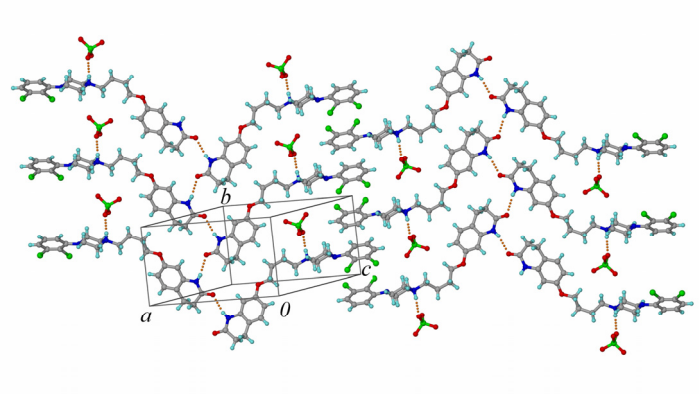
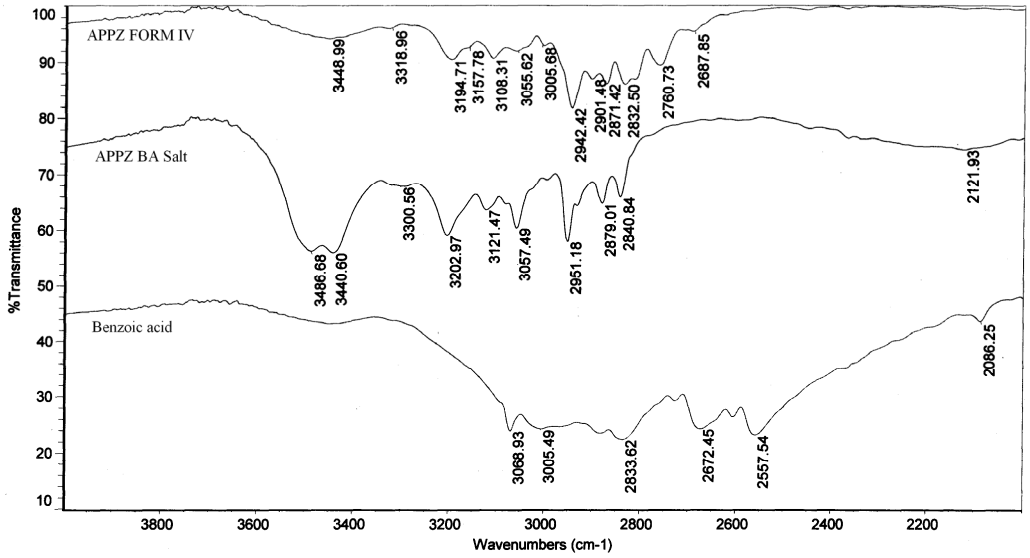


(c)

Figure S2. (a) Crystal packing diagram of aripiprazole hydrochloride salt (IV). (b) Aripiprazole nitrate salt.[11a] (b) Aripiprazole perchlorate salt.[11b] All three structures contain a twisted conformation and form amide N–H···O catemer. The space created due to twisting of the molecule has been used for accommodating the anionic counter ions and for close packing of the phenyl rings.



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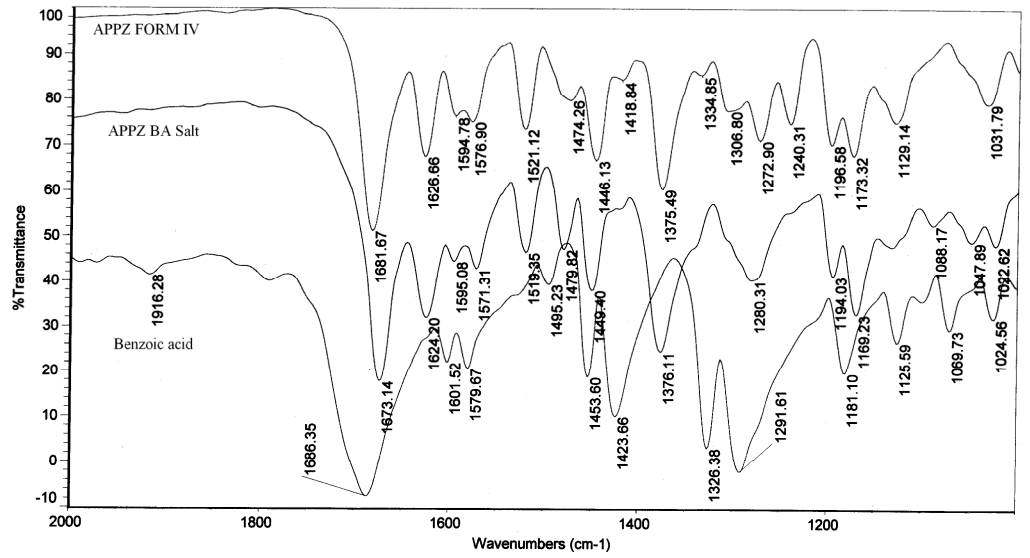
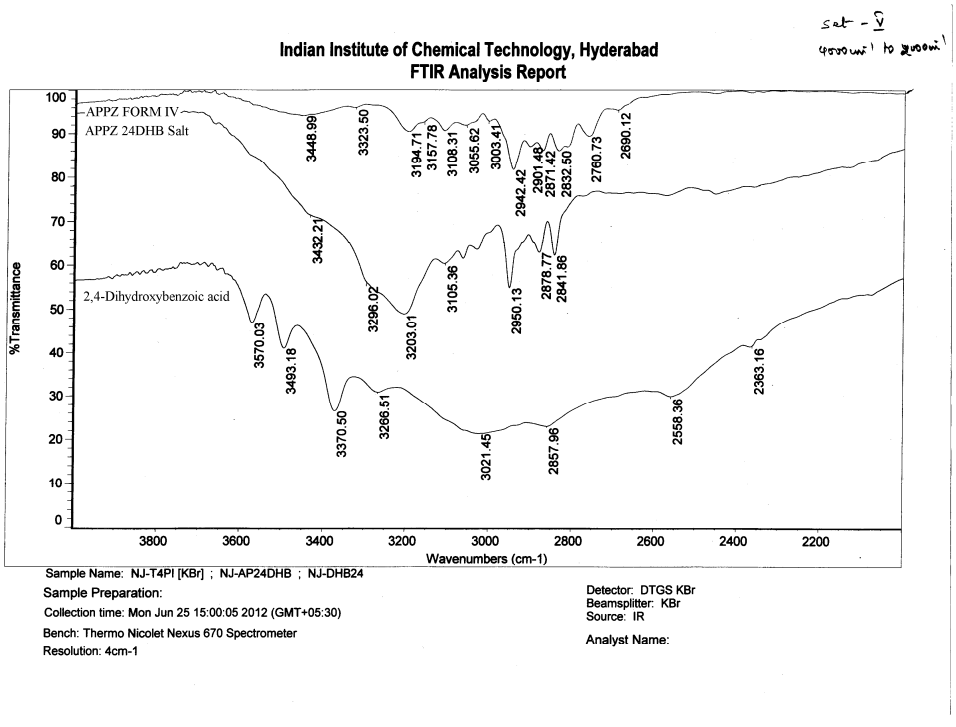


(b)

Figure S3. An overlay of FT-IR spectra on aripiprazole form IV, aripiprazole benzoate monohydrate, and benzoic acid. (a) Region 4000-2000 cm^{-1}. (b) Region 2000-1000 cm^{-1}. Upon protonation of N-alkyl of aripiprazole, the appearance of N^{+}–H vibrational mode band at ~2121.9 cm^{-1} is noticed. The carbonyl peak of the benzoic acid at 1688.3 cm^{-1} has moved towards lower frequency. The presence of water in the benzoate salt is identified from the peak at 3488.6 cm^{-1}.



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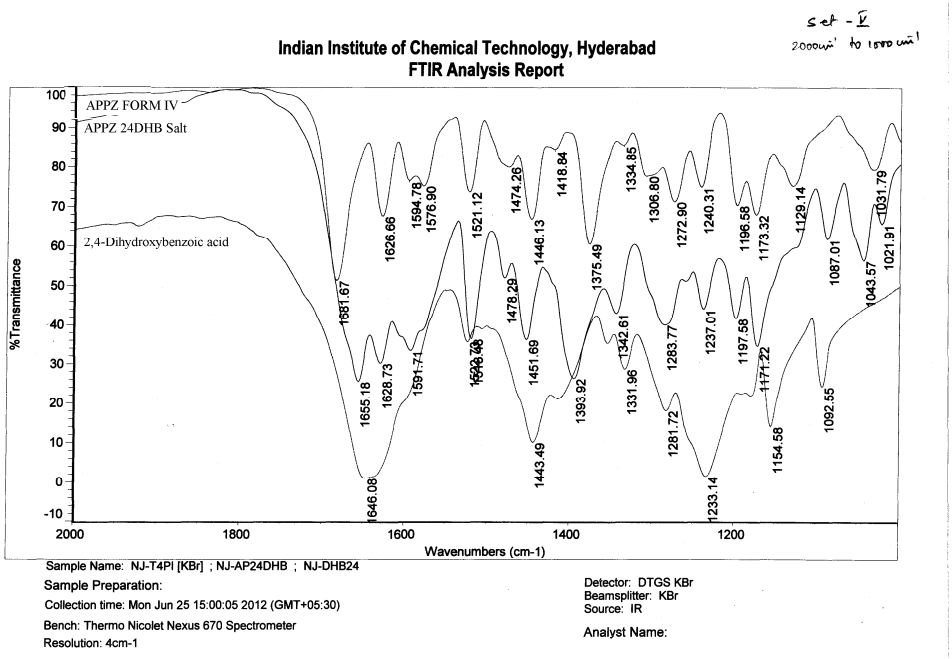
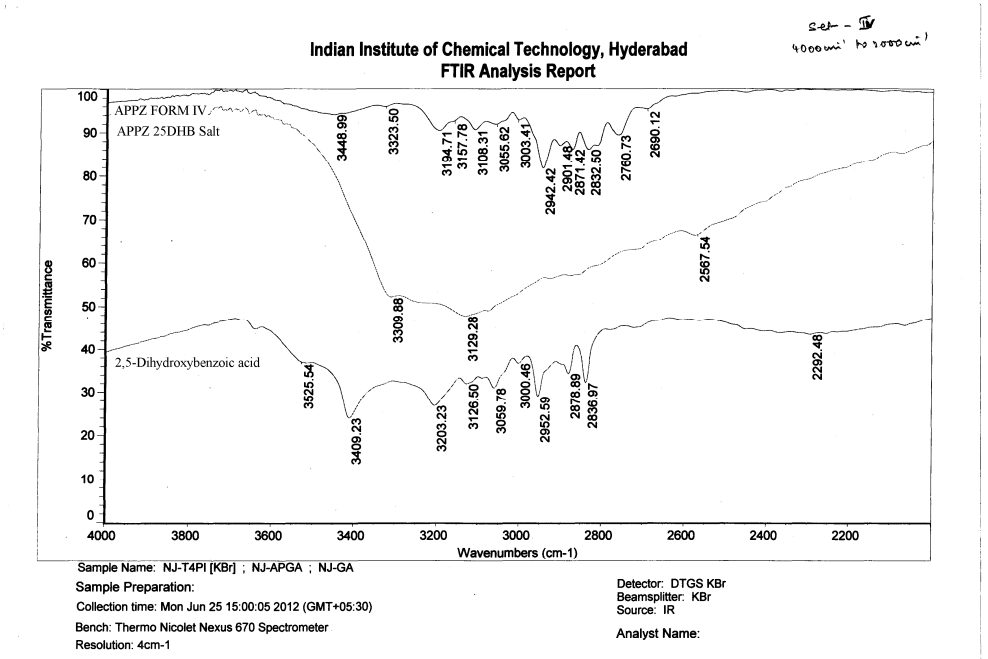


(b)

Figure S4. An overlay of FT-IR spectra on Aripiprazole form IV, Aripiprazole 2,4-dihydroxy benzoate and 2,4-dihydroxy benzoic acid. (a) Molecular region 4000-2000 cm^{-1}. (b) Molecular region 2000-1000 cm^{-1}.



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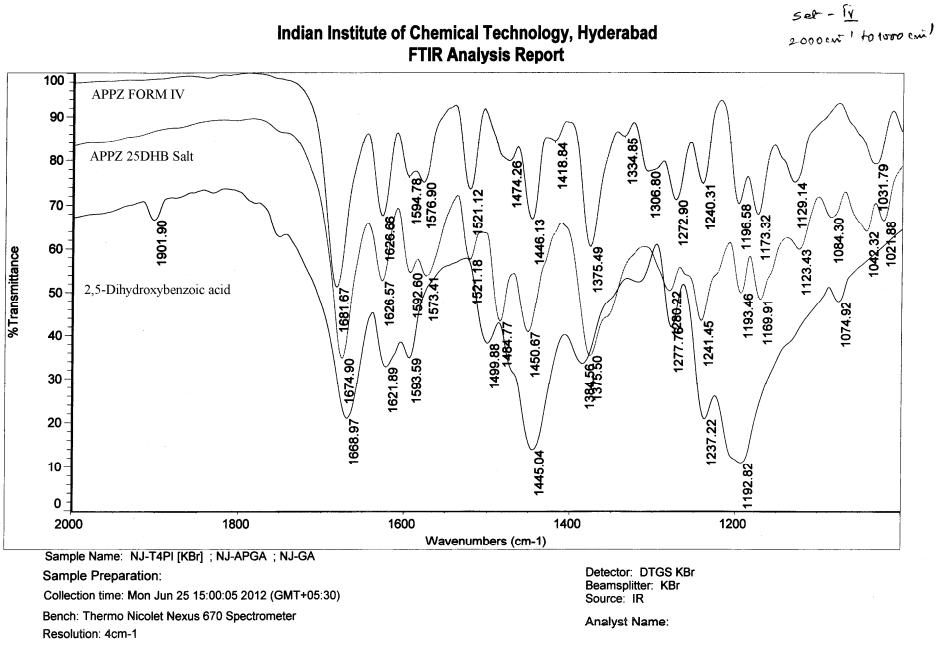
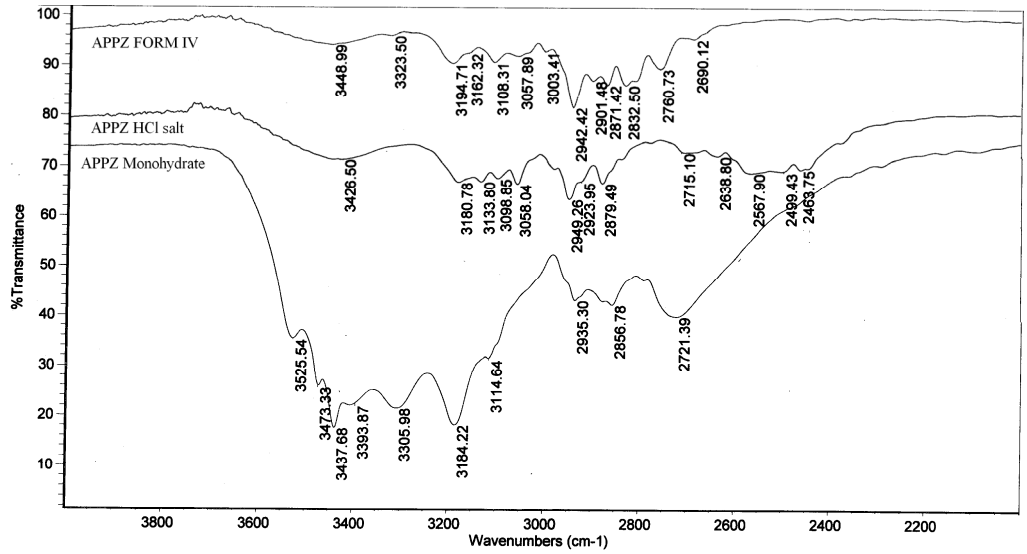


(b)

Figure S5. An overlay of FT-IR spectra on Aripiprazole form IV, Aripiprazole 2,5-dihydroxy benzoate hemihydrate and 2,5-dihydroxy benzoic acid. (a) Molecular region 4000-2000 cm^{-1}. (b) Molecular region 2000-1000 cm^{-1}.



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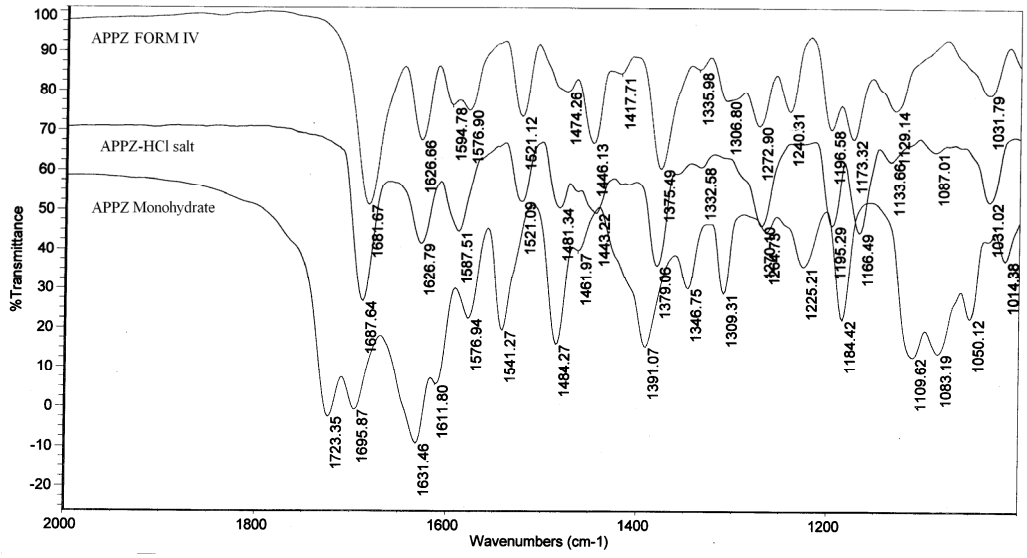
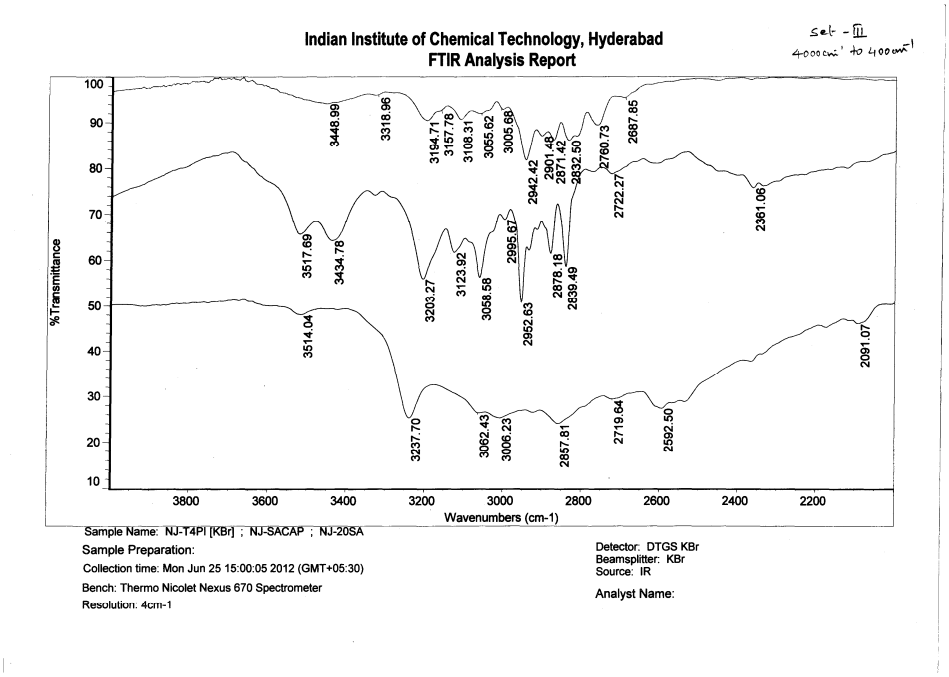


(b)

Figure S6. An overlay of FT-IR spectra on aripiprazole form IV, aripiprazole hydrochloride salt (IV), and aripiprazole monohydrate. (a) Region 4000-2000 cm^{-1}. (b) Region 2000-1000 cm^{-1}. Upon protonation of N-alkyl of aripiprazole, the appearance of N^{+}–H vibrational mode band at ~2500 cm^{-1} is a clear indicative of hydrochloride salt formation.



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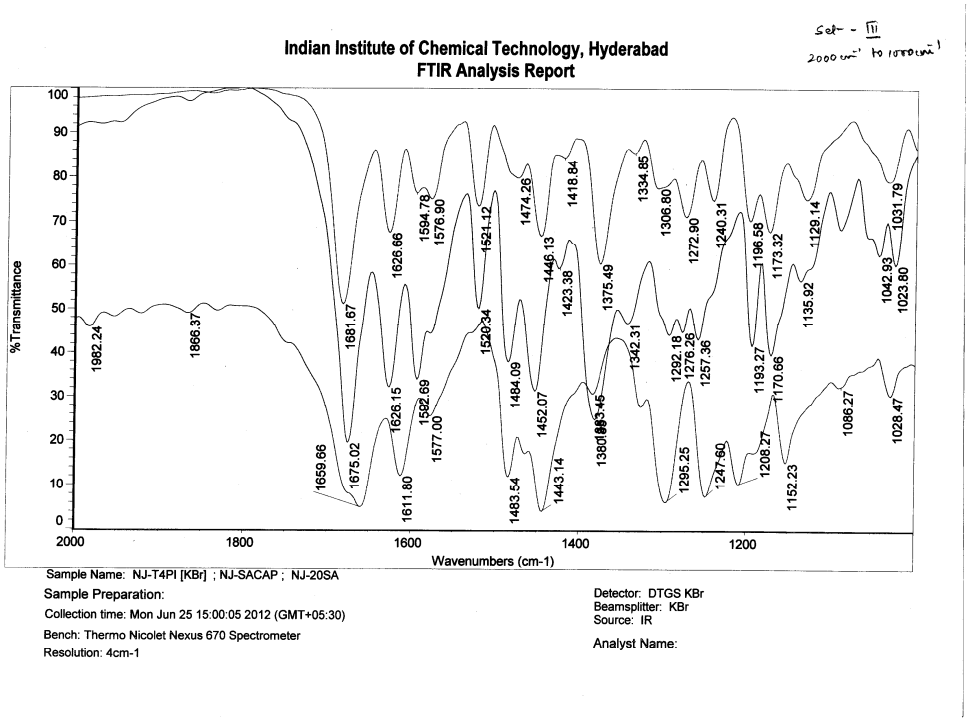
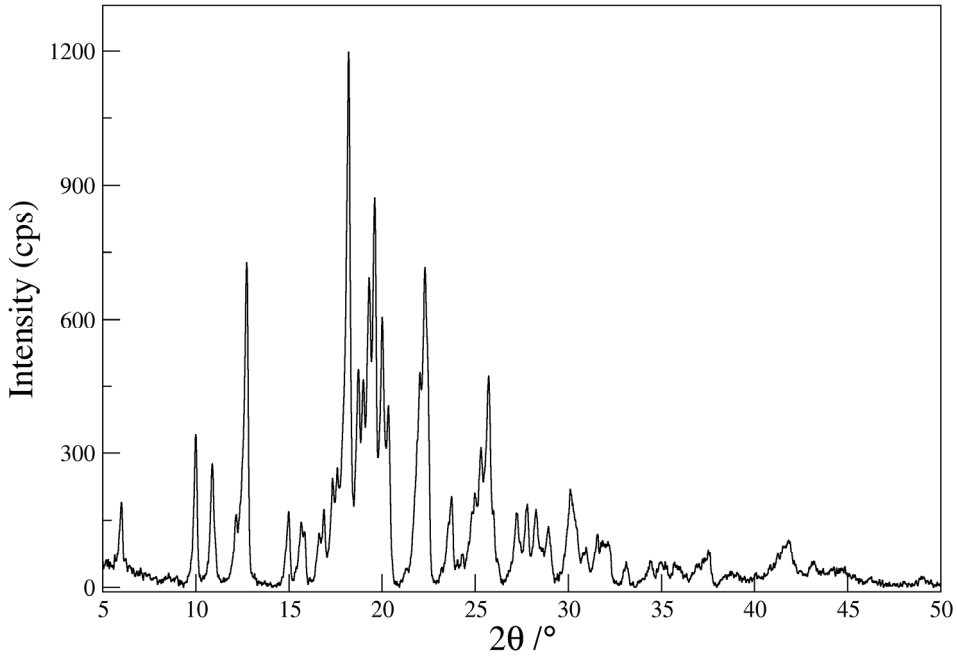


(b)

Figure S7. An overlay of FT-IR spectra on Aripiprazole form IV, Aripiprazole 2-dihydroxy benzoate (salicylate) and salicylic acid. (a) Molecular region 4000-2000 cm^{-1}. (b) Molecular region 2000-1000 cm^{-1}.



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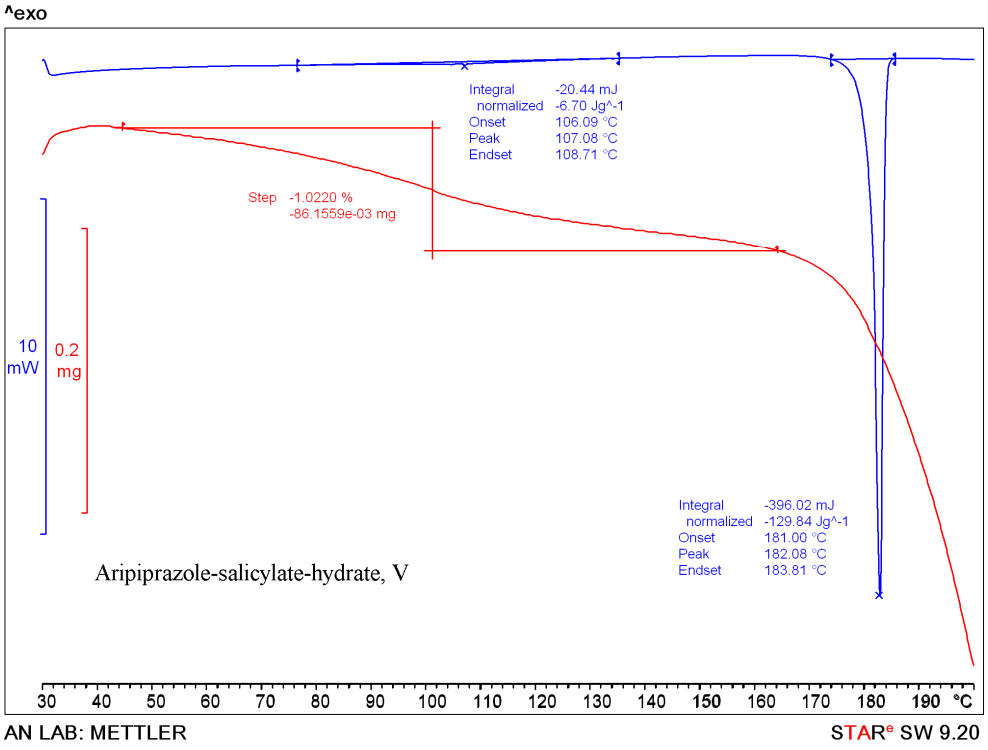
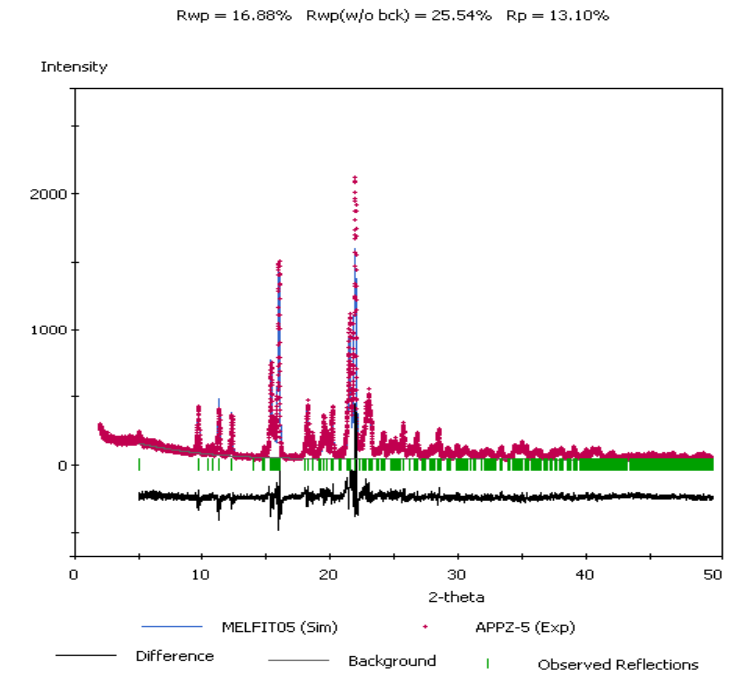


(b)

Figure S8. (a) PXRD of aripiprazole-salicylate (V) bulk material. (b) DSC and TGA of aripiprazole-salicylate crystals. Thermal analysis indicated that V is hydrate, which contains 1.02% water content in its crystal structure.



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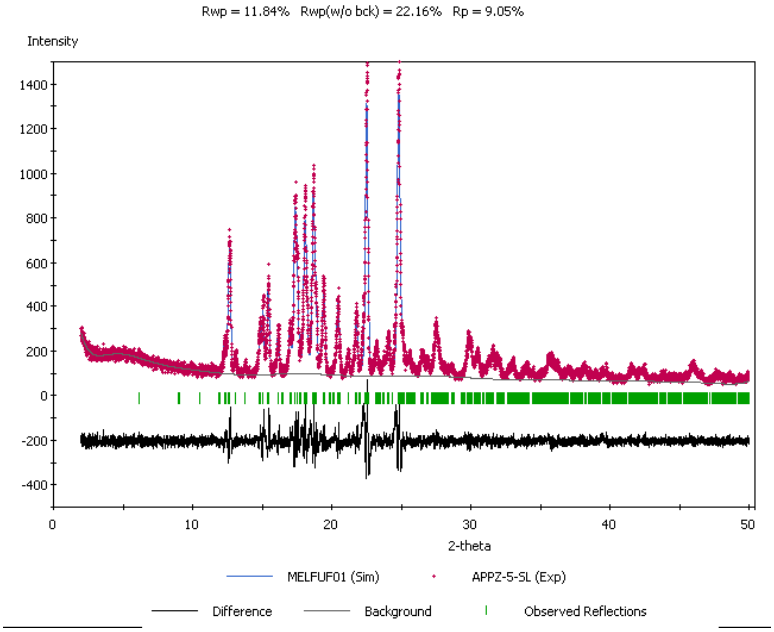
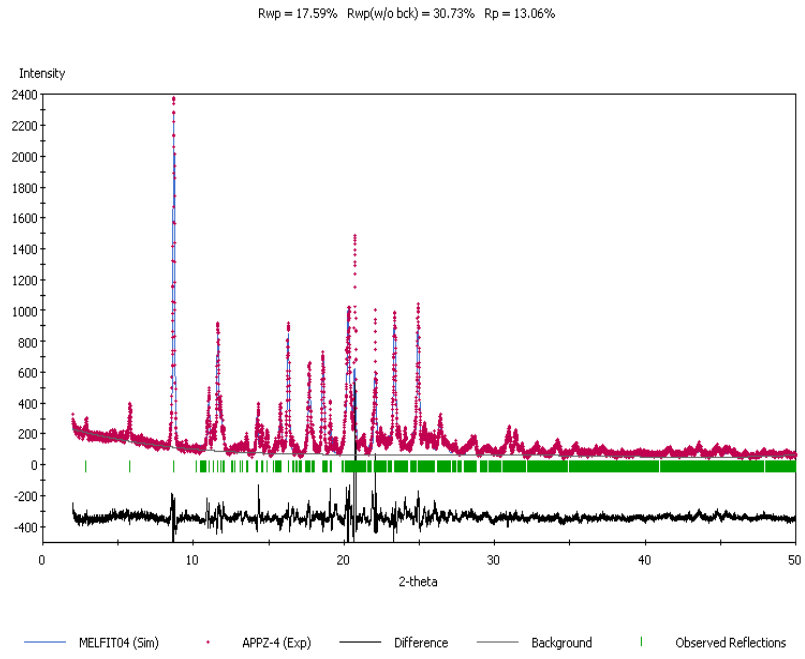


(b)

Figure S9. Slurry experiments of aripiprazole polymorph 5 as monitored by Rietveld refinement using the crystal structure model. Blue trace is the simulated powder pattern from crystal structure, red pattern is the experimentally observed diffraction pattern, black trace is the difference between the simulated and experimentally observed, green tics are systematic absences and grey line is the background model. The goodness of the fit is measured by R values in the Reitveld refinement: R_p and R_{wp} (a) Aripiprazole form 5 before the slurry experiment was initiated. (b) Aripiprazole form 5 after 1 day of slurrying. The entire PXRD pattern has changed. Refinement with the hydrate crystal structure indicated a good match thus confirming the anhydrate-to-hydrate transformation.



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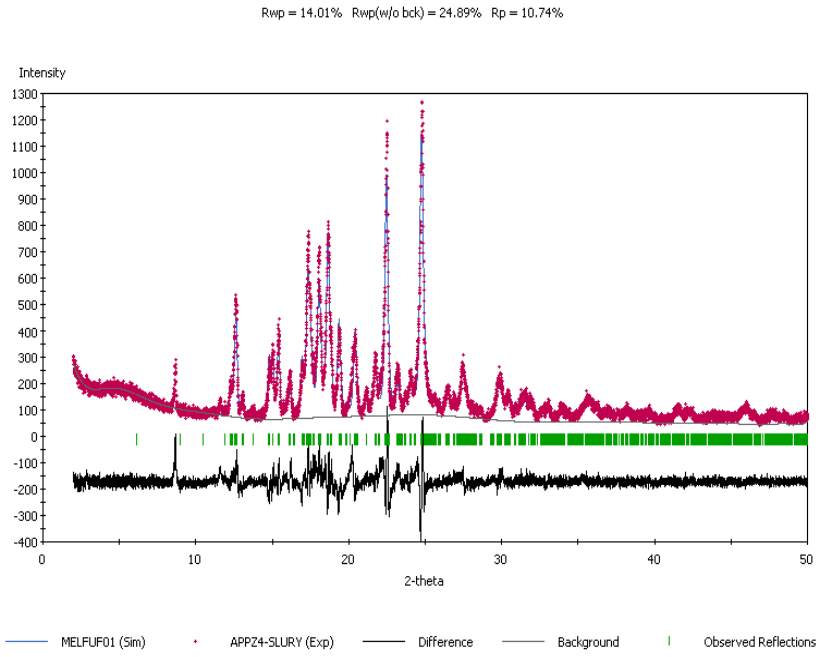
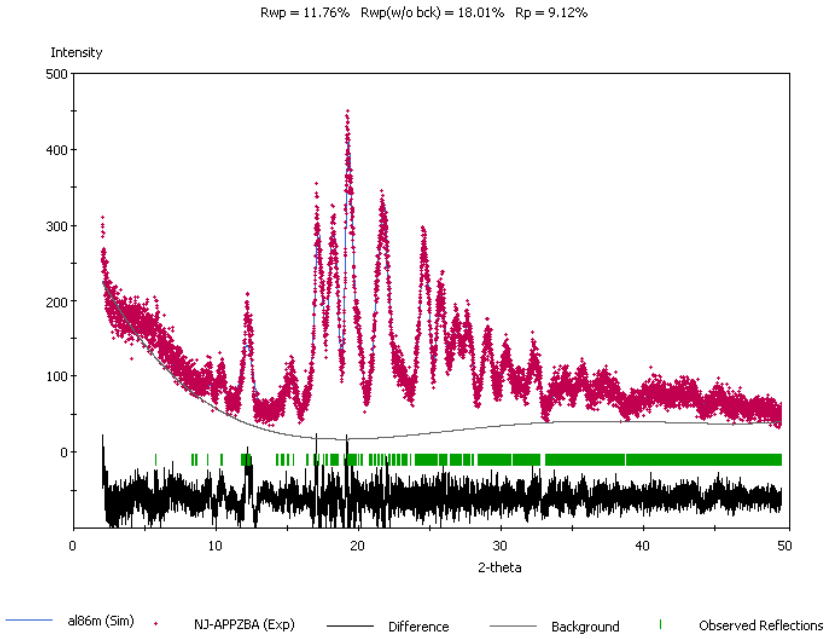


(b)

Figure S10. Slurry experiments of aripiprazole form 4, as monitored by Rietveld refinement using the crystal structure model. (a) Aripiprazole form 4 before the slurry experiment was initiated. (b) Aripiprazole form 4 after 1 day of slurrying. The entire PXRD pattern has changed. Refinement with the hydrate crystal structure indicated a good match thus confirming the anhydrate-to-hydrate transformation.



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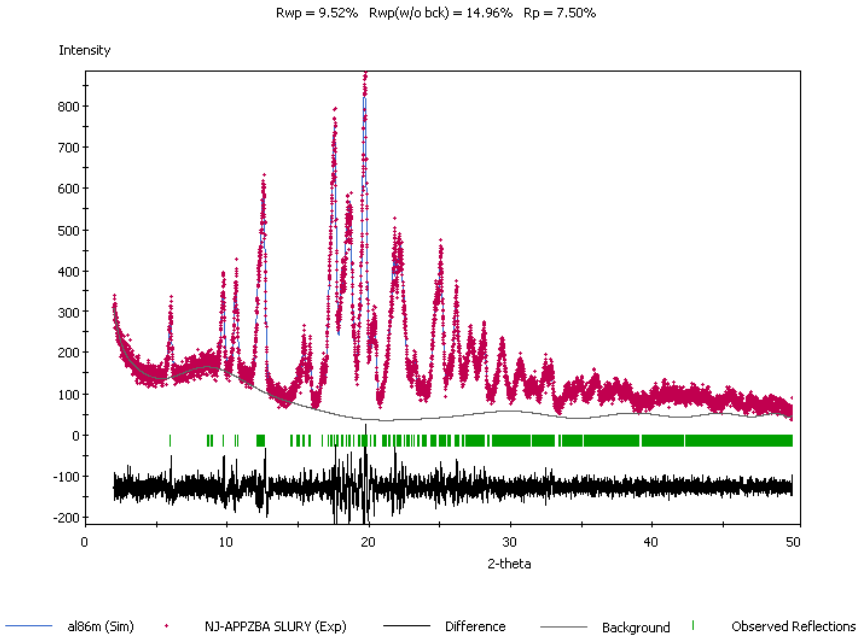
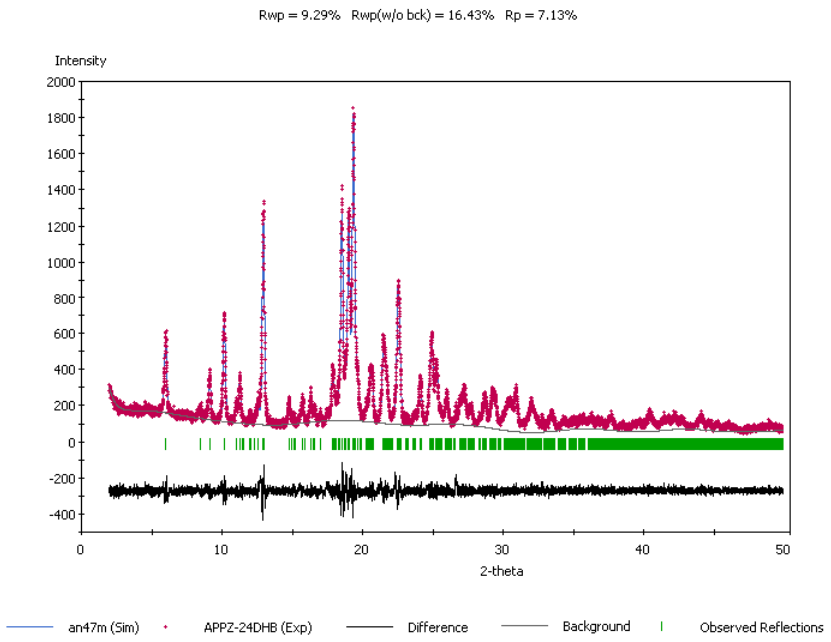
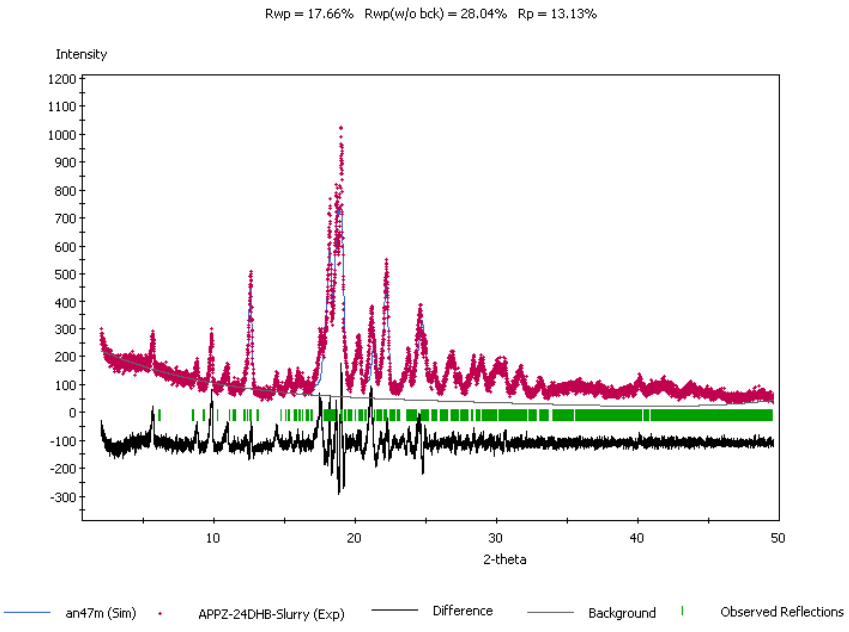


(b)

Figure S11. Slurry experiments of Aripiprazole benzoate monohydrate (salt I), as monitored by changes in the PXRD and Reitveld refinement using the crystal structure model. The material did not undergo any phase transformation as there are no additional peaks observed or the existing peaks were not disappeared, after 1 week slurrying.

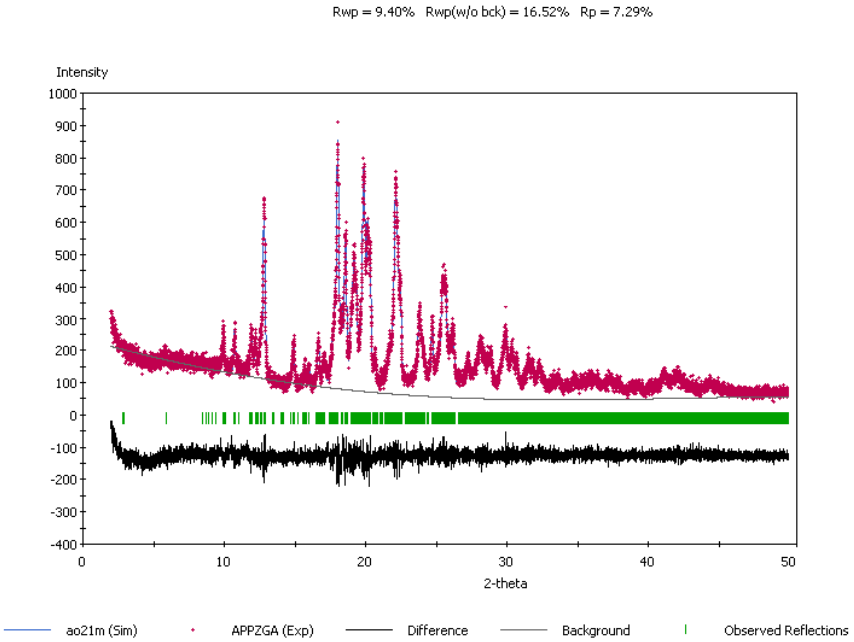


(a)



(b)

Figure S12. Slurry experiments of Aripiprazole 2,4-dihydroxybenzoate (salt II), as monitored by changes in the PXRD and Reitveld refinement using the crystal structure model. The material did not undergo any phase transformation as there are no additional peaks observed or the existing peaks were not disappeared, after 1 week slurrying.



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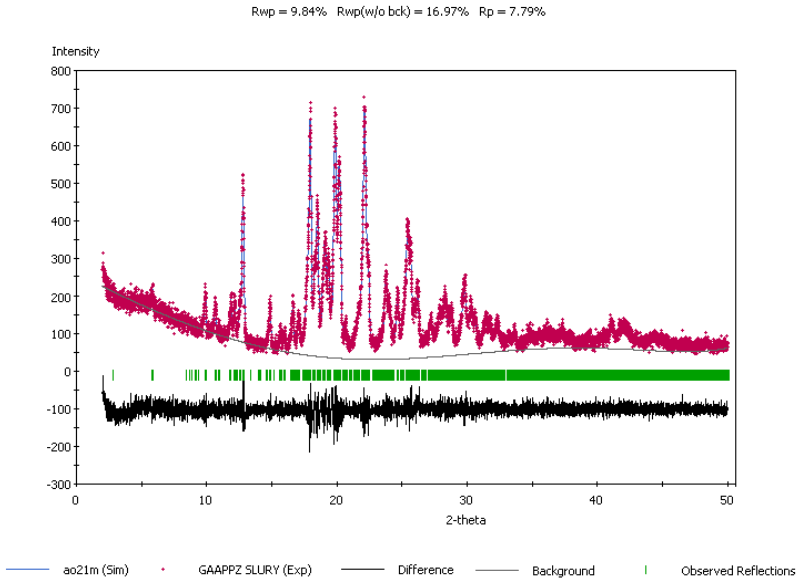
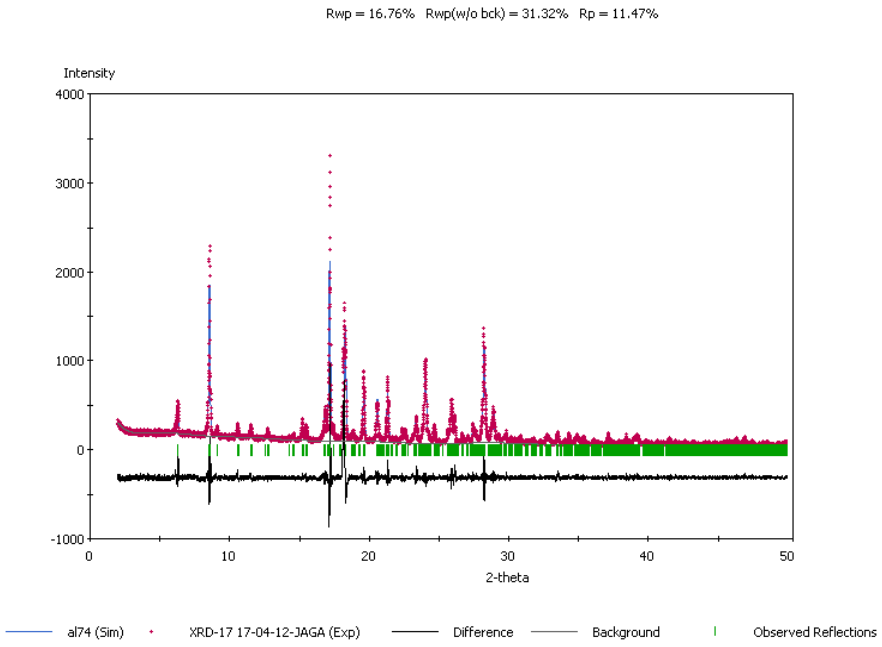


(b)

Figure S13. Slurry experiments of Aripiprazole 2,5-dihydroxybenzoate hemihydrate (salt III), as monitored by changes in the PXRD and Reitveld refinement using the crystal structure model. The material did not undergo any phase transformation as there are no additional peaks observed or the existing peaks were not disappeared, after 1 week slurrying.



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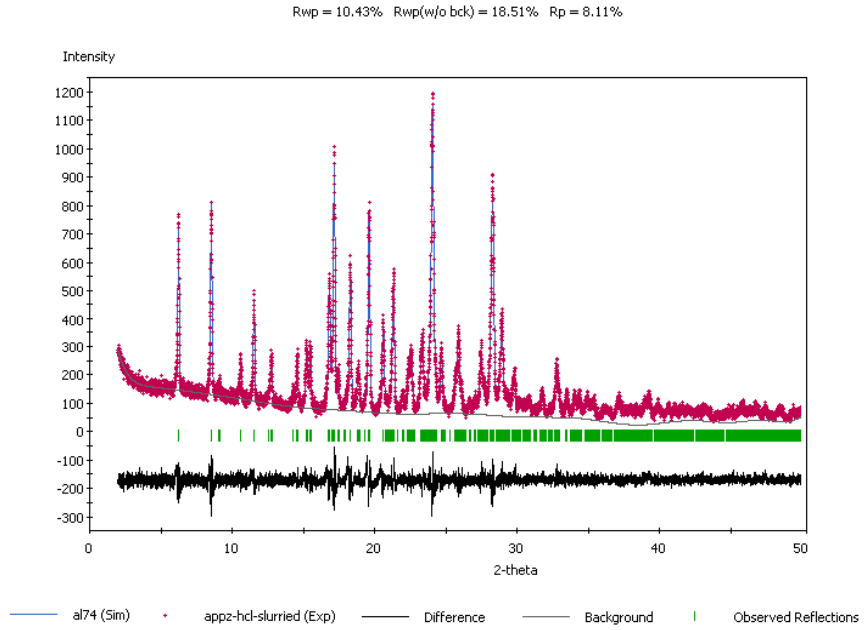

(b)

Figure S14. (a) Aripiprazole hydrochloride salt (salt IV) before the slurry experiment was initiated. (b) Aripiprazole hydrochloride salt after 1 week slurry experiment in water. The material did not undergo any phase transformation as there are no additional peaks observed or the existing peaks not disappeared. Preferred orientations of the peaks have been removed.