Crystal structures of commercial pharmaceuticals

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As part of a continuing project, the challenging room-temperature crystal structures of six commercial pharmaceutical APIs have been solved by Monte Carlo simulated annealing techniques using synchrotron X-ray powder diffraction data (11-BM at APS), and optimized using density functional techniques. **Bisoprolol fumarate**, $(C_{18}H_{33}NO_4)_2(C_4H_2O_4)$, crystallizes in *P1*, with *a* = 8.16570(5), *b* = 8.51639(12), *c* = 16.75179(18) Å, *α* = 89.142(1), *β* = 78.155(1), *γ* = 81.763(1)°, *V* = 1128.265(10) Å^3, and *Z* = 1. The structure was difficult to solve because the two ends of the bisoprolol cation are similar but not identical. **Hyoscyamine sulfate monohydrate**, $(C_{17}H_{24}NO_3)_2(SO_4)(H_2O)$, (generally described as a dihydrate) crystallizes in $P2_1$ with *a* = 6.60196(2), *b* = 12.95496(3), *c* = 20.93090(8) Å, *β* = 94.8839(2)°, *V* = 1783.680(5) Å^3, and *Z* = 2. The multiple fragments led to a low success rate. **Atropine sulfate monohydrate**, $(C_{17}H_{24}NO_3)_2(SO_4)(H_2O)$, (racemic hyoscyamine) crystallizes in $P2_1/n$ with *a* = 19.2948(5), *b* = 6.9749(2), *c* = 26.9036(5) Å, *β* = 94.215(2)°, *V* = 3610.86(9) Å^3, and *Z* = 4. The success rate of solution using DASH was only 1%, and required Mogul Distribution Bias and {010} preferred orientation. Despite being apparently orthorhombic **cefprozil monohydrate**, $C_{18}H_{19}N_3O_5S(H_2O)$, crystallizes in $P2_1$ with *a* = 11.26503(5), *b* = 11.34017(4), *c* = 14.72628(10) Å, *β* = 90.1249(4)°, *V* = 1881.24(2) Å^3, and *Z* = 4. DFT calculations suggest that the carboxylic acid proton on one (but not the other) of the two independent cefprozil molecules is transferred to an amino group, forming a salt. This suggestion needs to be confirmed by spectroscopic experiments and calculations of the vibrational spectrum. Despite being apparently monoclinic, **metolazone**, $C_{16}H_{16}ClN_3O_7$, crystallizes in *P1* with *a* = 8.1976(5), *b* = 14.4615(69), *c* = 16.0993(86) Å, *α* = 115.009(18), *β* = 90.096(7), *γ* = 106.264(4)°, *V* = 1644.52(9) Å^3, and *Z* = 4. The broad 021 peak indicates stacking faults in the structure. **Linagliptin**, $(C_{25}H_{28}N_8O_2)_2$(solvent)(H_2O), crystallizes in $P2_12_12$ with *a* = 24.85078(12), *b* = 21.5691(8), *c* = 9.74377(4) Å, *V* = 5222.77(3) Å^3, and *Z* = 8. The structure was solved by TEM electron tomography. Initial fit to the X-ray powder data was relatively poor, but the structure contains a channel, which is filled with water and solvent. Hydrogen bonding is important in all these crystal structures.