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\textsubscript{18}H\textsubscript{33}NO\textsubscript{4})\textsubscript{2}(C\textsubscript{4}H\textsubscript{2}O\textsubscript{4}), crystallizes in P1\textsuperscript{1}, with \(a = 8.16570(5), b = 8.51639(12), c = 16.75179(18) \text{ Å}, \alpha = 89.142(1), \beta = 78.155(1), \gamma = 81.763(1)^\circ, V = 1128.265(10) \text{ Å}^3, \) 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\textsubscript{17}H\textsubscript{24}NO\textsubscript{3})\textsubscript{2}(SO\textsubscript{4})(H\textsubscript{2}O), (generally described as a dihydrate) crystallizes in P2\textsubscript{1} with \(a = 6.60196(2), b = 12.95496(3), c = 20.93090(8) \text{ Å}, \beta = 94.839(2)^\circ, V = 1783.680(5) \text{ Å}^3, \) and \(Z = 2.\) The multiple fragments led to a low success rate. Atropine sulfate monohydrate, (C\textsubscript{17}H\textsubscript{24}NO\textsubscript{3})\textsubscript{2}(SO\textsubscript{4})(H\textsubscript{2}O), (racemic hyoscyamine) crystallizes in P2\textsubscript{1}/n with \(a = 19.2948(5), b = 6.9749(2), c = 26.9036(5) \text{ Å}, \beta = 94.215(2)^\circ, V = 3610.86(9) \text{ Å}^3, \) 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\textsubscript{18}H\textsubscript{19}N\textsubscript{3}O\textsubscript{5}S(H\textsubscript{2}O), crystallizes in P2\textsubscript{1} with \(a = 11.26503(5), b = 11.34017(4), c = 14.72628(10) \text{ Å}, \beta = 90.1249(4)^\circ, V = 1881.24(2) \text{ Å}^3, \) 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\textsubscript{16}H\textsubscript{16}ClN\textsubscript{3}O\textsubscript{7}, crystallizes in P1 with \(a = 8.1976(5), b = 14.4615(69), c = 16.0993(86) \text{ Å}, \alpha = 115.009(18), \beta = 90.096(7), \gamma = 106.264(4)^\circ, V = 1644.52(9) \text{ Å}^3, \) and \(Z = 4.\) The broad 021 peak indicates stacking faults in the structure. Linagliptin, (C\textsubscript{25}H\textsubscript{28}N\textsubscript{8}O\textsubscript{2})(solvent)(H\textsubscript{2}O), crystallizes in P2\textsubscript{1}2\textsubscript{1}2\textsubscript{1} with \(a = 24.85078(12), b = 21.5691(8), c = 9.74377(4) \text{ Å}, V = 5222.77(3) \text{ Å}^3, \) 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.