Crystal Structures of Large-Volume Commercial Pharmaceuticals

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As part of a continuing project, the challenging room-temperature crystal structures of four 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. Atorvastatin calcium trihydrate (Lipitor®), (C33H34FN2O5)2Ca(H2O)3 crystallizes in space group P1 (#1) with a = 5.44731(4), b = 9.88858(16), c = 29.5925(10) Å, a = 95.859(3), β = 94.211(1), g = 105.2790(1)°, V = 1521.277(10) Å³, and Z = 1. The structure was solved by removing the O atoms from the carboxylate groups of the anion, and using a CaO6 fragment. Pimecrolimus (Elidel), C43H68ClNO11, crystallizes in space group P21 (#4) with a = 15.28864(7), b = 13.31111(4), c = 10.95529(5) Å, β = 96.1542(3)°, V = 2216.649(9) Å³, and Z = 2. By default, simulated annealing programs did not give enough torsional degrees of freedom, so the macrocycle was broken, and re-formed at a low success rate. Ivermectin hemihydrate ethanolate, (C48H74O14)(H2O)0.5(C2H5O H)0.68, crystallizes in space group I2 (#5) with a = 14.94878(15), b = 9.26938(4), c = 39.27263(30) Å, β = 94.4017(7), V = 5425.80(5) Å³, and Z = 4. A reduced cell search yielded another solvate, and the guest species were identified using difference Fourier and spectroscopic techniques. Ceftriaxone sodium hemiheptahydrate (Rocefin), C18H16N8O7S3Na2(H2O)3.5, crystallizes in space group C2 (#5) with a = 30.56495(19), b = 4.75245(3), c = 18.55021(18) Å, β = 90.3551(7)°, V = 2694.521(24) Å³, and Z = 4. Some of the water molecules were difficult to locate conventionally, and were placed by progressively searching for smaller voids. Other new structures may be discussed as they become available.

Acta Cryst. (2020). A76, a1