CRYSTAL STRUCTURE OF *d*-MANNITOL

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Several polymorphic forms of anhydrous D-mannitol, a widely used pharmaceutical excipient, have been reported in the literature. We have used high-resolution synchrotron X-ray powder diffraction and simulated annealing methods to determine the crystal structure of the δ polymorph of D-mannitol. There is one molecule in the irreducible volume of the monoclinic cell, space group $P2_1$, dimensions a=5.0895Å, b=18.2501Å, c=4.9170 Å and β=118.302°.

To prepare the sample, aqueous mannitol solutions (10% w/v) were cooled in a tray freeze-dryer from 25°C to –50°C at 1°C/min, and held isothermally for 12 hours. The frozen solutions were subsequently heated at 1°C/min to the primary drying temperature of –15°C and dried for 60 hours at a pressure of 50 mTorr.

Powder diffraction data collection was carried out on the X3B1 beamline at the National Synchrotron Light Source, using monochromatic X rays of wavelength 0.7022 Å. Initial inspection of the diffraction pattern showed two mannitol polymorphs coexisting in the sample: β (whose structure was already known) and δ. We identified the latter by agreement with published diffraction patterns, *e.g.*, Powder Diffraction File entry 22-1794. We performed a Le Bail fit to the d phase with a simultaneous Rietveld refinement of the ß phase in order to extract estimated intensities of the former. Subsequent quantitative analysis based on the Rietveld refinements yielded 22% and 78% w/w of the β and δ forms respectively. We used the direct space simulated annealing program PSSP to determine the δ-mannitol structure, followed by Rietveld refinement. We find that the molecule is slightly distorted from its conformation in the ß phase.

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