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Structure of Aldose Reductase-Inhibitor Complexes at Ultra-High Resolution from Helium Cooled Crystals.

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Ultra-high resolution diffraction data were collected from crystals of human Aldose Reductase-inhibitor complexes cooled with helium. Data sets at 0.9Å were obtained using the Structural Biology Center beamline ID19, at the Advanced Photon Source. Cryotemperatures of 15 K and 60 K at the crystal were maintained with an open flow helium cryostat. Diffraction data were collected at 19 KeV using a 2theta offset on the SBC2 CCD detector and processed with HKL2000. Aldose Reductase (AR) is an enzyme of MW=36 Kdaltons involved in diabetes complications. For the AR IDD 676 complex, data were collected at 15 K, while for the AR IDD 594 complex, data were collected at 15 K and 60 K for a hydrogenated crystal and 15K for a perdeuterated crystal. The completed refinement of the AR IDD 676 complex structure with 15 K data shows a double conformation for the carboxylate head of the inhibitor, this was not resolved with the 100 K data. This double conformation, is also seen in a crystal structure at pH=8, and appears to be important for the proton donation mechanism. Refinement of the AR IDD 594 complex at different temperatures is in progress and it will be presented. Preliminary results show a decrease in B-factors with temperature.

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