## The First Structure from Ultralente Insulin Microcrystals

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Ultralente human insulin is one of the commercially available preparations for the treatment of diabetes type 1. Its long-acting activity arises from rhombohedral microcrystals, which are directly injected as an insulin-zinc suspension into the blood stream [1]. The slowly dissolving crystals provide a gradual release of insulin and hence a constant blood level over several hours.

The hexameric arrangement of the insulin heterodimers in Ultralente microcrystals has been elucidated by atomic-force microscopy [2]. Powder diffraction studies proposed the  $T_6$  conformer by comparison of the unit cell constants with those obtained from bigger insulin crystals grown from different crystallization conditions [3]. However due to the small crystal size of approximately 25 x 25 x 5  $\mu$ m<sup>3</sup> the three-dimensional structure has not been determined yet.

A suspension of Ultralente human insulin was provided by Novo Nordisk. A complete data set from one crystal (R3, 81.03 Å, 33.57 Å) could be collected up to a resolution of 1.9 Å at the micro diffractometer MD2 of beamline X06SA, Swiss Light Source, PSI. The structure was solved by molecular replacement. Results from the structure analysis will be discussed on the poster.

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[3] Richards J. P. et al., *J. Pharm. Sci.*, 1999, **88**, 867.

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