Coordination of selected metal ions in insulin

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Insulin is a polypeptide hormone that is synthesized in the β-cells of the pancreas. Although insulin is accumulated in the pancreas as a zinc containing hexamer, it is active as a monomer that does not contain zinc. Seventy years ago it was discovered that other metals (Co, Ni and Cd) can replace the zinc ion [1], but so far only two papers describing coordination of some other metal ions in insulin have been published [2, 3].
Replacement of zinc ions with selected essential elements (copper, nickel, molybdenum, cobalt, iron and vanadium) has been done and where possible the prepared insulin derivatives were structurally characterized. Single crystals of the insulin derivatives were prepared by the hanging drop vapor diffusion crystallization method at pH=6.4. All of the structurally investigated insulin derivatives belong to the T_6 hexamer form. Two metal ions (Cu^{2+}, Ni^{2+}, Mo^{6+}, Co^{2+}) in all insulin derivatives are situated on the crystallographic threefold axis and each is octahedrally coordinated by three crystallographically related His B10/D10 and additionally by three water molecules or three oxygen atoms (in the molybdenum derivative). There was no evidence of metal binding to the GluB13 or GluA17.
New $T_3R_3^f$ insulin derivative was crystallized in the presence of bromide ions. Single crystal data were collected both at 100K and at room temperature. This derivative undergoes a phase change – *c*-axis at room temperature was found to be halved in comparison to the structure at 100 K. Both axial and off-axial Zn ions are tetrahedrally coordinated. Powder diffraction data for bromo insulin derivate were also collected on laboratory instrument at room temperature.

References

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[3] J. Nicolson, L. Perkins & F. Korber, *Recent Res. Devel. Mol. Biol*. **3** (2006) 1-16.