The Discovery of Insulin

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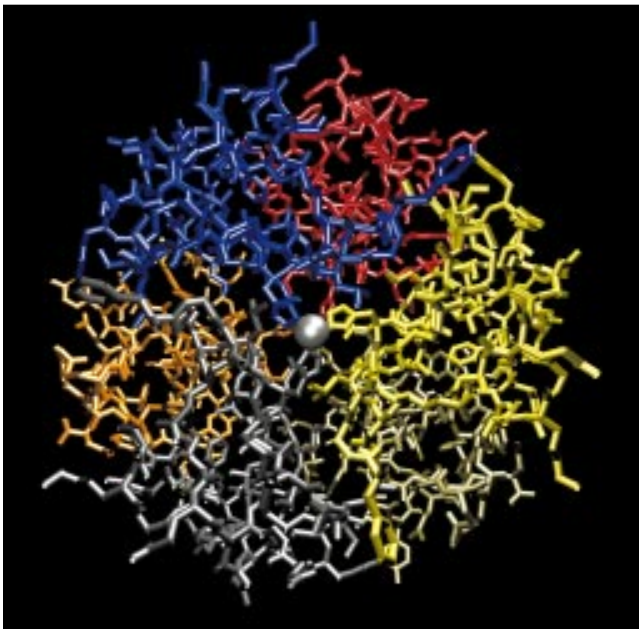
The focus for the front cover of *CJHP* in 2003 is important Canadian medical institutions and discoveries.



Insulin exists in solution (depending on concentration and pH) as monomers or dimers and in rhombohedral crystals as hexamers. This image shows insulin as a hexamer viewed down the 3-fold axis, showing the position of 2 superimposed zinc ions. The image is drawn with a molecular visualization program (VMD) that is used for displaying large biomolecular systems with 3-D graphics (http://www.ks.uiuc.edu/Research/vmd/). Image courtesy of Nicholas H. Keep, School of Crystallography, University of London.

Until 1920, having diabetes meant wasting away to almost certain death, but this started to change in the early 1920s. A few weeks after receiving an honours baccalaureate in physiology and chemistry from the University of Toronto in 1921, Charles Herbert Best jumped at the chance for summer work with Dr Frederick Banting. Over that summer, Banting used a surgical technique that he had developed to isolate an unpurified extract of insulin from the pancreas of beagles. It was Best's responsibility to complete the chemical assays related to this "antidiabetic component" of the pancreas. When the initial dog experiments proved successful, Professor John James Richard MacLeod, who provided laboratory space and general scientific direction for Banting and Best, put his entire research team to work on the production and purification of insulin. James Bertram Collip, who had graduated from the University of Toronto at 15 years of age, joined the team and developed the process by which insulin was purified in sufficient amounts for clinical trials and use in diabetic patients. The first tests were conducted on Leonard Thompson early in 1922, with spectacular success.

For this work, Banting was knighted in 1934 and shared the 1923 Nobel Prize in Physiology or Medicine with MacLeod. Best was accepted into medical school and, after completing doctorates in both medicine and physiology, was appointed professor of physiology at the University of Toronto in 1929. He served as Associate Director of the Connaught Laboratories from 1932 to 1941. Years later, Best was involved in isolating heparin.

The complete amino acid sequence of the insulin molecule was described in the early 1950s; in fact, insulin was the first protein to be sequenced in its entirety. This pioneering work was confirmed over the period 1963 to 1966, when several groups reported laboratory synthesis of biologically active insulin.[1,2] The 3-dimensional structure of the crystalline hormone was published in 1969.[3]

References

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