



Insulins Today and Tomorrow

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Successful extraction and introduction of Insulin in 1921 by Banting, Best, Collip and Macleod revolutionised the treatment of Diabetes Mellitus and went down in the history as one of the most outstanding medical achievements of 20th century. Even today, Insulin continues to offer hope and life to multitudes of Diabetics across the world.

In the 1930s, more than 50 years before emergence of incontrovertible evidence from both the Diabetes control and complication Trial (DCCT)(1) and the UK Prospective Diabetes Study(UKPDS)(2), Joslin had strongly advocated restoration of blood glucose to near normal concentrations to prevent the devastating complications of diabetes. Since then, Insulin has been an essential part of the armamentarium in the management of Diabetes Mellitus.

For the first half century of the Insulin era, Porcine or Bovine insulin were the only commercially available preparations(3). In the 1970s, highly purified (monocomponent) insulin became a commercial reality. It differed from the porcine insulin in its amino acid sequence at B30 position(4). The advent of recombinant DNA technology meant that human insulin could be made biosynthetically. This innovation has led to availability of mutant insulins(insulin analogues) that are designed mainly to have improved pharmacokinetic properties for subcutaneous administration.(5)

Notwithstanding the availability of a wide and ever increasing array of insulin preparations, today, the re-

placement of physiological insulin remains the most cherished goal. An unrelenting endeavour in this direction has led to the discovery of Insulin Glargine, a new long acting insulin analogue which was approved for use by the US Food and Drug Administration in April 2000 and by the European Agency for the Evaluation of Medicinal Products in June 2000. Insulin Glargine has become available in USA from May 2001.

A recombinant analogue of human insulin, Insulin glargine (HOE 901, 21(A)-Gly-30(B) a-L-Arg-30(B)b-L-Arg human insulin) is characterised by a shift in the isoelectric point producing a retarded absorption rate and an increased duration of action that closely mimics basal insulin secretion. It has been recommended for once-daily subcutaneous administration at bed time. Glargine is a peakless insulin, its action lasts nearly 24 hours and it closely mimics Continuous Subcutaneous Insulin Infusion (CSII), the gold standard of basal insulin replacement(6). In addition, compared to NPH insulin, Insulin Glargine carries a lower risk of nocturnal hypoglycemia or weight gain.(7).

Even as the fast acting insulin analogues (Lispro and aspart insulin) are already available, interesting experiments are under way with a new insulin analogue called Acylated Insulin which holds the promise of a protracted steady action not due to slow absorption after subcutaneous injection but due to reversible binding to albumin. Acylated Insulin is a long acting insulin analogue acylated with a 14-C fatty acid chain. Other new Insulin

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under trial include a large covalently linked thyroxyl-insulin analogue which exhibits relative hepatoselectivity but low hypoglycemic potency(8) thus offering a more physiological basal insulin supplementation.

However, the most long awaited breakthrough pertains to Oral Insulins. Oral insulins tried in the past proved to be a failure because of the gastric acidity. A new acrylic based gel like coating on the pill is now being tried to optimize the body's absorption of the future oral insulin. Meanwhile considerable advancement has been made towards buccal and pulmonary delivery of insulin.(9)

More exciting news about insulin seems to be in store in the years to come.

References

1. DCCT. The effect of intensive treatment of diabetes on development and progressing of long term complications in Insulin Dependent Diabetes Mellitus. *New Engl J Med* 1993 ; 329 : 977-86.
2. UKPDS-Intensive Blood Glucose control with sulphonylureas or Insulin compared with conventional treatment and risk of complications in patients with type 2 Diabetes Mellitus. *Lancet* 1998 ; 352 : 837-53.
3. Indian Diabetes Guidelines. *J Assoc Physicians India* 2002 ; 50 : 319.
4. Jitendra Singh. In Defence of Animal Insulin. *J Ind Med Assoc* 2002 ; 100 : 171-72.
5. Brange J, Volund A. Insulin Analogues with improved pharmacokinetic profiles. *Advanced Drug Delivery Reviews* 1999 ; 35 : 307-55.
6. Bolli G.B. Physiological insulin replacement in Type 1 Diabetes Mellitus. *Exp Clin Endocrinol Diabetes* 2001 ; 109 : 5317-32.
7. Rosenstaock J. Basal insulin therapy in Type 2 Diabetes: 2 week comparison of insulin glargine (HOE 901) and NPH insulin. *Diabetes Care* 2001 ; 24(4) : 631-36.
8. Shojaee-Moradie F, Eckey H, Jacson NC *et al*. Novel hepatoselective insulin analogues: studies with covalently linked thyroxyl-insulin complexes. *Diabet Med* 1998 ; 15 : 928-36.
9. Das S, Mahapatra SK. *Medicine Update API*. Editor Thakur BB. 2000 ; 10 : 501-7.

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