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Structure, Biosynthesis and Regulation of Insulin

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Editorial Note

Insulin is potentially considered as a polypeptide hormone whose production is stimulated by the β cells of islet of Langerhans of pancreas (a part of endocrine system). It has tremendous influence on the metabolism of carbohydrate (glucose), lipids (fats) and protein (aminoacids). Insulin is also considered as anabolic hormone as it promotes the synthesis of glycogen, fats and proteins. This hormone has been implicated in the development of diabetes mellitus. Insulin occupies a special place in the field of biochemistry and medicine. Insulin was the first hormone to be isolated, purified, synthesized, sequenced and also first hormone to be produced by recombinant DNA (r-DNA) technology.

Human insulin contains a total of 51 amino acids arranged in two polypeptide chains. The chain A has 21 amino acids while chain B has 30 amino acids which are held together by two interchain disulfide bridges connecting A7 to B7 and A20 to B19. In addition to this, there is an intrachain disulfide link in chain A between the amino acids 6 and 11.

Insulin production is stimulated by β cells of the islets of Langerhans of pancreas and the gene for this protein synthesis (insulin) is located on chromosome 11. The synthesis of insulin involves two precursors, namely pre-proinsulin with 108 amino acids and proinsulin with 86 amino acids. They are gradually degraded to form the active hormone insulin and a connecting peptide which is indicated as C-peptide. Insulin and C-peptide are produced in equal concentration. The estimation of C-peptide in the plasma serves as a useful index for the endogenous production of insulin although it has no biological activity. In the β cells insulin and proinsulin combines with zinc to form complexes. In this form, insulin is stored in the granules of the cytosol which is released in stimulus to exocytosis.

About 40-50 units of insulin is secreted by human pancreas in our day to day life. The normal insulin concentration in plasma is 20-30 μ U/ml. The important factors that influence the release of insulin from the β cells of pancreas are glucose, amino acids and gastrointestinal hormones. Glucose is considered to be the one of the most important enhancer for insulin release whereas the epinephrine is considered to be the inhibitor. The effect is most considered when glucose is administered orally (either directly or through a carbohydrate rich meal). A slight increase in blood glucose level is a signal for insulin secretion. Amino acids influence the secretion of insulin which is particularly observed after the ingestion of protein rich meal that causes transient rise in plasma amino acid concentration. Among the amino acids, arginine and leucine are potent enhancers of insulin release. Gastrointestinal hormones (secretin gastrin, pancreozymin) enhance the secretion of insulin. The gastrointestinal hormones are released after the ingestion of food. In emergency situation like stress, intense exercise and trauma, the nervous system stimulates adrenal medulla to release epinephrine. Epinephrine inhibits insulin release and promotes metabolism by mobilizing energy yielding compounds such as glucose from the liver and fatty acids from adipose tissue. In the plasma, insulin has a normal half-life of 4-5 minutes. This short half-life allows rapid metabolic changes in accordance to the alterations in the circulating levels of insulin. This is advantageous for the therapeutic purposes. A protease enzyme, namely insulinase which is mainly found in liver and kidney is known to degrade insulin.