Insulin Therapy for Type -1 Diabetic Patients

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ABSTRACT: Insulin is a peptide hormone produced by cells of the pancreatic islets encoded by the insulin gene. It regulates the metabolism of carbohydrates, fats, and protein by promoting the absorption of glucose from the blood into the cells of the liver, fat, and skeletal muscles. Insulin is used in the treatment of type-1 diabetes (insulin dependent diabetes). Recent advances in insulin therapy include ultra-rapid-acting insulin and ultra-long-acting basal insulin therapies. LEVEMIR is the most common insulin used in the treatment of diabetes.

INTRODUCTION

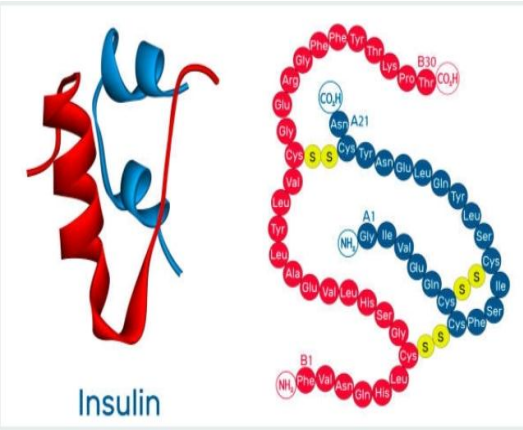
The insulin molecule consists of 51 amino acids arranged in two chains, an A chain (21 amino acids) and B chain (30 amino acids) that are linked by two disulfide bonds. Pro insulin is the insulin precursor that is transported to the Golgi apparatus of the beta cell where it is processed and packaged into granules. Pro insulin, a single-chain 86 amino acid peptide, is cleaved into insulin and C-peptide both are secreted in equimolar portions from the beta cell upon stimulation from glucose and other insulin secretagogues. While C-peptide has no known physiologic function, it can be measured to provide an estimate of endogenous insulin secretion.

HISTORY

Insulin was first discovered by Frederick G Banting, Charles H Best and JJR Macleod at the University of Toronto in 1921 from dog's pancreas. It was later purified by James B Collip. On July 27 the insulin was discovered. T he term insulin was discovered from a Latin word "Insula" with reference to the Langherans islands.

With the availability of human insulin by recombinant DNA technology in the 1980s, use of animal insulin declined dramatically. Beef insulin, beef-pork, and pork insulin are no longer commercially available in the United States. The United States FDA may allow for personal importation of beef or pork insulin from a foreign country if a patient cannot be treated with human insulin. Beef insulin differs from human insulin by 3 amino acids and pork insulin differs by one amino acid.

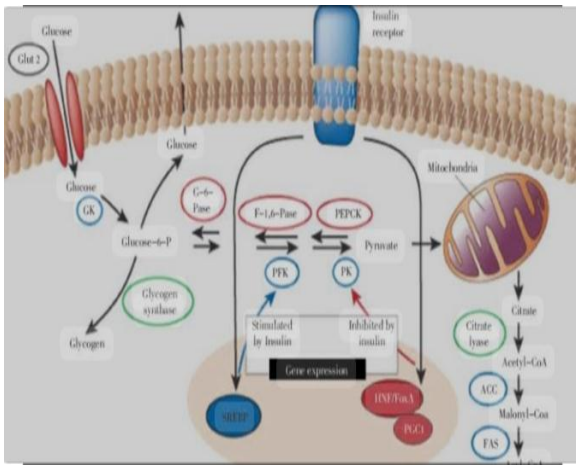
Recombinant DNA technology has allowed for the development and production of analogs to human insulin. With analogs, the insulin molecule structure is modified slightly to alter the pharmacokinetic properties of insulin, primarily affecting the absorption of the drug from the subcutaneous tissue. The B26-B30 region of the insulin molecule is not critical for insulin receptor recognition and it is in this region that amino acids are generally substituted.



MECHANISM OF ACTION OF INSULIN

The primary action of insulin is the regulation of glucose metabolism. Insulin promotes the cellular uptake of glucose, particularly in muscle and adipose tissues, promotes energy storage via glycogenesis, opposes catabolism of energy stores, increases DNA replication and protein synthesis by stimulating amino acid uptake by liver, muscle and adipose tissue, and modifies the activity of numerous enzymes involved in glycogen synthesis and glycolysis. It binds to the insulin receptors, a heterotetrameric protein consisting of two extracellular alpha units. The binding of insulin to the alpha sub unit of IR stimulates the tyrosine kinase activity intrinsic to the beta sub unit of the receptor. The bound receptor is able to phosphorylate numerous intracellular substracts (IRS) proteins, Cbl, APS, Shc, and Gab 1. These activated proteins in turn lead to the activation of downstream signaling

molecules including PI3 kinase and AKt. AKt regulates the activity of glucose transporter 4 (GLUT 4) and protein kinase C (PKC) which plays a critical role in metabolism and catabolism.



CLINICAL APPLICATIONS

- The major purpose of insulin is to regulate the body's energy supply by balancing micro nutrient levels during the fed state.
- Insulin is critical for transporting intracellular glucose to insulin-dependent cells/tissues like liver and adipose tissue

EFFICACY AND BENEFITS

It helps your body turn food into energy and manages your blood sugar levels. If you have diabetes, your body can't make enough insulin or can't use it properly. Your healthcare provider can prescribe manufactured insulin that you take through an injection (shot), injectable pen or pump.

ADVERSE REACTIONS

- Hypoglycaemia (hypos) Insulin can make your blood glucose levels fall too low (hypoglycaemia, or hypos).
- Itching or redness where you inject.
- Pain when you inject.
- Bleeding or bruising where you inject.
- Fatty lumps under the skin (lipohypertrophy).
- Changes in your vision.

ONGOING RESEARCH AND FUTURE DIRECTIONS

- Recent developments in insulin therapy have potential for reducing some of the negative aspects of current methods. Long-acting insulin, such as insulin degludec, may require less frequent injections. Fast-acting insulin, such as Viaject, has been shown to improve postprandial glycemic control and reduce hypoglycemia.
- New research from a phase 2b study suggests that an oral insulin formulation is now closer than ever before to becoming reality, and a coin-sized "smart" insulin patch has shown promise in recent animal studies. A novel, super-long-acting basal insulin — dosed as a once-weekly injection — is also in early development.

CONCLUSION

Insulin moves glucose from your blood into cells all over your body. Glucose comes from both the food and drinks you consume and your body's natural release of stored glucose (glycogen). Glucose is your body's main — and preferred — source of energy. All of your body's cells need energy.

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