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25years of Humulin, the first genetically engineered drug approved by the FDA

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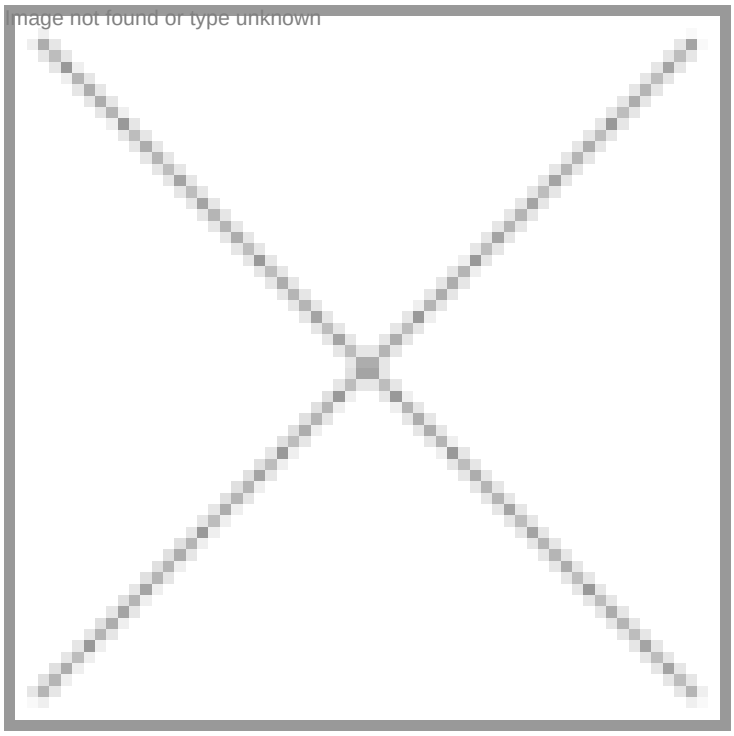

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Till date, insulin therapy is the only effective treatment for Type 1 diabetes and is also generally required for the treatment of Type 2 diabetes as the disease progresses.

Insulin was isolated for the first time in 1921 from animal sources and commercialized within 12 months. Decades later, it took just four years for developers to move from expressing recombinant insulin in bacteria to launching the world's first biotechnology drug product.

Composition

Insulin consists of a 21-amino acid A chain and a 30-amino acid B chain, linked by two disulfide bonds. It can be produced either by generating the chains separately and chemically combining them or by creating a single-chain precursor, human proinsulin, and cleaving out a 35-amino acid connecting peptide. For manufacturing the drug, the proinsulin route is favored because it requires a single fermentation and isolation step.

A breakthrough

In 1978, the US-based biotech company Genentech and City of Hope National Medical Center, jointly produced human insulin in the laboratory using recombinant DNA (rDNA) technology. City of Hope scientists had synthesized the genes for the

protein's two chains before inserting them into Escherichia coli.With its expertise in purifying and handling insulin and the desire to remain a leader in the field, Lilly, a US-based pharmaceutical company, immediately licensed recombinant insulin from Genentech and set about developing it. Fortunately, Lilly also had experience isolating antibiotics from fermentation processes. Because rDNA guidelines at the time allowed the expression of only inactive protein products, Lilly had to use the two-chain method.

Clinical studies began in 1980. In 1982, Lilly's Humulin became the first genetically engineered drug approved by the US Food and Drug Administration. The US approval came just one month after British regulatory authorities allowed its introduction in the UK. Although the development of Humulin took just four years, it was a major undertaking for both the developers and regulators, breaking new ground.

Humulin was the first drug produced by genetic engineering techniques to gain the FDA approval for human use. It was made by inserting human genes responsible for insulin production into E. Coli bacteria, thus stimulating the bacteria to synthesize insulin. Because this technique could produce large quantities of insulin, the artificial insulin was expected to help alleviate a shortage of animal insulins predicted to occur within the next decade. Humulin had proved to be safe and effective in FDA clinical trials involving more than 400 patients. It is used by more than 4 million people with diabetes around the world everyday. Today Humulin is available in both a vial and a disposable prefilled pen and this helps in choosing a convenient way of taking Humulin.

The pioneer

Today Genentech is a purely biotechnology company that discovers, develops, manufactures and markets human pharmaceuticals produced by recombinant DNA technology for significant unmet medical needs. More recently, producers have used genetic engineering to create insulin analogs that differ in a few amino acids as a way to control their onset and duration of activity.

Technological developments

DNA technology has led to the ability to synthesize insulin analogs. To date, more than 300 insulin analogs have been produced. The purity of insulin has increased and the needle size for injections has decreased, thus reducing the discomfort associated with subcutaneous insulin injections.

Traditionally, diabetics who use insulin have to inject themselves via a syringe. However, alternative approaches for insulin delivery, including nasal and oral methods, are being studied. Biocon Ltd, India's premier biotechnology company, has recently presented the results of Phase I studies on the oral insulin product-IN-105, a novel analog of insulin at the European Association for Study of Diabetes (EASD) meeting held at Amsterdam. The product has special properties that make it feasible for delivery of insulin in tablet form. Alternatives to syringe injections may help ensure patient compliance to insulin therapy by making insulin delivery easier and more convenient. New technologies are also under development to provide automatically controlled insulin delivery. One such device uses a glucose sensor implanted into the patient.

The production of human insulin through recombinant DNA technology represented an important advance in the treatment of patients with diabetes. The increased incidence of diabetes, coupled with the introduction of alternative delivery methods that rely on higher doses, is expected to result in a substantial escalation in the demand for affordable insulin in the future.