BIOTECHNOLOGICAL APPLICATIONS IN MEDICINE

The advancements in recombinant DNA technologies have revolutionized the landscape of healthcare, leaving a profound impact. These innovative processes have ushered in a new era of therapeutic development with several notable advantages:

1) Facilitation of Mass Production: Recombinant DNA technologies empower the mass production of therapeutic agents, enabling widespread availability and accessibility to patients in need.
2) Enhanced Safety and Efficacy: Through meticulous engineering, these technologies yield drugs that are not only more potent but also safer for consumption. This heightened level of efficacy ensures better treatment outcomes for patients.
3) Mitigation of Immunological Risks: Unlike traditional products derived from non-human sources, recombinant therapeutics mitigate the risk of triggering unwanted immunological responses. This characteristic enhances the overall safety profile of these drugs.

Presently, the global pharmaceutical landscape boasts approximately 30 approved recombinant therapeutics, signifying the widespread acceptance and adoption of this cutting-edge approach. In India specifically, 12 of these recombinant products have already penetrated the market, highlighting the nation's embrace of innovative healthcare solutions.

The therapeutic products that have received approval for use in India encompass a diverse range, including:

1) Human Insulin
2) Streptokinase
3) Erythropoietin
4) Hepatitis B vaccine
5) Human Growth Hormone
6) Human Interleukin
7) Granulocyte Colony-Stimulating Factor (GCSF)
8) Granulocyte-Macrophage Colony-Stimulating Factor (GMCSF)
9) Alpha-interferon (Charles Weissman)
10) Gamma-interferon
11) Blood Factor VIII
12) Follicle-Stimulating Hormone

These therapeutic agents represent a significant milestone in medical science, as they are synthesized from genes cloned in bacteria and/or eukaryotic cells, or through a process known as pharming. Notably, all of these products, except for the hepatitis B vaccine, are currently imported and utilized within the Indian healthcare system. This underscores the nation's reliance on global pharmaceutical sources to meet its medical needs and highlights the importance of international collaboration in ensuring access to vital therapeutic interventions.

Recombinant Insulin, also known as Genetically Engineered Insulin

Insulin, a crucial hormone synthesized by the ß cells within the islets of Langerhans situated in the pancreas, plays a pivotal role in regulating blood glucose levels. Deficiency in insulin production leads to the manifestation of diabetes mellitus, a condition characterized by high blood sugar levels. To mitigate the symptoms of diabetes, patients often require a regimen of insulin injections to supplement the insufficient production of the hormone by their pancreas. Historically, insulin used for diabetes treatment was obtained from the pancreases of slaughtered cattle and pigs. While animal-derived insulin proved effective for many patients, it posed allergic reactions in some individuals.

It's worth noting that oral administration of insulin to diabetic patients isn't feasible due to its degradation within the digestive tract.

Recombinant DNA techniques have provided a breakthrough in insulin production, offering several advantages:

Elimination of Post-Translation Modification

Unlike traditional insulin extraction methods, recombinant DNA techniques produce insulin that doesn't necessitate modification after translation. This streamlines the manufacturing process and ensures the production of insulin molecules with consistent biological activity.

Structural Suitability

Insulin, being a relatively small protein composed of two polypeptide chains (the A chain consisting of 21 amino acids and the B chain consisting of 30 amino acids), linked together by disulfide bonds, is structurally well-suited for production via recombinant DNA techniques. This structural simplicity facilitates the synthesis of insulin with high purity and efficacy.

The adoption of recombinant DNA technologies has not only revolutionized insulin production but has also improved the quality and accessibility of insulin therapy for diabetic patients worldwide.

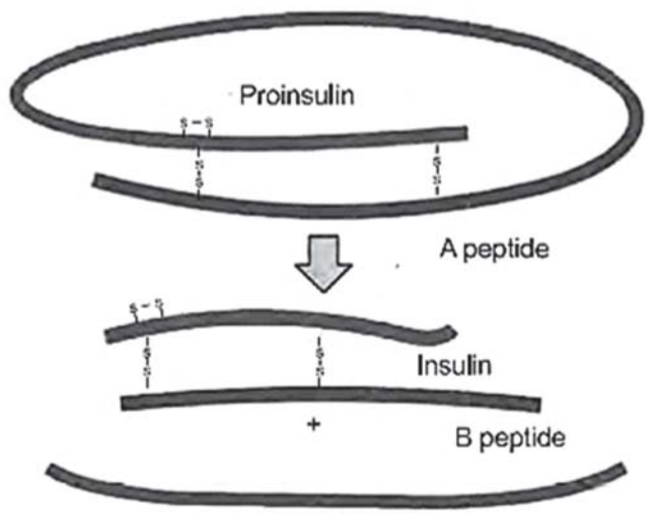

Fig. : Maturation of pro-insulin into insulin (simplified)

In mammals, including humans, insulin undergoes synthesis as a pro-hormone, akin to a pro-enzyme, requiring processing before attaining full maturity and functionality. The gene responsible for orchestrating this protein synthesis is situated on chromosome 11. This pro-hormone contains an additional segment known as the C peptide, which is absent in the mature insulin and is consequently excised during the maturation process.

One of the primary hurdles encountered in producing insulin via recombinant DNA (rDNA) techniques was achieving its assembly into a mature form. In 1983, Eli Lilly, an American pharmaceutical company, tackled this challenge by synthesizing two DNA sequences corresponding to the A and B chains of human insulin. These sequences were then inserted into plasmids such as pBR322 and subsequently introduced into Escherichia coli (E. coli) bacteria to induce insulin chain production. The sequences for the A and B chains were coupled with the lac Z gene, which encodes for the enzyme β-galactosidase, and integrated into the pBR322 plasmid. Through a process known as blue-white screening, transformed E. coli bacteria capable of producing the insulin chains were selectively identified.

The A and B chains of insulin were generated separately, extracted, and then amalgamated by forming disulfide bonds, culminating in the formation of human insulin. This intricate process marked a significant milestone in biotechnology, paving the way for the mass production of insulin through rDNA techniques and revolutionizing the treatment of diabetes.

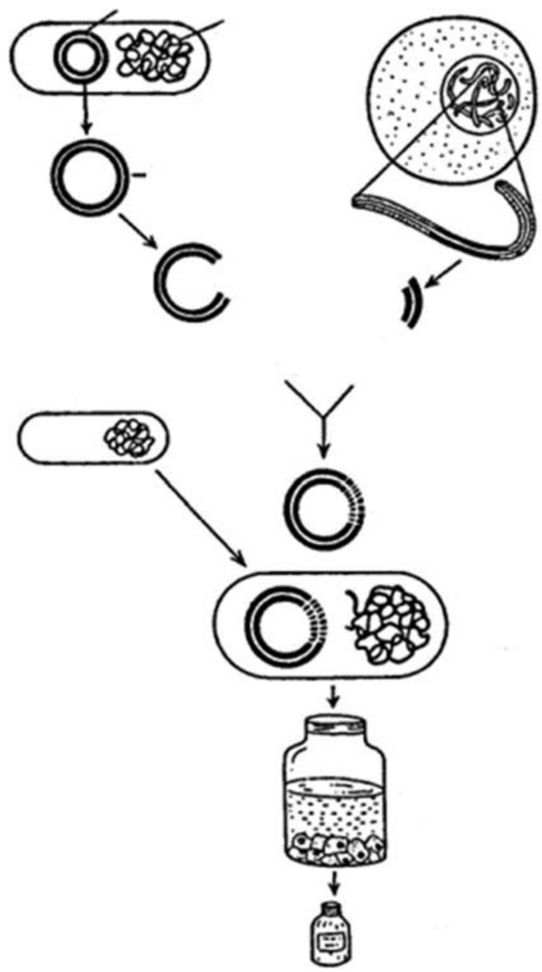

Fig.: Steps involved in gene transfer for the production of human insulin

Gene Therapy

Gene therapy is a new medical approach that aims to treat certain inherited diseases like SCID and hemophilia. It involves fixing a faulty gene found in a person's cells and tissues to address a disease. This process can include inserting healthy genes into the individual or embryo to replace non-functioning ones. The first instance of clinical gene therapy was administered in 1990 to a 4-year-old girl with ADA deficiency, a condition where the immune system lacks a crucial enzyme. While bone marrow transplants or enzyme replacement therapy can help manage ADA deficiency, they aren't always completely curative. Gene therapy offers a promising solution by introducing functional genes into the patient's cells, potentially providing a permanent cure, particularly if applied at an early embryonic stage.

Medical Diagnosis of Disease (Molecular diagnosis)

Early diagnosis and understanding the underlying causes of a disease are vital for effective treatment. Conventional diagnostic methods like serum and urine analysis often fail to detect diseases in their early stages. However, advanced techniques such as recombinant DNA technology, Polymerase Chain Reaction (PCR), and Enzyme Linked Immunosorbent Assay (ELISA) enable early detection. PCR, for instance, can identify pathogens like HIV before symptoms appear and is increasingly used to detect genetic mutations in suspected cancer patients. ELISA, on the other hand, relies on the interaction between antigens and antibodies to identify infections or antibodies produced in response to pathogens. These molecular diagnostic methods offer powerful tools for detecting diseases at their earliest stages.