Biotechnological Applications of Enzymes : enzymes as targets for drug design. Clinical uses of enzymes, enzyme therapy, enzymes and recombinant DNA technology

Enzymes are crucial in medicine, acting as both primary **targets for drug design** and as therapeutic agents themselves in **enzyme therapy**. The development and large-scale production of many therapeutic enzymes have been made possible by **recombinant DNA technology**.

Enzymes as Targets for Drug Design

Most modern drugs target specific enzymes to modulate their activity, typically through inhibition. By understanding an enzyme's catalytic mechanism and three-dimensional structure, scientists can design highly potent and specific inhibitors that interfere with the enzyme's function and alter disease processes.

Key examples of successful enzyme-targeting drugs include:

- **ACE (Angiotensin-Converting Enzyme) inhibitors** (e.g., enalapril, lisinopril) for treating hypertension and heart failure by blocking the production of the vasoconstrictor angiotensin II.
- **HIV Protease inhibitors** (e.g., ritonavir, lopinavir) that interfere with the HIV virus's ability to replicate and mature.
- **Tyrosine kinase inhibitors** (e.g., imatinib) for cancer treatment by blocking signaling pathways crucial for cancer cell growth.
- **Statins** which inhibit HMG-CoA reductase, a key enzyme in cholesterol synthesis, to manage high cholesterol levels.
- **Allopurinol**, a xanthine oxidase inhibitor used to reduce uric acid levels in patients with gout.

Clinical Uses of Enzymes

Enzymes are used in medicine for diagnosis, therapy, and pharmaceutical manufacturing.

Diagnostic Uses

- **Biomarkers:** Measuring the levels of specific enzymes in the blood can indicate organ damage. For example, elevated levels of creatine kinase (CK) or aspartate aminotransferase (AST) suggest heart damage or liver disease, respectively.
- **Biosensors:** Enzymes like glucose oxidase are integrated into test strips to monitor blood glucose levels for diabetic patients.
- **Genetic Disease Diagnosis:** Enzymes are used in techniques like PCR (polymerase chain reaction) to diagnose genetic diseases such as sickle cell anemia at the prenatal stage.

Therapeutic Uses

Enzymes are directly administered as drugs to perform specific biochemical functions:

- **Thrombolytic agents:** Streptokinase and urokinase are used to dissolve dangerous blood clots in patients who have had a heart attack or stroke.
- **Cancer treatment:** L-asparaginase is used to treat certain types of leukemia by depriving cancer cells of the amino acid asparagine, which they cannot synthesize themselves.
- **Wound healing:** Proteases like trypsin and collagenase are used to remove dead tissue from wounds (debridement), promoting healing.
- **Digestive aids:** Amylase, lipase, and protease supplements are given to individuals with pancreatic insufficiency or lactose intolerance to aid digestion.
- **Cyanide poisoning:** Rhodanese, a mitochondrial enzyme, is used as part of an antidote to detoxify cyanide into less toxic thiocyanate.

Enzyme Therapy

Enzyme therapy primarily involves **Enzyme Replacement Therapy (ERT)** for genetic disorders caused by a specific enzyme deficiency, such as lysosomal storage diseases. In these conditions, an exogenous (externally produced) enzyme is administered intravenously to compensate for the missing or non-functional natural enzyme.

Examples of ERT:

- **Gaucher disease:** Treated with imiglucerase, a modified enzyme that breaks down the fatty substance (glucocerebroside) that would otherwise accumulate in organs.
- **Fabry disease:** Treated with agalsidase beta, which replaces the deficient alpha-galactosidase A enzyme.
- **Pompe disease:** Involves the use of alglucosidase alfa to break down glycogen buildup in muscles.
- **Severe Combined Immunodeficiency (SCID):** Treated with PEG-ADA, a modified adenosine deaminase enzyme, to break down toxic metabolites and restore immune function.

Enzymes and Recombinant DNA Technology

Recombinant DNA (rDNA) technology has revolutionized the field of therapeutic enzymes by enabling the large-scale, cost-effective, and safe production of high-purity enzymes.

- **Production in host organisms:** The gene encoding a human enzyme is inserted into a vector and introduced into host cells, such as bacteria (e.g., *E. coli*), yeast (*Saccharomyces cerevisiae*), or mammalian cell lines (e.g., Chinese hamster ovary or CHO cells).
- **Enhanced efficacy and safety:** Recombinant enzymes minimize the risk of transmitting pathogens found in animal or human-derived sources. Molecular modifications, such as linking enzymes to polyethylene glycol (PEGylation), can also increase the enzyme's half-life in the body and reduce the risk of an immune response.
- **Novel treatments:** rDNA technology allows for the engineering of enzymes with improved properties, such as enhanced stability, altered specificity, or better drug delivery capabilities (e.g., in gene therapy where a correct gene is inserted).

In essence, enzymes are pivotal in modern medicine, with drug discovery often focusing on modulating their activity, and biotechnology providing the means to produce them for life-saving therapies.