BIOTECHNOLOGY AND ITS APPLICATIONS

Biotechnology has many applications such as **biopharmaceuticals, therapeutics, diagnostics, genetically modified crops, processed food, bioremediation, waste treatment and energy production.**

Biotechnology has 3 critical research areas:

a. **Providing the best catalyst** in the form of improved organism usually a microbe or enzyme.
b. **Creating optimal conditions** through engineering for a catalyst to act.
c. **Downstream processing technologies** to purify the protein/organic compound.

APPLICATIONS IN AGRICULTURE

3 options for increasing food production:

a. **Agro-chemical based agriculture:** It uses fertilizers & pesticides. Expensive. Causes environmental pollution.
b. **Organic agriculture:** Expensive.
c. **Genetically engineered crop-based agriculture:** It uses genetically modified crops. **Genetically Modified Organisms** (**GMO**) are the plants, bacteria, fungi & animals whose genes are altered by manipulation.

Advantages of genetic modification in plants:

- It makes crops more tolerant to abiotic stresses (cold, drought, salt, heat etc.).
- Pest-resistant crops reduce the use of chemical pesticides.
- It reduces post-harvest losses.
- It increases efficiency of mineral usage by plants (it prevents early exhaustion of soil fertility).
- It enhances nutritional value of food. E.g. Golden rice (Vitamin A enriched rice).
- To create tailor-made plants to supply alternative resources (starches, fuels, pharmaceuticals etc.) to industries.

Pest Resistant Plants

- They act as **bio-pesticide.**
- It reduces the need for insecticides.
- E.g. Bt cotton, Bt corn, rice, tomato, potato, soyabean etc.

Bt Cotton:

- Some strains of *Bacillus thuringiensis* have proteins that kill insects like coleopterans (beetles), lepidopterans (tobacco budworm, armyworm) & dipterans (flies, mosquitoes).
- *B. thuringiensis* forms an insecticidal protein **(Bt toxin)** crystal during a phase of their growth. It does not kill the *Bacillus* as it exists as inactive *protoxins.*
- When an insect ingests the toxin, it becomes active due to alkaline pH of the gut which solubilise the crystals. Toxin binds to surface of mid-gut epithelial cells creating pores. It causes cell swelling and lysis and death of the insect.
- **Bt toxin genes** were isolated from *B. thuringiensis* and incorporated into crop plants such as cotton.
- Most Bt toxins are insect-group specific. They are coded by **cry genes**. E.g. proteins encoded by *cryIAc* & *cryIIAb* genes control cotton bollworms. Protein of *cryIAb* gene controls corn borer.

Nematode resistance in tobacco plants:

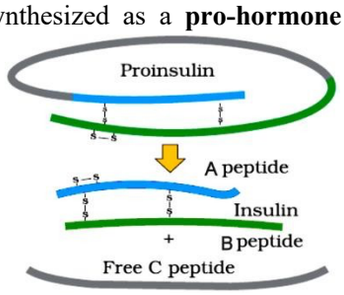
- A nematode *Meloidogyne incognita* infects the roots of tobacco plants causing a reduction in yield.
- It can be prevented by **RNA interference** (RNAi) strategy.
- **RNAi** is a method of cellular defense in all eukaryotic organisms. It prevents translation of a specific mRNA (silencing) due to a complementary dsRNA molecule.
- The source of this complementary RNA is from an infection by RNA viruses or mobile genetic elements (transposons) that replicate via an RNA intermediate.
- Isolate Nematode-specific genes (DNA). It is introduced into host plant using *Agrobacterium* vectors. It produces both sense & anti-sense RNA in host cells. These RNAs are complementary. So they form double stranded (ds) RNA. It initiates RNAi and silences the specific mRNA of nematode. Thus the parasite cannot survive in a transgenic host expressing specific interfering RNA.

APPLICATIONS IN MEDICINE

- Recombinant DNA technology helps for mass production of safe and more effective **therapeutic drugs.**
- Products from non-human sources cause unwanted immunological responses. But recombinant therapeutics does not have such problems.
- At present, about 30 recombinant therapeutics have been approved. Of these, 12 are being marketed in India.

1. Genetically Engineered Insulin

- Insulin is used to manage adult-onset diabetes.
- Insulin from the pancreas of animals (cattle & pigs) causes allergy or other types of reactions to the foreign protein.
- Now, it is possible to produce human insulin using bacteria.
- Insulin consists of two short **polypeptide chains (chain A & chain B)** that are linked by disulphide bridges.
- In mammals, insulin is synthesized as a **pro-hormone (pro-insulin).** It is processed to become mature and functional hormone.



- The pro-hormone contains an extra stretch called **C peptide**. This is removed during maturation into insulin.
- In 1983, **Eli Lilly** (an American company) prepared two DNA sequences corresponding to A & B chains of human insulin and introduced them in plasmids of *E. coli* to produce insulin chains. Chains A & B were combined by creating disulfide bonds to form human insulin ***(Humulin).***

2. Gene Therapy

- It is a method to correct a gene defect in a child/embryo.
- Here, genes are inserted into a person's cells and tissues to treat a hereditary disease. It compensates for the non-functional gene.
- First clinical gene therapy (1990) was given to a 4-year old girl with **adenosine deaminase (ADA) deficiency.**
- This is caused due to the deletion of a gene of ***adenosine deaminase*** (an enzyme for the functioning of immune system). It can be cured by **bone marrow transplantation** or by **enzyme replacement therapy** (injection of ADA). But these are not completely curative.
- **Gene therapy for ADA deficiency:** Collect **lymphocytes** from the patient's blood and grow in a culture → Introduce a functional **ADA cDNA** into lymphocytes (using a retroviral vector) → They are returned to the patient.
  This should be periodically repeated as lymphocytes are not immortal.
- If the **ADA gene** from marrow cells is introduced into cells at early embryonic stages, it could be a permanent cure.

3. Molecular Diagnosis

- Conventional methods (serum & urine analysis) are not suitable for early diagnosis of diseases.
- It is possible by techniques such as **Recombinant DNA technology, PCR & ELISA.**

PCR (Polymerase Chain Reaction):

- Presence of a pathogen is normally suspected only based on symptoms. By this time, the concentration of pathogen is already very high in the body.
- However, very low concentration of a bacteria or virus can be detected by amplification of their nucleic acid by PCR.
- **Uses of PCR:**
  - To detect HIV in suspected patients.
  - To detect gene mutations in suspected cancer patients.
  - To identify many other genetic disorders.
- A single stranded DNA or RNA, tagged with a radioactive molecule (probe) is hybridized to its complementary DNA in a clone of cells. It is detected by autoradiography. The clone having mutated gene will not appear on photographic film, because the probe will not have complementarity with mutated gene.

ELISA (Enzyme Linked Immuno-Sorbent Assay):

- It is based on **antigen-antibody interaction.**
- Infection by pathogen can be detected by the presence of **antigens** (proteins, glycoproteins, etc.) or by detecting the **antibodies** synthesized against the pathogen.

TRANSGENIC ANIMALS

- These are the animals whose genome has been altered by introduction of a foreign gene by manipulation.
- E.g. Transgenic rats, rabbits, pigs, sheep, cows and fish.
- Over 95% of the transgenic animals are mice.

Benefits of transgenic animals

- **To study regulation of genes and their action on normal physiology & development:** E.g. Study of **insulin-like growth factor.** Genes (from other species) that alter formation of this factor are introduced and the biological effects are studied. This gives information about biological role of the factor.
- **To study the contribution of genes in the development of a disease and thereby new treatments:** E.g. transgenic models for human diseases such as cancer, cystic fibrosis, rheumatoid arthritis & Alzheimer's.
- **Biological products:** Some medicines contain expensive biological products. Transgenic animals can be used to produce biological products by introducing genes which codes for a particular product.
  They are used to treat diseases such as emphysema, phenylketonuria (PKU), cystic fibrosis etc. E.g. **human protein (α-1-antitrypsin)** used to treat emphysema.
  In 1997, **Rosie** (first transgenic cow) produced human protein-enriched milk (2.4 gm per litre). It contains **human α-lactalbumin.** It is nutritionally more balanced product for human babies than natural cow-milk.
- **Vaccine safety testing:** Transgenic mice are used to test the safety of the polio vaccine. If it is reliable, they can replace the use of monkeys to test the safety of vaccines.
- **Chemical safety testing (toxicity testing):** Some transgenic animals carry genes which make them more sensitive to toxic substances than non-transgenic animals. They are exposed to the toxic substances and the effects studied. It gives immediate results.

ETHICAL ISSUES

- **Problem of unpredictable results:** Genetic modification may cause unpredictable results.
  Indian Government has set up organizations like **GEAC** (Genetic Engineering Approval Committee) to make decisions about the validity of GM research and the safety of GM-organisms for public services.
- **Bio-piracy:** It is the use of bio-resources by multinational companies and other organizations without proper authorization from the countries and people concerned. Certain companies have got patents for products and technologies that make use of the genetic materials, plants etc. that have been identified, developed and used by farmers and indigenous people of a country. E.g. Basmati rice, herbal medicines (turmeric, neem etc.).
  Basmati rice has unique aroma & flavour. India has 27 varieties of Basmati. In 1997, an American company got patent rights on Basmati rice through the **US Patent and Trademark Office.** This allowed the company to sell a 'new' variety of Basmati. This was actually derived from Indian farmer's varieties. Indian Basmati was crossed with semi-dwarf varieties and claimed as a novelty. Other people selling Basmati rice could be restricted by patent.

Generally, industrialized nations are poor in biodiversity and traditional knowledge. The developing and underdeveloped world have rich biodiversity and traditional knowledge related to bio-resources.

It has to develop laws to prevent unauthorized exploitation of bio-resources and traditional knowledge.

Indian Parliament has cleared the second amendment of the **Indian Patents Bill** that has considered patent terms emergency provisions and research and development initiative.

MODEL QUESTIONS

1. There are many advantages of genetic modification in plants. Mention any four advantages.
2. Now a days Bt Brinjal has been much in the news. Being a GM Food is it advantageous or disadvantageous? List out any two points each.
3. Transgenic animals are said to be beneficial to humans. Justify this statement by giving two reasons.
4. Genetically modified tomato has some significance. Comment.
5. With an example, explain how biotechnology has been applied in each of the following:
   a) In curing Diabetes mellitus b) In rising pest resistant plants
   c) In producing nutritionally balanced milk.
6. Briefly explain the terms: a) cry gene b) C peptide
7. Explain RNA interference (RNAi) strategy.
8. Biotechnology has provided some techniques for early diagnosis of diseases. Mention any 2 examples.
9. Expand the following abbreviations:
   a) GMO b) PCR c) ADA d) ELISA e) GEAC
10. Do you think it is ethical to manipulate organisms for human benefits? Justify your answer.
11. What do you understand by the term Biopiracy?