CHAPTER-10

BIOTECHNOLOGY AND ITS APPLICATIONS

Topic-1

Applications of Biotechnology in Agriculture and Medicine

Concepts Covered • *Applications of Biotechnology, Stem cell technology, Gene therapy, Molecular diagnosis.*

Revision Notes

- **Applications of Biotechnology**
  - Biotechnology essentially deals with industrial-scale production of biopharmaceuticals using genetically modified microbes, fungi, plants and animals.
  - The applications of biotechnology include therapeutics, diagnostics, and genetically modified crops for agriculture, processed food, **bioremediation**, waste treatment and energy production.
  - **Three critical research areas of biotechnology are :**
    (a) Providing the best catalyst in the form of an improved organism usually a microbe or pure enzyme.
    (b) Creating optimal conditions through engineering for a catalyst to act.
    (c) Downstream processing technologies to purify the protein / organic compound.

Key Word

Bioremediation : Branch of biotechnology which use living organisms, like microbes and bacteria to remove pollutants, contaminants, etc. from soil, water, etc.

- **Biotechnological Applications in Agriculture :**
  - **Three options for increasing food production are are :**
    (a) Agro-chemical based agriculture.
    (b) Organic agriculture.
    (c) Genetically engineered crop-based agriculture.
  - The Green Revolution succeeded in tripling the food supply.
  - Increased yields have partly been due to the use of improved crop varieties, but mainly due to the use of better management practices and use of agrochemicals (fertilisers and pesticides).
  - Genetically Modified Organisms (GMO) or transgenic organisms are the plants, bacteria, fungi and animals whose genes are altered by manipulation.
- **Advantages of Genetic Modification in Plants**
  (a) It makes crops more tolerant to abiotic stresses (cold, drought, salt, heat, etc).
  (b) It helps to reduce post-harvest losses.
  (c) It increases the efficiency of mineral usage by plants (this prevents early exhaustion of fertility of soil).
  (d) It enhances the nutritional value of food e.g., Vitamin 'A' enriched rice.
  (e) GM is used to create tailor-made plants to supply alternative resources to industries in the form of starch, fuels and pharmaceuticals.

Key Fact

Some of the genetic material that make our DNA is not of the human origin. Viruses and bacteria have inserted some of it in a process called horizontal DNA Transfer.

- **Pest Resistant Plants**
  - Pest Resistant Plants reduce the use of chemical 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* produce proteins that kill insects like coleopterans (beetles), lepidopterans (tobacco, budworm, armyworm) and dipterans (flies, mosquitoes).

- *B. thuringiensis* forms a toxic insecticidal protein (Bt toxin) crystal during a particular phase of their growth. It does not kill the *Bacillus* as it exists as inactive protoxins.
- When an insect ingests the inactive toxin, it is converted into an active toxin due to the alkaline pH of the gut which solubilises the crystals.
- The toxin binds to the surface of midgut epithelial cells and create pores.
- It causes cells to swell and undergo lysis and ultimately leading to the 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.
- The toxin is coded by a gene named cry e.g., the proteins encoded by the genes *cryIAc* and *cryIIAb* control the cotton bollworms and that of *cryI Ab* controls corn borer.

Biotechnological Applications in Medicine

- The recombinant DNA technology helps for the mass production of safe and more effective **therapeutic** drugs.
- The recombinant therapeutics does not induce unwanted immunological responses as it is common in the case of similar products isolated from non-human sources.
- At present, about 30 recombinant therapeutics have been approved for human use in the world including India.
- In India, 12 of these are presently being marketed.

Genetically Engineered Insulin

- The management of adult-onset diabetes is possible by taking insulin at regular time intervals.
- Now, it is possible to produce human insulin using bacteria.
- Insulin from the pancreas of animals (cattle and pigs) causes allergy or other types of reactions to the foreign protein.
- Insulin consists of two short polypeptide chains (chain A and chain B) that are linked together by disulphide bridges.
- In mammals, insulin is synthesized as a pro-hormone.
- The pro-hormone needs processing before it becomes a fully mature and functional hormone.
- The pro-hormone contains an extra stretch called the C peptide.
- This is removed during maturation into insulin.
- In 1983, Eli Lilly an American company prepared two DNA sequences corresponding to A and B chains of human insulin and introduced them in plasmids of *E. coli* to produce insulin chains.
- The chains A and B were produced separately, extracted and combined by creating disulfide bonds to form human insulin.

Key Words

Therapeutic : Related to the treatment of disease or disorders by remedial agents or methods.

Pluripotent cell : A cell capable to develop into many different types of cells or tissues in the body.

Malignant disease : In such type of diseases, abnormal cells divide without control and invade nearby cells or blood and lymph.

Stem Cell Technology :

- Stem cells are undifferentiated or "blank" cells.
- They are special human cells which are capable to develop into many different cell types.
- This can range from muscle cells to brain cells. In some cases, they can also fix damage tissues.
- Stem cells can be obtained from an embryo, or by using a specialized body cells (developed by a technique) which behave like embryonic stem cells. These cells are known as induced **pluripotent** stem cells (IPS cells).
- They are used in treating several clinical problems like : (i) Tissue regeneration. (ii) Damaged myocardium after heart infarction. (iii) Brain after stroke. (iv) Spinal cord after mechanical injury.
- Advantages of stem cells technology : Stem cell technology is a rapidly developing field that combines the efforts of cell biologists, geneticists, and clinicians and offers hope of effective treatment for a variety of **malignant** and **non-malignant** diseases. The regenerative property of stem cell can be used in replacing any organ which is not working or damaged. It can help in studying human growth and cell development. It can be used to test the effects of medicinal drugs and medicine without the use of animals.

Key Word

Non-malignant diseases : In this case, tumors may grow larger but do not spread to other parts of the body.

Vaccine production:

Vaccines are the substances which protect the human body from various diseases by recognizing and destroying the harmful foreign pathogens. A dead or weakened microbe is used to produce the vaccine.

Generally, there are four types of vaccines which include:

1. **Live attenuated vaccine:** This type of vaccine contains weakened form of viruses. e.g., Rubella, Measles, Mumps etc.

2. **Inactivated vaccines**: These vaccines are made from small pieces of virus or bacteria or from their proteins. e.g., The whooping cough vaccine.
3. **Toxoid vaccines:** These vaccines contain the toxin produced by the bacteria or virus. e.g., Tetanus and diphtheria vaccine.
4. **Biosynthetic vaccines:** These are the man-made vaccines which are produced from the substances or chemicals similar to the pieces of virus or bacteria. e.g., Hepatitis-B.

- **Gene Therapy :**
  - It is a method to correct a gene defect diagnosed 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 was given in 1990 to a four year old girl with adenosine deaminase (ADA) deficiency.
  - This disorder is caused due to the deletion of the gene for *Adenosine deaminase* (the enzyme crucial for the immune system to function).
  - This can be cured by bone marrow transplantation or by enzyme replacement therapy (injection of functional ADA) but these approaches are not completely curative.
  - In gene therapy, lymphocytes from the patient's blood are grown in a culture.
  - Then, a functional ADA cDNA (using a retroviral vector) is introduced into these lymphocytes.
  - They are then returned to the patient.
  - This should be periodically repeated as these cells are not immortal.
  - However, if the ADA gene (from bone marrow cells) is introduced into cells at the early embryonic stages, it could be a permanent cure.
- **Molecular Diagnosis**
  - Recombinant DNA technology, PCR and Enzyme Linked Immunosorbent Assay (ELISA) are some techniques for early diagnosis.
  - The presence of a pathogen is normally suspected only when the pathogen has produced a symptom.
  - By this time, the concentration of the pathogen will be already very high in the body.
  - However, a very low concentration of a bacteria or virus can be detected by amplification of their nucleic acid by PCR.
  - PCR is used to detect HIV in suspected AIDS patients.
  - It is also used to detect mutations in genes in suspected cancer patients.
  - It is a powerful technique to identify many other genetic disorders.
  - A single-stranded DNA or RNA, tagged with a radioactive molecule (probe) is allowed to hybridise to its complementary DNA in a clone of cells followed by detection using autoradiography.
  - The clone having the mutated gene will hence not appear on the photographic film, because the probe will not have complementarity with the mutated gene.
  - ELISA is based on the principle of 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.

IMPORTANT DIAGRAMS

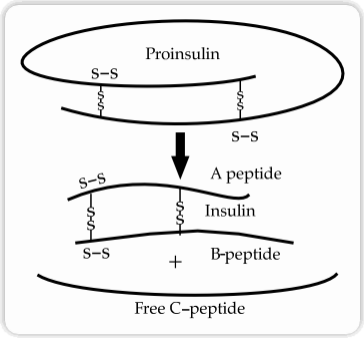

Fig. 10.1 : Genetically Engineered Insulin

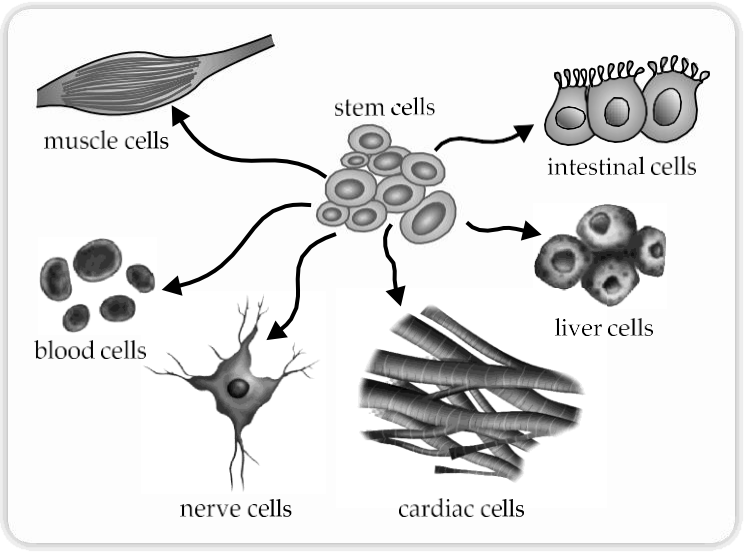

Fig 10.2: Stem cells

Mnemonics

Concept: Achievement through transgenic crops or GM crops.

Mnemonic: Proper **P**ackage of **M**uscular **b**ody **: H**ardwork **C**an **T**ransform

Interpretations: Achievements of :

		Example
Protein of interest	:	**H**irudin
Production of desired genotype	:	***C**ry* protein (Crystal protein)
Modification of existing **B**iosynthetic pathway	:	**T**ransgenic rice (higher content of vitamin A)

Example 1

Q. Why does the insecticidal protein produced by *Bacillus thuringiensis* not kill the bacterium, but kills the cotton bollworm ? Explain.

Sol. (i) The Bt toxin protein exist as inactive protoxin and hence does not kill the *Bacillus* but once an insect ingest the inactive toxin, it is converted into an active form of toxin due to the alkaline pH of the gut which solubilise the crystals.

(ii) The activated toxin binds to the surface of midgut epithelial cells and create pores that cause cell swelling and lysis and eventually cause death of the insect.

Topic-2 Transgenic Animals and Bioethical Issues

Concepts Covered • *Transgenic animals, advantages of transgenic animals, Ethical issues.*

Revision Notes

- **Transgenic Animals**
  - These are the animals whose genome has been altered by the introduction of an extra (foreign) gene by manipulation. e.g., Transgenic rats, rabbits, pigs, sheep, cows and fish.
  - Over 95% of all existing transgenic animals are mice.
- **Advantages or Benefits of Transgenic Animals**
  - **To study normal physiology and development :**
    (a) Transgenic animals are used to study how genes are regulated and how they affect the normal body functions and their development.

(b) For example study of complex factors such as insulin-like growth factor. Genes (from other species) that alter the formation of this factor are introduced and the biological effects are studied. This gives information about the biological role of the factor in the body.

- **To Study the contribution of genes in the development of a disease :**
  (a) Transgenic models help for the investigation of new treatments for human diseases.
  (b) For example: transgenic models for many human diseases such as Cancer, Cystic Fibrosis, Rheumatoid arthritis and Alzheimer's disease.
- **Biological products :**
  (a) Some medicines contain biological products, but they are often expensive.
  (b) Transgenic animals are used to produce useful biological products by introducing genes that codes for a particular product. e.g., human protein (α-1-antitrypsin) used to treat emphysema, products for the treatment of Phenylketonuria (PKU) and Cystic fibrosis, etc.
  (c) In 1997, *Rosie* (first transgenic cow) produced human protein-enriched milk (2.4 gm per litre).
  (d) It contains the human alpha-lactalbumin and is nutritionally more balanced product for human babies than natural cow-milk.
- **Vaccine safety testing :** Transgenic mice are being developed and used in testing the safety of **vaccines** before they are used for humans. The polio vaccine was tested in mice.
- **Chemical safety testing (toxicity testing) :** Transgenic animals are made to know the effect of **toxic** chemicals. This is also known as toxicity / safety testing.

Key Fact

Mice have been genetically modified to naturally produce human antibodies for use as therapeutics. Seven out of the eleven monoclonal antibody drugs approved by the FDA between 2006 and 2011 were derived from transgenic mice.

Ethical Issues

- **Problem of unpredictable results**
  (a) Genetic modification may cause unpredictable results when such organisms are introduced into the ecosystem.
  (b) Therefore, Indian Government has set up organizations like **GEAC** (Genetic Engineering Approval Committee), which makes decisions about the validity of GM research and the safety of GM-organisms for public services.
- **Problems of patent**
  (a) 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 specific country.
  (b) E.g., Basmati rice, herbal medicines like turmeric, neem, etc.
  (c) Basmati rice has unique aroma and flavour.
  (d) India has 27 varieties of Basmati.
  (e) In 1997, an American company got patent rights on Basmati rice through the US Patent and Trademark Office.
  (f) This allowed the company to sell a 'new' variety of Basmati which had actually been derived from Indian farmer's varieties.
  (g) Indian Basmati was crossed with semi-dwarf varieties and claimed as a novelty.
  (h) Other people selling Basmati rice could be restricted by the patent.
- **Biopiracy :**
  (a) It is the use of bio-resources by multinational companies and other organizations without proper authorization from the countries and people concerned.
  (b) Most of the industrialized nations are poor in biodiversity and traditional knowledge.
  (c) The developing and the underdeveloped world have rich biodiversity and traditional knowledge related to bio-resources.
  (d) It has to develop laws to prevent unauthorized exploitation of **bio-resources** and traditional knowledge.
  (e) Indian Parliament has cleared the second amendment of the Indian Patents Bill that takes such issues into consideration, including **patent** terms, emergency provisions and research and development initiative.

Key Words

Vaccines : It is a liquid, containing a dead or attenuated pathogen or it is antigen that provides temporary or permanent immunity to disease.
Toxic : Substance which is harmful to living organisms or cells.
Biopatent : A patent is a right granted by a government to an inventor to prevent others from commercially using his invention. When patents are granted for biological entities and for products derived from them, these patents are called biopatents.
Bio-resources : These are natural renewable sources, Bio-resources are laboratory animals, plants, cells, genes, and microorganisms, used for researches.

Example 2

Q. What do you understand by Ethical issues?

Sol. Ethical issues occur when a given decision, scenario or activity creates a conflict with a society's moral principles. Both individuals and businesses can be involved in these conflicts, since any of their activities might be put to question from an ethical standpoint. For e.g., 27 varieties of Basmati are cultivated in India. This variety is known for its unique flavour and long grains. An American company cross-bred their semi-dwarf varieties with the Indian Basmati and claimed it to be a 'new' variety. The company even got the patent rights for the new variety without giving any compensation to the respective country or the farmers. This is known as biopiracy. This would severely affect the biodiversity of the concerned areas and harm the indigenous livelihoods. This is an ethical issue related to Genetically Modified Organisms.