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RESEARCH ARTICLE

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BIOTECHNOLOGY: PAST, PRESENT و AND FUTURE: A REVIEW

ABSTRACT:

Knowledge of biotechnology dates back to the start of human civilization. In present day world, ever increasing demand of food due to rapid increase in population is among one of the big challenges for human race. Biotechnology is playing a key role in Agriculture, Food technology, Livestock by introducing genetically improved organisms that has high production, disease resistance and improved nutritious value. Modern industrialization has increasing requirement of energy and waste treatment. Biofuels and bioremediation are the most focused areas to meet these demands as it provides environment friendly, renewable and economical solutions. Health industry is being revolutionized by the introduction of improved vaccines, better diagnostic techniques, gene therapy and bioinformatics tools. Future biotechnology has wider scope and will lead certain fields of science and technology.

KEY WORDS:

Biotechnology, Agriculture, Medicine, Aquaculture, Environmental, Animal, Past, Present, Future.

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INTRODUCTION:

Biotechnology is defined as the use of living organisms through some logic for the benefit of mankind. The first ever process in which biotechnology is used by man is fermentation done thousands of years ago when milk is converted into the yogurt (Herbst, 2001). In the earliest documents, the production of cheese from the milk is mentioned. Egyptians used fungi in bread making in 4000 BC (Demain, 1981). Therefore, biotechnology is not a new science which is invented recently by the scientists. History of biotechnology date back to thousands of years when the human used it in food and medicine production (Bateson and Mendel, 1909).

In 500BC, moldy crud was used by the Chinese to treat boils (Wieczorek and Munster, 2006). Greeks started crop rotation in 250 BC to increase the fertility of their soils. In 1590, the microscope was developed by Hans Jansen (Bradbury, 2014) that helped

L. Hooke to discover the cell in 1663. Leading to the Leeuwenhoek discovery of bacteria in 1675 (Smit and Heniger, 1975). In 1797 Jenner vaccinated the child against small pox first time in the history of mankind (Willis, 1997; Winkelstein, 1992). Then historical event of using term "biology" occurred first time in 1802 by Jean Baptiste Lamarck (Hoffmeyer, 2001). In 1830, the discovery of proteins take place. In 1833 cell nucleus (Brown, 1833) and in 1855 *E.coli* was discovered by Theodor Escherich (Feng *et al.*, 2002).

Modern biotechnology started in the past hundred years and its foundation is laid down by Louis Pasture, R. Koch and Mendel (Bateson and Mendel, 1909; Mendel, 1996; Sakula, 1982).

Era of modern biotechnology starts from 1869. This field was first called biotechnology by K. Erkey in 1919 (Murphy and Perrella, 1993). He refered it to the production of beneficial products from live organisms with the help of raw material (Ereky, 1917; Goujon, 2001). Watson and Crick in 1953 explained DNA structure (Watson and Crick, 1953). After discovering the fact that the genetic information is passed from one generation to other in 1954 the biotechnology picks up the speed and many new discoveries were made in the second half of the 20th century.

Discovery of the procedure to inject foreign DNA into an organism happened in 1970's when restriction enzyme was discovered by Smith and Welcox. He used the ligase enzyme to join together the two restricted cites in the form of plasmid. This was the start of recombinant DNA technology (Smith and Welcox, 1970).

In 1983 artificial chromosome was developed (Murray and Szostak, 1983). Following the discovery of DNA finger printing technique in 1984 (Bjorvatn *et al.*, 1984). In the same year first genetically-engineered vaccine was made (Paoletti *et al.*, 1984; Watson and Enquist, 1984). The microorganisms in bioremediation was first time used in the 1989 (Heitkamp and Cerniglia, 1989).

Development of PCR by the K Mullis in 1990 changed the entire field of biotechnology and revolutionized it (Mullis, 1990).

Present day biotechnology has provided the researchers enough tools and data so that they can manipulate their desired traits with the help of genetic biotechnology. The result of this is very obvious in every field of science and on all human beings living in today's world. For example, in health and medicine biotechnology helped a lot in the development of recombinant proteins and drugs used as therapy and diagnosis to different diseases now days. Also the genetic disorders previously troughed to be incurable are now treated with the help of gene therapy. Biotechnology is now even used in the crime scene and many countries in the world have legalized their use in judicial system to solve crimes. Biotechnology is also used in bioremediation of different contaminants which are toxic and cause pollution in the environment (Deutschbauer *et al.*, 2006).

On 11th march, 2014 APEC R&D Leaders' Forum scientists said that the human population is supposed to be doubled by 2050 (Sheeha, 2007) and we are unable to provide food to them by the current technologies. They proposed biotechnology can bring revolution in the current technologies of food and energy production to cope up the upcoming challenges. In past few years biotechnology is booming and many new technologies and developments had made (Lim, 2009).

In 1970 the major development took place in the field of biotechnology as recombinant DNA formation occurs. In 1976 the industrial applications of biotechnology took place as scientists and engineers can now change the characteristics of an organism at genetic level. The scientists modified the genetic material of the organisms to obtain their desired product (Flavell and Smith, 1976; Galán *et al.*, 1990; Law *et al.*, 1976).

RESULTS:

Agriculture:

In 1960 the production of agrochemicals brings the green revolution by doubling the production with negligible amount of increase in land under cultivation (Shiva, 1991). The rate at which world population is increasing this boost in food production will soon be saturated. Also the impact of chemicals on the environment is also very dangerous and world is facing many problems due to it like greenhouse effect. To meet this challenge genetically modified organisms and crops are in spot light and in near future these will bring revolution. But genetically modified organisms are live as compare to agrochemicals and are no trustable. GMO's when released into the environment it is very difficult to control them and they can bring drastic changes in the environment. Some scientists are trying to improve the nutritional value of the plants by improving them through Genetic Engineering. For example, rice is deficient in many essential nutrients like iron and Vitamin A. And is food for almost half of the world population. Scientists at Zurich's Federal Institute of Technology (ETH) are successful in implanting the genes into the rice for the production of iron and vit. A (Ye *et al.*, 2000).

The biotechnological applications mainly used in agriculture include tissue culture, genetic engineering, somatic hybridization, marker aided selection, analysis of the whole genome sequence of the species (Vincze, 2009).

Introduction of biotechnology in the field of agriculture has a revolutionary effect on it. Two bacteria played a major role in this regard, first is *Agrobacterium tumefaciens* and second is *Bacillus thuringiensis*. Tumor producing capability of first bacteria was used and its genes were recognized that were present on its plasmid (called tumor inducing plasmid) (Van Larebeke *et al.*, 1974). This plasmid is extensively used to incorporate the foreign genes into the plants to produce transgenic plasmid (Hernalsteens *et al.*, 1980; Hoekema *et al.*, 1983; Hooykaas-Van Slogteren *et al.*, 1984; Stachel and Zambryski, 1986). The second bacteria is used as bio pesticide due to presence of cry gene in its plasmid (Battisti *et al.*, 1985; Miteva, 1978; Nickerson, 1980). This property of the bacteria is being used and the gene after separation is being incorporated into the plants so that they can protect themselves from pests (Barton *et al.*, 1987; Fischhoff *et al.*, 1987). As in market there is no chemical pesticide present which is effective against viruses that attack plants due to which in near future there will be vast production and demand of bio pesticide, bio herbicide, bio fungicide etc. This will be due to their effectiveness and cheapness (Rajasekaran, 2008).

Virus resistant varieties are also very important to increase the production and in future this is going to happen. At present viral coat protein and multiple genes are transferred for this purpose (Thomson, 2003). A gene that codes for the viral coat proteins of the virus is inserted into the plant. This viral coat protein act as virus in the plant and produces immunity but do not produce disease. This technique is being used at present (Abel *et al.*, 1986; Beachy *et al.*, 1990).

Scientists are trying at their level best to decrease the anti-nutritional factors in the plants (Clarke and Wiseman, 2000; Enneking and Wink, 2000; Gupta and Shrivastava, 2015). A research on potato to decrease glycoalkaloids content is done by adding antisense genes to the plants. Anti-sense genes block the activity of glucose glucosyltransferase enzyme which is responsible for the production of glycoalkaloids. This substance cause damage to intestine and health. This research is carried out to decrease its contents (Wood, 1997).

Bioinformatics:

Research in genetics leads to the development of tools that helps the researchers to investigate about their gene (Jiang *et al.*, 2015; Manor and Segal, 2015; Rezaei-Ghaleh *et al.*, 2015; Setoain *et al.*, 2015). During previous years problems was faced to arrange and store the massive data of genes coming from different research institutions which leads to the development of tools used today (Brown *et al.*, 2015; Edgar *et al.*, 2002; Goujon *et al.*, 2010; Sherry *et al.*, 2001). Genetic sequence of different microorganisms like Archea bacteria and other bacteria was done in the late 1999 also the sequence of human genome (chromosome 22) was done in this era. During nineties, the Gene Bank which is the major data bank for the storage of DNA sequence grown to 4.86 million organism sequence. Human genome sequence project was started in 2000 and completed in 2003. At present private companies are providing the services to the researches for sequencing their genes. In future bioinformatics is going to become an industry as the use of genomics in the every research project is becoming essential(Reed, 2000).

Biotechnology in Medicine:

Biotechnology brought a revolution in the field of medicine by producing cheaper, faster and safest medicines. Now the researches are able to identify the genes which cause the disease. After identifying their enemy, now they are in better position to fight and eliminate them (Ohlstein *et al.*, 2006; Passos *et al.*, 2016; Tafsiri *et al.*, 2016; Zajtchuk, 1999).

At present almost 400 private companies are producing medicine with the help of biotechnology and in future this will increase to several hundred thousand. It is estimated by the scientists that by 2020 every one will be using genetically engineered medicines for common disease like diabetes and hepatitis and by 2040 individual based genetically engineered medicines will be developed. So the future of health and medicine is pharmacogenomics (Shastry, 2005).

After the completion of human genome, it is now challenge to discover the function of each gene which will revolutionize the field of medicine and genetics. Development in Omics (proteomics, genomics, metabolomics and transcriptomics) will help in invention of novel medicines.

Vaccines:

In 19th century Edward Jenner (Willis, 1997; Winkelstein, 1992) and L. Pasteur (Debré, 2000; Geison, 2014; Pasteur *et al.*, 2002) discovered the vaccine and many techniques have been developed to improve the vaccine at present. Traditionally vaccine was produced by attenuating or killing the bacteria with the help of chemicals (Holmgren and Svennerholm, 1992). Attenuated vaccine

sometimes revert into the live pathogens causing disease in the patient (Baba *et al.*, 1999) while killed vaccines contains toxic components which cause toxicity (Trollfors, 1984). But after the progress in biotechnology recent techniques have developed which help in overcoming such problems like subunit vaccines (Morein and Simons, 1985; Wunner *et al.*, 1983). Subunit vaccines contain only a portion of the pathogenic bacteria instead of the full bacteria and have no effect on the health of patient (Pecora *et al.*, 2012; PURCELL and GERIN, 1975). First subunit vaccine produced in yeast was hepatitis B vaccine. Bioinformatics methods (Setoain et al., 2015) also revolutionized this field. The sequencing of pathogens at low cost also helps in recognizing the immunogenic parts of the pathogens. Gene bank and online data bases contain whole genome sequences of most of the pathogens (Benson *et al.*, 2015). Hundreds of important bacterial genomes are in the process of sequencing and hopefully will be available in near future (Rajasekaran, 2008).

Biopolymers and Bio plastic:

Manufacturing of today's world plastic is done with the help of petroleum-based chemicals. These chemicals have a severe impact on the environment and scientists are trying to develop biodegradable source to produce plastic as it is environment friendly (Ivanov *et al.*, 2015). In 1992 scientists produced the bio plastic polyhydroxyalkanoate (PHA) by inserting the genes that codes specifically this protein into the plant (Poirier *et al.*, 1992).

Bio plastic is mainly used in packaging, bowls, pots, bags, plastic piping, fuel lines and crockery (Chen and Patel, 2011). It is used as medical implants to save patients from operations (Hamad *et al.*, 2015). Starch made mulch films are being used in Agriculture that are not collected from the field after use (Scarascia-Mugnozza *et al.*, 2006).

The production of bio plastic with the help of corn is 300 times more expensive and in future more research is needed on this subject.

Enzyme production:

For the production of enzymes fermentation was the best suited method before the start of modern biotechnology. After the development of recombinant biotechnology, it was rapidly accepted by the companies due to its rapid impact on production and efficiency. At present the industrial production of enzyme worth 1.6 billion dollars. Enzyme industry is growing at very fast pace and pharmaceutical industry is now also using enzymes in their products because microbial enzymes are now proved to be effective for many diseases like ribonuclease enzyme that is an effective antiviral medicine. Enzyme production from microbes is preferred over the plants due to their easy and cheap process of production. Therapeutic proteins production has an estimated market of 200 billion dollars at present. For example, proteins like interleukin-2 is very effective in renal carcinoma. In future the discovery of novel pathways and microorganisms of both aquatic and terrestrial will help a lot in the development of enzyme production industry (Nielsen, 1980).

Food Technology:

Genetically modified foods or GMO's (Genetically Modified Organisms) are modified plants at laboratory to resist insects, herbs and to increase production. For example, gene of an organism resistant to pest is isolated and incorporated in our desired plant to make it genetically modified. For example *Bacillus thuringiensis* gene which kills the pest larva by the production of crystals is incorporated into the plants (Whitman, 2000). At present there are few GM crops that are accepted in international food markets. These are *Bt* maize, rape oilseed, herbicide resistant soybean and insect resistant cotton.

Citric acid is widely used in food applications. Its production is about half million tons per year. This is mainly produced through fermentation process. Previously it was produced from lemon but now the major portion is produced by fungus *Aspergillus niger* in very huge fermenters. Lactic acid is also very important organic acid produced through fermentation and used in food products as a food additive, strain improvement to increase the production is needed at present and research work is going on. But it is a slow process as mutation and isolation are very much laborious and time consuming process. Development of rapid and easy technique will help in this regard. In the era of modern biotechnology first of all enzyme were produced to be used in food products followed by organic and amino acids production. In future the more emphasis will be on the improvement of nutrition value and quality of the food products (Pai, 2003).

Livestock:

Researchers are discovering the ways to increase the production of livestock and poultry with the help of biotechnology (Armstrong and Gilbert, 1985; Burt, 2002). Scientists have increased the production of casein protein in the milk which increased the nutritional value of the milk (Brophy *et al.*, 2003). Researches are trying to develop the disease resistant and enhanced egg and meat production gene to get favorable results from it (Bacon *et al.*, 2000; Sasaki *et al.*, 2004).

Animal genomics plays an important role in the increase and quality of production of animals. Biotechnology plays a vital role in

this. Molecular markers are now gaining popularity in selection and characterization of different species of animals. These include Restriction Fragment Length Polymorphism (RFLP), Amplified Fragment Length Polymorphism (AFLP), Randomly Amplified Polymorphic DNA (RAPD) and Single Nucleotide Polymorphism (SNP). MAS (Marker Assisted Selection) is used to identify and select the animal with desirable traits (Fan *et al.*, 2010).

Due to rapid increase in the population of the world the demand of the fish is also increased and it will increase many folds in the coming years. The fish population is declining due to over fishing so aquaculture is the only solution to overcome this problem. But the aquaculture now days is facing many problems like feed conversion ratio, weight gain, diseases and reproduction rate etc.

Demand of fish is increasing day by day. Biotechnologist tried to introduce genes into the fish to speed up growth, disease resistant and increase weight. This resulted in 3 to 5 times more growth and disease resistant than the non-transgenic ones (FAO/WHO, November 2003).

Bioremediation:

Hydrocarbons contamination is today's most harmful agent to the environment. The seepage of the oil into the environment is due to the accidental leakage of oil, refineries processing and other natural phenomenon. The leakage during the transportation of oil by sea is a regular phenomenon. Also during storage, processing and refining leakage of oil occur. These all things cause an estimated of 600000 to 200000 metric ton of oil seepage into the environment (Kvenvolden and Cooper, 2003).

Microorganisms play a vital role in the removal of this contaminant from the environment. Several bacterial species take up hydrocarbons and transform it into simpler, nontoxic compounds (Medina-Bellver *et al.*, 2005).

During recent years the production of genetically modified organisms has increase the potential of bioremediation. These organisms has a gene incorporated into their genome which code for an enzyme responsible for the degradation of environmental contaminants into nontoxic forms (Jain and Bajpai, 2012).

There are two types of bioremediation in-situ and ex-situ. In-situ bioremediation is the treatment of the contaminant with the help of microorganisms on the spot while ex-situ bioremediation is the treatment of the contaminant elsewhere. Mostly bacteria, yeast and fungi play vital role in biodegradation. Efficiency of biodegradation is different in different organisms. (Das and Mukherjee, 2007; Jones *et al.*, 1970; Margesin and Schinner, 1997; Pinholt *et al.*, 1979). In future economical and efficient algae strains will be produced with the help of biotechnology to meet fuel demand (Mata *et al.*, 2010).

Genetic engineering has help the scientists in modifying the bacteria for the purpose of bioremediation for example *Deinococcus radiodurans* (the most radio resistant microorganism known) is being used on nuclear waste to detoxify toxic metals like mercury and toluene (Brim *et al.*, 2000).

Biofuels:

An interest in the biotechnology is increasing by the concept of biofuel production. The reason behind it include the scarcity of fossil fuel we are facing today which will even go more worse in the future (Şensöz *et al.*, 2000). Also biofuels are biodegradable and environment friendly. Private companies are taking interest in it as it will be the fuel in the future when fossil fuel deplete from earth. China has desire to be a leader of industrial biotechnology due to its high demand of fuel and ever increasing population (Nesbitt, 2009).

Algae which is a third generation biofuel (Dragone *et al.*, 2010) is very much in focus now a days for its potential to produce bioethanol (John *et al.*, 2011). It was the era of Second World War when some researchers discovered the potential benefits of the algae and used it as a replacement to animal protein for humans (Cannell, 1990; Spolaore *et al.*, 2006).

Algae do not require any land to grow and some algae strains can even grow in salt water. So there is no competition between the land crops and algae (Chisti, 2007; Harvey *et al.*, 2012; Milledge *et al.*, 2014). The biomass production of algae is also high as compare to land crops (Tredici, 2010; Walker, 2009; Williams and Laurens, 2010). Therefore algae is the future biomass for biofuel production (Menetrez, 2012). These are the bio factories to convert carbon dioxide and water into fuel in the presence of sunlight (Chisti, 2007). But to date the extraction of fuel from the algae is not economical and technology is needed in this regard. Hopefully in coming years we will be using biofuel in our cars extracted from algae (Aresta *et al.*, 2005; Milledge and Heaven, 2014).

Diagnosis of Infectious Diseases:

As today's world is become a global village the tools to detect transboundary infectious diseases has got important and biotechnology plays its role in it. PCR is an effective tool with its different types in the diagnosis of infectious diseases (Habib *et al.*, 2014; Yang, 2007; Yang and Rothman, 2004; Yang *et al.*, 2007) to carry out global trade. Other techniques include Fluorescent Antibody Test (Dean *et al.*, 1996), ELISA (Engvall and Perlmann, 1971), DNA

microarrays (Schena *et al.*, 1995) and probes, Genomic sequencing (Church and Gilbert, 1984; Shah *et al.*, 2011), Nucleic acid extraction etc. (Manual, 2012).

Future techniques that will increase the diagnosis accuracy, sensitivity and specificity include Multiplex ELISA (one ELISA for multiple infectious diseases), potentiometric Elisa, Multiplex protein assay, Proximity ligation assays (PLA) and many others. Hopefully in future the diagnosis with the help of biotechnology will be more cheap, accurate and handy (Belák *et al.*, 2009).

Scientists are now working on cow milk to produce bactericidal enzymes which kill bacteria by lysis like lysostaphin. This will help in the reduction of diseases like mastitis as this enzyme will lyse the causative bacteria (Oldham and Daley, 1991).

Bacteriophages:

Most abundant organisms on earth are bacteriophages. These are viruses having protein coat and genetic material (either DNA or RNA) (Clark and March, 2006).

Bacteriophages were first used as therapeutic agents in humans in 1919 (Summers, 2001). In 1940 antibiotics were discovered and phage therapy died in America while in Russia it is in use till now (Sulakvelidze and Kutter, 2004). But now it is admitted that

Future of Biotechnology:

Biotechnology is an emerging field of science and it has a bright future. Development in Omics (proteomics, genomics, metabolomics, transcriptomics, etc.) will help in future progress in every field of science linked with biotechnology. The technologies that are at experimental level will be at commercial level in future. Proteomics and Bioinformatics are among the emerging subjects in the field of biotechnology. Proteomics will help in revealing the cause of alteration in the bacterial proteomes by the change in the environment. Biotechnology will change the future, as this field is supported by both the academic institutes as well as private companies. In future there will be a greater demand of biotechnologists as compared to any other field of science. Pakistan is a developing country, so there should be focus on the products of biotechnology and preparation of the biotechnologists for the market as well as for institutes to meet the future demand (Niazi and Riaz-ud-Din, 2006).

With all these positive impact of biotechnology on the society there are concerns that genetically modified organisms would escape into the environment. For example, if an organism containing an enzyme to degrade the cellulose is escaped into the forest we cannot imagine what will damage it cause. Also the escape of genetically engineered fish, cattle and other organism cause serious ecological consequences (Muir and Howard, 1999; Muir and Howard, 2001; Muir and Howard, 2002).

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