STUDY ON MODERN TRENDS IN MICROBIOLOGY WITH SPECIAL REFERENCE TO HUMAN HEALTH

Bibhudatta Mohanty, **Dr. Akhilesh Kumar

***Assistant Professor, Govt. PG college, Narnaul, Haryana*
**Research Scholar, Monad University, Hapur, Ghaziabad (U.P)*

ABSTRACT

The first genetically engineered products were medicines designed to treat human diseases. To cite one example, in Genentech developed synthetic humanized insulin by joining its gene with a plasmid vector inserted into the bacterium Escherichia coli. Insulin, widely used for the treatment of diabetes, was previously extracted from the pancreas of abattoir animals the resulting genetically engineered bacterium enabled the production of vast quantities of synthetic human insulin at relatively low cost. According to a 2003 study undertaken by the International Diabetes Federation (IDF) on the access to and availability of insulin in its member countries, synthetic 'human' insulin is considerably more expensive in most countries where both synthetic 'human' and animal insulin are commercially available:
E.g. within European countries the average price of synthetic 'human' insulin was twice as high as the price of pork insulin. Yet in its position statement, the IDF writes that "there is no overwhelming evidence to prefer one species of insulin over another" and "[modern, highly purified] animal insulins remain a perfectly acceptable alternative.

Key words: *Abattoir animals, synthetic 'human' insulin, pork insulin, plasmid vector.*

INTRODUCTION

For thousands of years, humans have used selective breeding to improve production of crops and livestock to use them for food. In selective breeding, organisms with desirable characteristics are mated to produce offspring with the same characteristics. For example, this technique was used with corn to produce the largest and sweetest crops. In the early twentieth century scientists gained a greater understanding of microbiology and explored ways of manufacturing specific products. In 1917, Chaim Weizmann first used a pure microbiological culture in an industrial process, that of manufacturing corn starch using *Clostridium acetobutylicum*, to produce acetone, which the United Kingdom desperately needed to manufacture explosives during World War I.

REVIEW OF LITERATURE

Microbiology has led to the development of antibiotics. In 1928, Alexander Fleming discovered the mold *Penicillium*. His work led to the purification of the antibiotic compound formed by the mold by Howard Florey, Ernst Boris Chain and Norman Heatley - to form what we today know as penicillin. In 1940, penicillin became available for medicinal use to treat bacterial infections in humans.

he field of modern biotechnology is generally thought of as having been born in 1971 when Paul Berg's (Stanford) experiments in gene splicing had early success. Herbert W. Boyer (Univ. Calif. at San Francisco) and Stanley N. Cohen (Stanford) significantly advanced the new technology in 1972 by transferring genetic material into a bacterium, such that the imported material would be reproduced. The commercial viability of a biotechnology industry was significantly expanded on June 16, 1980, when the United States Supreme Court ruled that a genetically modified microorganism could be patented in the case of *Diamond v. Chakrabarty*.[12] Indian-born Ananda Chakrabarty, working for General Electric, had modified a bacterium (of the *Pseudomonas* genus) capable of breaking down crude oil, which he proposed to use in treating oil spills. (Chakrabarty's work did not involve gene manipulation but rather the transfer of entire organelles between strains of the *Pseudomonas* bacterium.

Revenue in the industry is expected to grow by 12.9% in 2008. Another factor influencing the biotechnology sector's success is improved intellectual property rights legislation—and enforcement—worldwide, as well as strengthened demand for medical and pharmaceutical products to cope with an ageing, and ailing, U.S. population.

Rising demand for biofuels is expected to be good news for the biotechnology sector, with the Department of Energy estimating ethanol usage could reduce U.S. petroleum-derived fuel consumption by up to 30% by 2030. The biotechnology sector has allowed the U.S. farming industry to rapidly increase its supply of corn and soybeans—the main inputs into biofuels—by developing genetically modified seeds which are resistant to pests and drought. By boosting farm productivity, biotechnology plays a crucial role in ensuring that biofuel production targets are met.

Most traditional pharmaceutical drugs are relatively small molecules that bind to particular molecular targets and either activate or deactivate biological processes. Small molecules are typically manufactured through traditional organic synthesis, and many can be taken orally. In contrast, Biopharmaceuticals are large biological molecules such as proteins that are developed to address targets that cannot easily be addressed by small molecules. Some examples of biopharmaceutical drugs include Infliximab, a monoclonal antibody used in the treatment of autoimmune diseases, Etanercept, a fusion protein used in the treatment of autoimmune diseases, and Rituximab, a chimeric monoclonal antibody used in the treatment of cancer. Due to their larger size, and corresponding difficulty with surviving the stomach, colon and liver, biopharmaceuticals are typically injected.

Modern biotechnology is often associated with the use of genetically altered microorganisms such as *E. coli* or yeast for the production of substances like synthetic insulin or antibiotics. It can also refer to transgenic animals or transgenic plants, such as Bt corn. Genetically altered mammalian cells, such as Chinese Hamster Ovary cells (CHO), are also used to manufacture certain pharmaceuticals. Another promising new biotechnology application is the development of plant-made pharmaceuticals.

microbiology is also commonly associated with landmark breakthroughs in new medical therapies to treat hepatitis B, hepatitis C, cancers, arthritis, haemophilia, bone fractures, multiple sclerosis, and cardiovascular disorders. The biotechnology industry has also been instrumental in developing molecular diagnostic devices that can be used to define the target patient population for a given biopharmaceutical. Herceptin, for example, was the first drug approved for use with a matching diagnostic test and is used to treat breast cancer in women whose cancer cells express the protein HER2.

MATERIAL AND METHOD:

Modern biotechnology can be used to manufacture existing medicines relatively easily and cheaply. The first genetically engineered products were medicines designed to treat human diseases. To cite one example, in 1978 Genentech developed synthetic humanized insulin by joining its gene with a plasmid vector inserted into the bacterium *Escherichia coli*. Insulin, widely used for the treatment of diabetes, was previously extracted from the pancreas of abattoir animals (cattle and/or pigs). The resulting genetically engineered bacterium enabled the production of vast quantities of synthetic human insulin at relatively low cost.[17] According to a 2003 study undertaken by the International Diabetes Federation (IDF) on the access to and availability of insulin in its member countries, synthetic 'human' insulin is considerably more expensive in most countries where both synthetic 'human' and animal insulin are commercially available: e.g. within European countries the average price of synthetic 'human' insulin was twice as high as the price of pork insulin.[18] Yet in its position statement, the IDF writes that "there is no overwhelming evidence to prefer one species of insulin over another" and "[modern, highly purified] animal insulins remain a perfectly acceptable alternative.

Modern biotechnology has evolved, making it possible to produce more easily and relatively cheaply human growth hormone, clotting factors for hemophiliacs, fertility drugs, erythropoietin and other drugs.[20] Most drugs today are based on about 500 molecular targets. Genomic knowledge of the genes involved in diseases, disease pathways, and drug-response sites are expected to lead to the discovery of thousands more new targets.

There are basically two ways of implementing a gene therapy treatment:

1. ***Ex vivo***, which means "outside the body" – Cells from the patient's blood or bone marrow are removed and grown in the laboratory. They are then exposed to a virus carrying the desired gene. The virus enters the cells, and the desired gene becomes part of the DNA of the cells. The cells are allowed to grow in the laboratory before being returned to the patient by injection into a vein.

2. ***In vivo***, which means "inside the body" – No cells are removed from the patient's body. Instead, vectors are used to deliver the desired gene to cells in the patient's body.

As of June 2001, more than 500 clinical gene-therapy trials involving about 3,500 patients have been identified worldwide. Around 78% of these are in the United States, with Europe having 18%. These trials focus on various types of cancer, although other multigenic diseases are being studied as well. Recently, two children born with severe combined immunodeficiency disorder ("SCID") were reported to have been cured after being given genetically engineered cells.

CONCLUSION:

Gene therapy faces many obstacles before it can become a practical approach for treating disease. At least four of these obstacles are as follows:

1. ***Gene delivery tools*.** Genes are inserted into the body using gene carriers called vectors. The most common vectors now are viruses, which have evolved a way of encapsulating and delivering their genes to human cells in a pathogenic manner. Scientists manipulate the genome of the virus by removing the disease-causing genes and inserting the therapeutic genes. However, while viruses are effective, they can introduce problems like toxicity, immune and inflammatory responses, and gene control and targeting issues. In addition, in order for gene therapy to provide permanent therapeutic effects, the introduced gene needs to be integrated within the host cell's genome. Some viral vectors effect this in a random fashion, which can introduce other problems such as disruption of an endogenous host gene.

2. ***High costs*.** Since gene therapy is relatively new and at an experimental stage, it is an expensive treatment to undertake. This explains why current studies are focused on illnesses commonly found in developed countries, where more people can afford to pay for treatment. It may take decades before developing countries can take advantage of this technology.

3. ***Limited knowledge of the functions of genes*.** Scientists currently know the functions of only a few genes. Hence, gene therapy can address only some genes that cause a particular disease. Worse, it is not known exactly whether genes have more than one function, which creates uncertainty as to whether replacing such genes is indeed desirable.

4. ***Multigene disorders and effect of environment.*** Most genetic disorders involve more than one gene. Moreover, most diseases involve the interaction of several genes and the environment. For example, many people with cancer not only inherit the disease gene for the disorder, but may have also failed to inherit specific tumor suppressor genes. Diet, exercise, smoking and other environmental factors may have also contributed to their disease.

REFERENCES

Cornell Chronicle, May 14, 1987, page 3.Biologists invent gun for shooting cells with DNA

Sanford JC et al (1987) Delivery of substances into cells and tissues using a particle bombardment process. Journal of Particulate Science and Technology 5:27-37.

Klein, TM et al (1987) High-velocity micro projectiles for delivering nucleic acids into livingcells. Nature 327:70-73.

*Lee LY, Gelvin SB (February 2008). "T-DNA binary vectors and systems". PlantPhysiol. **146** (2):325–332. doi:10.1104/pp.107.113001. OCLC 1642351.PMC 2245830. PMID 18250230.*

*Park F (October 2007). "Lentiviral vectors: are they the future of animal transgenesis?". Physiol. Genomics **31** (2): 159–173.doi:10.1152/physiolgenomics.00069.2007. OCLC 37367250. PMID 17684037.*

*Jackson, DA; Symons, RH; Berg, P (1 October 1972). "Biochemical Method for Inserting New Genetic Information into DNA of Simian Virus 40: Circular SV40 DNA Molecules Containing Lambda Phage Genes and the Galactose Operon of Escherichia coli". PNAS **69** (10): 2904– 2909. Bibcode:1972PNAS 69.2904J.doi:10.1073/pnas.69.10.2904. PMC 389671. PMID 43429 68.*

M. K. Sateesh (25 August 2008). Bioethics and Biosafety. I. K. International Pvt Ltd. pp. 456–. ISBN 978-81-906757-0-3. Retrieved 27 March 2013.

*Jefferson R. A. Kavanagh T. A. Bevan M. W. (1987). "GUS fusions: beta-glucuronidase as a sensitive and versatile gene fusion marker in higher plants". EMBO journal **6**(13): 3901– 3907. ISSN 0261-4189. PMC 553867. PMID 3327686.*

Nosowitz, Dan (15 September 2011) Suntory Creates Mythical Blue (Or, Um, Lavender-ish)Rose Popular Science, Retrieved 30 August 2012

Phys.Org website. April 4, 2005 Plant gene replacement results in the world's only blue rose

Kyodo (11 September 2011 Suntory to sell blue roses overseas The Japan Times, Retrieved 30 August 2012

Wired Report 2011

Gasdaska JR et al (2003) Advantages of Therapeutic Protein Production in the Aquatic Plant Lemna. Bio Processing Journal Mar/Apr 2003 pp 49–56 [1]

(10 December 2012) Engineering algae to make complex anti-cancer 'designer' drug PhysOrg, Retrieved 15 April 2013

Büttner-Mainik, A., et al (2011): Production of biologically active recombinant human factor Hin Physcomitrella. Plant Biotechnology Journal 9, 373–383. [2]

Baur, A., R. Reski, G. Gorr (2005): Enhanced recovery of a secreted recombinant human growth factor using stabilizing additives and by co-expression of human serum albumin in the moss Physcomitrella patens. Plant Biotech. J. 3, 331–340 [3]

Protalix website – technology platform

Gali Weinreb and Koby Yeshayahou for Globes May 2, 2012. FDA approves Protalix Gaucher treatment http://www.agf.gov.bc.ca/pesticides/infosheets/bt.pdf. Retrieved 21 January 2011

Hope, Alan (3 April 2013), News in brief: The Bio Safety Council...", Flanders Today, Page 2;In 2013, the Flemish Institute for Biotechnology was supervising a trial of 448poplar trees genetically engineered to produce less lignin so that they would be more suitable for conversion into bio-fuels.

*Nielsen, K. M. (2003). "Transgenic organisms—time for conceptual diversification?" Nature Biotechnology **21** (3): 227–228. doi:10.1038/nbt0303-227. PMID 12610561.edit*

*Schouten, H.; Krens, F.; Jacobsen, E. (2006). "Cisgenic plants are similar to traditionally bred plants: international regulations for genetically modified organisms should be altered to exempt cisgenesis". EMBO Reports **7** (8):750–753.doi:10.1038/sj.embor.7400769. PMC 1525145. PMID 16880817. edit*

Prins, T.W. and Kok, E.J. (2010) Food and feed safety aspects of cisgenic crop plant varieties Report 2010.001, Project number: 120.72.667.01, RIKILT – Institute of Food Safety, Netherlands. Retrieved 6 September 2010.

*Melo, Eduardo O.; Canavessi, Aurea M. O.; Franco, Mauricio M.; Rumpf, Rodolpho (2007). "Animal transgenesis: state of the art and applications". J. Appl. Genet. **48**(1): 47–61. doi:10.1007/BF03194657. PMID 17272861. Archived from the original on 26 September2009.*

*Leader, Benjamin; Baca, Qentin J.; Golan, David E. (January 2008). "Protein therapeutics: a summary and pharmacological classification". Nat Rev Drug Discov. A guide to drug discovery **7** (1): 21–39. doi:10.1038/nrd2399. PMID 18097458.Leader 2008 — Fee required for access to full text.*

*Walsh, Gary (April 2005). "Therapeutic insulins and their large-scale manufacture".Appl.Microbiol. Biotechnol. **67** (2): 151–159. doi:10.1007/s00253-004-1809-x.PMID 15580495. Walsh 2005 — Fee required for access to full text.*

Summers, Rebecca (24 April 2013) Bacteria churn out first ever petrol-like biofuel New Scientist, Retrieved 27 April 2013

*Pipe, Steven W. (May 2008). "Recombinant clotting factors". Thromb. Haemost. **99** (5): 840–850. doi:10.1160/TH07-10-0593. PMID 18449413.*

Bryant, Jackie; Baxter, Louise; Cave, Carolyn B.; Milne, Ruairidh; Bryant, Jackie (2007). "Recombinant growth hormone for idiopathic short stature in children and adolescents". In Bryant, Jackie. Cochrane Database Syst Rev (3):CD004440. doi:10.1002/14651858.CD004440.pub2. PMID 17636758. Bryant 2007 — Fee required for access to full text.

Baxter L, Bryant J, Cave CB, Milne R (2007). "Recombinant growth hormone for children and adolescents with Turner syndrome". In Bryant, Jackie. Cochrane Database Syst Rev (1): CD003887. doi:10.1002/14651858.CD003887.pub2.PMID 17253498.

Panesar, Pamit et al (2010) "Enzymes in Food Processing: Fundamentals and Potential Applications", Chapter 10, I K International Publishing House, ISBN 978-9380026336

EFSA (2012). Genetically modified animals. Europe:EFSA. http://www.efsa.europa.eu/en/topics/topic/gmanimals.htm.

Murray, Joo (20). Genetically modified animals. Canada:Brain waving. http://www.brainwaving.com/2010/07/28/genetically-modified-animals/.

*Jaenisch, R. and Mintz, B. (1974). "Simian virus 40 DNA sequences in DNA of healthy adult mice derived from preimplantation blastocysts injected with viral DNA.". Proc. Natl. Acad. Sci. **71** (4):1250–1254. Bibcode:1974PNAS...71.1250J.doi:10.1073/pnas.71.4.1250. PMC 388203. PMID 4364530.*

rudinko, larisa (20). Guidance for industry. USA: Center for veterinary medicine Link.

*Sathasivam K, Hobbs C, Mangiarini L, et al. (June 1999). [http: //journals.royalsociety.org/openurl.asp?genre=article&issn=0962- 8436 &volume=354& issue=1386& spage=963 "Transgenic models of Huntington'sdisease"]. Philos. Trans. R. Soc. Lond., B, Biol. Sci. **354** (1386): 963–9.doi:10.1098/rstb.1999.0447. PMC 1692600. PMID 10434294.*

*Spencer, L; Humphries, J; Brantly, M. (12 May 2005). "Antibody Response to Aerosolized Transgenic Human Alpha1-Antitrypsin". New England Journal of Medicine **352**: 19. Retrieved 28 April 2011.*

"The Nobel Prize in Chemistry 2008". The Official Web Site of the Nobel Foundation. Retrieved2012-08-31.

*Cabot, R. A.; Kühholzer, B.; Chan, A. W. S.; Lai, L.; Park, K. -W.; Chong, K. -Y.; Schatten, G.; Murphy, C. N. et al. (2001). "Transgenic Pigs Produced Using in Vitro Matured OocytesInfected with a Retroviral Vector". Animal Biotechnology **12** (2): 205–214. doi:10.1081/ABIO- 100108347. PMID 11808636. edit*

Lai, L.; Park, K. W.; Cheong, H. T.; k Hholzer, B.; Samuel, M.; Bonk, A.; Im, G. S.; Rieke, A. et al. (2002). "Transgenic pig expressing the enhanced green fluorescent protein produced by nuclear transfer using colchicine-treated fibroblasts as donor cells". Molecular Reproduction andDevelopment ***62*** *(3): 300–306.doi:10.1002/mrd.10146. PMID 12112592. edit*

Hogg, Chris (12 January 2006) Taiwan Breeds Green-Glowing Pigs BBC, Retrieved 31 August2012

Staff (8 January 2008) Fluorescent Chinese pig passes on trait to offspring AFP, Retrieved 31 August 2012

Kawarasaki, T.; Uchiyama, K.; Hirao, A.; Azuma, S.; Otake, M.; Shibata, M.; Tsuchiya, S.; Enosawa, S. et al. (2009). "Profile of new green fluorescent protein transgenic Jinhua pigs as an imaging source". Journal of Biomedical Optics ***14*** *(5):054017. doi:10.1117/1.3241985. PMID 19895119. edit*

Randall S. et al (2008) Genetically Modified Pigs for Medicine and Agriculture Biotechnology and Genetic Engineering Reviews – Vol. 25, 245–266, Retrieved 31 August 2012

Staff (2006) NTU produces green fluorescent pigs for medical research Taiwan Central News Agency, Retrieved 31 August 2012

Wongsrikeao P, Saenz D, Rinkoski T, Otoi T, Poeschla E (2011). "Antiviral restriction factor transgenesis in the domestic cat". Nature Methods ***8*** *(10):853–9.doi:10.1038/nmeth.1703. PMID 21909101.*

Staff (3 April 2012) Biology of HIV National Institute of Allergy and Infectious Diseases,Retrieved 31 August 2012.

Sasaki, E.; Suemizu, H.; Shimada, A.; Hanazawa, K.; Oiwa, R.; Kamioka, M.; Tomioka, I.; Sotomaru, Y. et al. (2009). "Generation of transgenic non-human primates with germline transmission". Nature ***459*** *(7246):523–527.Bibcode:2009Natur.459..523S. doi:10.1038/nature08090. PMID 19478777. edit*

Schatten, G.;Mitalipov, S. (2009). "Developmental biology: Transgenic primateoffspring". Nature ***459*** *(7246): 515–516. Bibcode:2009Natur.459..515S.doi:10.1038/459515a. PMC 2777739. PMID 19478771. edit*

Cyranoski, D. (2009). "Marmoset model takes Centre stage". Nature ***459*** *(7246):492–492. doi:10.1038/459492a. PMID 19478751. edit*

Louis-Marie Houdebine (2009) Production of Pharmaceutical by transgenic animals.Comparative Immunology, Microbiology & Infectious Diseases 32(2): 107–121 [4]

Britt Erickson, 10 February 2009, for Chemical & Engineering News. FDA Approves Drugfrom Transgenic Goat Milk Accessed October 6, 2012

Guelph (2010). Enviropig. Canada: http://www.uoguelph.ca/enviropig/index.shtml/.

Schimdt, Sarah. Genetically engineered pigs killed after funding ends, Postmedia News, June 22,2012. Accessed July 31, 2012.

Canada. "Enviropig — Environmental Benefits | University of Guelph". Uoguelph.ca. Retrieved 8 March 2010.

Stevenson, Heidi (2011). Scientists Use Human Genes in Animals, So Cows Produce Human-Like Milk—Or Do They? USA: http://www.gaia-health.com/articles401/000433-human-genes-cows-produce-human-milk.shtml/.

Classical Medicine Journal (14 April 2010). "Genetically modified cows producing humanmilk."

Yapp, Robin (11 June 2011). "Scientists create cow that produces 'human' milk". The Daily Telegraph (London). Retrieved 15 June 2012.

Jabed, A.; Wagner, S.; McCracken, J.; Wells, D. N.; Laible, G. (2012). "Targeted micro RNA expression in dairy cattle directs production of -lacto globulin-free, high-casein milk". Proceedings of the National Academy of Sciences.doi:10.1073/pnas.1210057109.

*Lai L et al. (2006). "Generation of cloned transgenic pigs rich in omega-3 fatty acids". Nature Biotechnology **24** (4):435–436. doi:10.1038/nbt1198.PMC 2976610. PMID 16565727.Retrieved 2009-03-29.*

Zyga, Lisa (2010). Scientist bred goats that produce spider silk. Link.