CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3827672

Available online at: http://www.iajps.com *Review Article*

ROLE OF BIOTECHNOLOGY IN PHARMACEUTICAL RESEARCH: A COMPREHENSIVE REVIEW

Indira Padhy*[1], Abikesh P K Mahapatra[2], Dr.Rohit Saraswat[3], Jianwu Song[4]

[1]Khallikote Autonomous College, Berhampur, Ganjam, Odisha-760001, INDIA
muluskaa@gmail.com
[2]OPJS University, School of Pharmacy, Churu, Rajasthan-331303, INDIA,
abikeshmahapatra@gmail.com
[3] OPJS University, School of Pharmacy, Churu, Rajasthan-331303, INDIA,
saraswatrohit20s@gmail.com
[4]Shandong Zibo Mytechpharm, No. 1 Lutai Ave, Zibo City, Shangdong, CHINA
9549069@qq.com

Article Received: March 2020 **Accepted:** April 2020 **Published:** May 2020

Abstract:
Biotechnology is a multidisciplinary scientific research field which uses living organisms or their parts to develop or modify products, or improve plants, animals and microorganisms. Biotechnology and the world of colors are always connected with each other through biotech applications. This has encouraged the requirement to construct a classification system based on colors. Advance technologies and products are developed within the areas include medicine (development of new medicines and therapies), agriculture (development of genetically modified plants, biofuels, biological treatment) or industrial biotechnology (production of chemicals, paper, textiles and food), environment (maintenance of biodiversity, bioremediation) etc. However, Biotechnology achieved considerable progress in the branch of healthcare sector. Pharmaceutical biotechnology is a relatively new and growing field in which the principles of biotechnology are applied to the development of drugs. A majority of therapeutic drugs in the current market are bioformulations, such as antibodies, nucleic acid products and vaccines. Biotechnology helps the pharmaceutical industry to develop new products, new processes, methods and services and to improve existing ones. This article is an inclusive review of use of biotechnology in the development of novel pharmaceutical products. It also covers the impact of biotechnology in research and invention related to different aspects of medicine. There is a widespread list of biopharmaceutical products in healthcare management available for therapeutic use. In this review we are discussed about various classes of biotechnology-based products such as gene therapy, monoclonal antibody, DNA fingerprinting, vaccines, biopharmaceuticals, stem cell therapy, pharmacogenomics along with their therapeutic applications.

Key words: *Pharmaceuticals in biotechnology,Gene therapy,Monoclonal antibody,Pharmacogenomics, DNA fingerprinting, Stem cell therapy.*

Corresponding author:
Indira Padhy,
Khallikote Autonomous College,
Berhampur, Ganjam, Odisha-760001,
INDIA
E-Mail: muluskaa@gmail.com

QR code

Please cite this article in press Indira Padhy et al, ***Role Of Biotechnology In Pharmaceutical Research: A Comprehensive Review.,****Indo Am. J. P. Sci, 2020; 07(05).*

INTRODUCTION:

Biotechnology can be defined as the technical application of living systems, organisms, or biologically derived materials to make products. It is a rapidly growing branch of science and technology working for human welfare [1].The word biotechnology was first coined by karoly Ereky in1919 in a book entitled Biotechnologie der Fleisch-, Fett- und Milcherzeugung im landwirtschaftlichen Grossbertriebe (Biotechnology of Meat, Fat and milk production in an Agrictural Large-Scale Farm) based on raw materials into useful product [2]. Biotechnology is a multidisciplinary field using various technologies, applied to living cells including not only biology but also areas enclosing microbiology, chemistry, biochemistry, genetics, molecular biology, immunology, cell and tissue culture and physiology, as well as genetic engineering for applications in industrial, agriculture and the pharmaceutical industry [3].

In early days, people were using techniques but did not know their working as field of biotechnology. As compared to current stage, it can be three types: Ancient biotechnology, Classical biotechnology and modern biotechnology. Early examples of traditional biological applications were baking bread, brewing alcoholic beverages, using microbes to make cheese and breeding animal and crops etc [4].

Modern biotechnology can be out lined with the development of the microscope by Zacharias Janssen in 1590 to the discovery of the cell by Robert Hooke. It also extended to the discovery of bacteria by Antonij van Leeuwenhoek. In the late 19th century, the rate of biotechnology has grown rapidly [5]. In this time the success rate of biotechnology started with the discovery of penicillin by Alexander Fleming in 1928. With the discovery of double helical structure of genetic material (DNA) in 1953, Watson and Crick set the stage for a new era of biotechnology for which they got Nobel Prize along with Hugh Wilkins, in 1962. Recombinant product human insulin was developed by Genentech became the first biopharmaceutical drug marketed. Recent advances in molecular biology have captured the attention into genomic era. Modern biotechnology comes up with breakthrough products and technologies can have a remarkable influence on the world economy and community [6].

The techniques in the biotechnology include the use of recombinant DNA for gene cloning and gene transfer between organisms through vector methods, culture of plant and animal tissues, DNA fingerprinting, PCR, Monoclonal antibody techniques, the regeneration of whole plants from single scale (totipotency), protoplast fusion of plant and animal cells , embryo manipulation technology, large scale fermentation processes using some of microbes for the production of pharmaceutical, diagnostics tests for diseases, food additives, enzymes, and hormones [7]. Today, the power of biotechnology is impacting all the aspects (food, health and animal life etc.) of everyday life. Biotechnology plays a major role to carry out biological transformations including enzymes, bacteria, yeast and other fungi, mammalian and insect cells and plant cell cultures, and transgenic animals. Industrial products including chemicals, biofuels and biopolymers, medical products including micro molecules (antibiotics), therapeutic proteins, vaccines and specific cell based products and finally, agricultural and food based products are the results of biological transformations and also used to recycle the waste materials and produce biological weapons [8].

There are other aspects of biotechnology that are promising and have the potential for greatly improving medicine. For example, gene therapy, which involves the correction of defects in the genes, is a promising approach that is being investigated for the ability to treat various diseases related to genetic mutations such as hypertension, diabetes, and cancer [9,10]. Another promising area is pharmacogenomics, which deals with the use of information derived from the genomics of the patient to help the physicians in making better therapeutic decisions [11].

Classification of Biotechnology:

Biotechnology and the world of colors are always connected with each other through biotech applications. A large number classification of biotechnology is available, but the classification based on color code is widely used. This is known as Rainbow code of biotechnology [12]. The briefly description of this classification is described in figure 1:

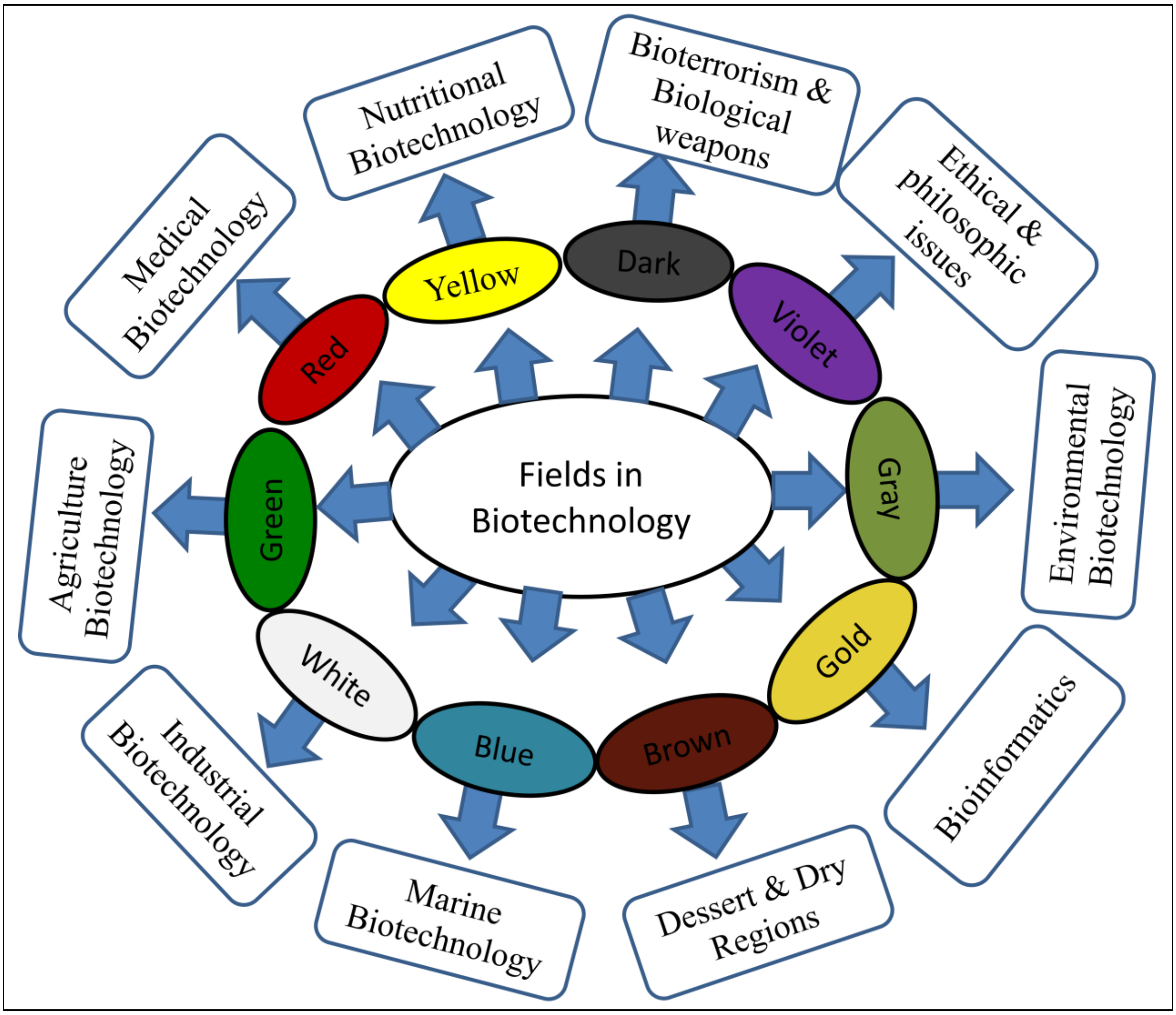

Figure 1: Classification of biotechnology based on color.

Green biotechnology:
Now a day, growth of population has increased the demand for basic needs like food, energy, fuel, medicines and other materials. To fulfil this demand, agricultural plays an important role in providing raw materials [13]. Green biotechnology is related to agricultural process with the aim of improving the nutritional quality, production of disease-resistant plants that have superior qualities, increased productivity and reduced production costs. Major applications of this field are tissue cultivation and micropropagation, development of genetically modified organisms, production of synthetic seeds for commercial uses, the use of molecular markers can map thousands of genes and production of biopolymers from renewable sources for power generation and the prevention of environmental pollution [14].

White biotechnology:
White biotechnology is related to industrial process. It is the modern application that uses minimum resource than traditional processes used to produce industrial goods and using living cells such as yeast, fungi, bacteria, plants and their enzymatic systems [15]. Such process are worldwide used in industrial fields including chemicals, pharmaceuticals, food & feed, detergents, pulp & paper, textiles, materials and polymers as well as in energy sectors. In this field biotechnology deals with less energy consumption, emissions of greenhouse gases and recycling of waste materials, and production of bio-based value added chemicals from fossil fuel. The raw materials which are used for this process including crops and organic byproducts from agricultural sources and sugars are obtained from household materials. For example, the use of enzymes as industrial catalysts to reduce hazardous pollutants and production of valuable chemicals like pharmaceuticals, cosmetics, fine chemicals and food additives [16].

Blue Biotechnology:
Blue or marine biotechnology is based on the use of marine and aquatic organisms for requirement of new substances that are used in various industrial

sectors and also for the conservation of the environment. The obtained macromolecules (proteins and enzymes) from marine organisms are necessary in pharmaceutical industry in the form of antioxidants and antibiotics agents. The materials derived from macro & micro algae and cyanobacteria used in food, cosmetics and biofuel industry. Blue biotechnology aims to explore and apply marine biodiversity into new products [17].

Brown biotechnology:
Brown biotechnology is related to management of desert and dry regions which makes larger part of the earth. Main purpose of this arid zone biotechnology is improved seeds and high-quality disease-free plants [12].

Gold biotechnology:
Gold biotechnology is related to bioinformatics. It can be focused into two main functions: creation and maintenance of databases of biological information & designing and manipulating of biological materials. It is connected with areas of life science, computer science, statistics and also specialized areas of biology such as genomics, proteomics, waste generation, agricultural and drug discovery [18].

Gray Biotechnology
Gray or environmental biotechnology is related to environment applications. It can be divided into two basic ways: the maintenance of biodiversity and the elimination of pollutants using microorganisms (bioremediation). Gray biotechnology plays a vital role in solving environmental problems through the application of biological systems in waste treatment and management, and for the protection and restoration of the environment. Organisms and their environments are dynamic and interdependent. It includes everything (biotic as well as abiotic factors) that surrounds an organism. It is an eco-friendly method has reduced the overexploitation and pollution of the ecosystem and is using various methods such as Bioremediation, phytoremediation, biodiversity and microbial ecology and its activities in protecting the environment [19].

Violet biotechnology:
Violet biotechnology is related to law, ethical and philosophic issues. Biotechnology achieved significant progress in various areas like industrial, agricultural production, fight against disease. Some social, ethical, moral and religious issues also exist in this field [20].

Dark biotechnology:
Dark biotechnology is related to bioterrorism and biological weapons. This field is easy to access and creates a wide range of disease producing biological agents with low production costs and easy transportation from one place to another. The raw materials which are used in this field are use of microbes and toxins, especially microorganisms, plant and animal origin to produce disease and death in humans, crops and living things [21].

Yellow biotechnology:
It is an older branch of biotechnology which deals with production of human and animal food. The main purpose of yellow biotechnology is improvement of certain food to obtain the most nourishing one. Besides, In this branch techniques are used to produce or modify a food, from living substance or develop microorganisms involved in its preparation, such as functional foods, are those who without therapeutic capacity, improve health or prevent against certain diseases [22].

Red biotechnology:
Red or medical biotechnology is related to the application of biological techniques that can be used for the diagnosis, prevention, and treatment of diseases [23]. Generally, medical biotechnology deals with proper use of the recombinant DNA technology in different therapeutic processes. The best-known products of medical biotechnology are antibiotics that are used to treat bacterial infections. Some exceptional products of medical biotechnology can be produced outside the body like insulin. The desirable applications of medical biotechnology are needed for a substantial degree of organization, regulation and making of careful policy and execution. The probabilities and possibilities behind this kind of attention towards medical biotechnology may be due to its potential to encourage the wealth as well as health problems [24].

Biotechnology in medicine:
Biotechnology is the scientific research field which provides numerous applications to various other fields of science. Medical biotechnology is a relatively advanced and growing field in which the principles of biotechnology are applied to the development of drugs. Biotechnology influences the medicine industry in different ways and has the ability to change the features of the medical field [25]. A majority of therapeutic drugs such as antibodies, nucleic acid products and vaccines are widely used for the molecular diagnostics in the current market are the result of bio formulations of biotechnology. One of the classic examples is Insulin which was the first biotechnologically manufactured medicine. Apart from that, biotechnology also provides advanced medical services and equipments for both preventive and diagnostic purposes [26]. In medicine, the

following biological techniques are helpful for treatment of various diseases:

Pharmaceutical Biotechnology:

Biotechnology refers to the application of biological systems, living organisms, or their derivatives in making or modifying products or processes for specific use. Biotechnology is used in various fields including agriculture, food science, and pharmaceuticals. Pharmaceutical companies use biotechnology for manufacturing drugs, pharmacogenomics, gene therapy, and genetic testing.

Biotech companies make biotechnology products (morespecifically said biotech pharmaceutical products) by manipulating and modifying organisms, usually at molecular level [27].

Pharmaceutical Biotechnology companies use recombinant DNA technology, which entails genetic manipulation of cells, or a monoclonal antibody for making their biotechnological.These biotech pharmaceutical products made by the biotech companies are widely used in prevention, diagnosis or treatment of many types of diseases products.

The conventional pharmaceutical formulations are relatively simple molecules manufactured mainly through trial and error technique for treating the symptoms of a disease or illness. On the other hand, biopharmaceuticals are complex biological molecules, commonly known as proteins, that usually aim at eliminating the underlying mechanisms for treating diseases. However, this is not true in all cases as in the case of type 1 diabetes mellitus where insulin is used to treat only the symptoms of the disease and not the underlying causes. Pharmaceutical biotechnology, essentially, is used to make complex larger molecules with the help of living cells (like those found in the human body such as bacteria cells, yeast cells, animal or plant cells). Unlike the smaller molecules that are given to a patient throughtablets, the large molecules are typically injected into the patient's body [28]. Details of some biopharmaceutical products are described in Table 1 and 2 [29,30].

Table 1: Some examples of disease and respective biopharmaceuticals used in treatment

Disease	**Active substance**
Hepatitis C	Interferon α
Multiple Sclerosis	Interferon β
Renal Cancer	Interleukin
Haemophilia	Factor VIII and Factor IX
Diabetes	Human Insulin
Anaemia	Erythropoietin

Table 2: Pharma and Biotech Companies With Marketed Biotechnology Products, By Number of Products, 1980–2014

Company	**No. of products**	**Blockbuster products**
Sanofi	23	Gardasil, Lantus
Roche	21	Actemra, Avastin, Herceptin, Lucentis, Pegasys, Rituxan, Xolair
Novartis	18	Eyelea, Lucentis, Sandostatin, Xolair
Pfizer	14	Enbrel, Prevnar 13
Merck KGaA	12	Erbitux, Rebif
Novo Nordisk	11	Levemir, Norditropin, NovoLin/-Log NovoMix, NovoRapid, NovoSeven, Victoza
Johnson & Johnson	10	Procrit, Remicade, Simponi, Stelara
Merck	10	Gardasil, Remicade, Simponi
Amgen	9	Aranesp, Enbrel, Epogen, Neulasta, Neupogen, Prolia, Xgeva
GlaxoSmithKline	7	Pediarix/Infarix
Teva	7	Biosimilars, Copaxone
AbbVie	7	Humira, Lupron, Synagis
Eli Lilly	7	Erbitux, Forteo, Humalog, Humulin
Takeda	6	Enbrel, Lupron
Biogen Idec	6	Avonex, Rituxan, Tysabri
AstraZeneca	5	Synagis
Bristol Myers Squibb	5	Erbitux, Orencia
Dainippon Sumitomo	4	None
Sigma-Tau	4	None
Ipsen	4	None
Baxter	4	Advate
Eisai	4	None
Organogenesis	4	None
Bayer	3	Betaseron, Eyelea, Kogenate

SOURCE Authors' analysis. **NOTES** A blockbuster product is defined as one that has $1 billion or more in annual sales. Another fifty-eight companies with seventy-six additional products (including two blockbuster products) are not shown because of space limitations.

Pharmaceuticals and Biotechnology- Benefits of Combination:

When the two disciplines- pharmaceuticals and biotechnology- come together, they result in many advantages for humankind in terms of healthcare.

This is possible through pharmacogenomics (derived from pharmacology'and'genomics') which refers to the study of how the genetic inheritance affects individual human body's respone to drugs [31].

1. Biopharmaceutical drugs aim at designing and producing drugs that are adapted to each person's genetic makeup.
   Thus pharmaceutical biotechnology companies may develop tailormade medicines for maximum therapeutic effects.
2. Also, biotechnology drugs can be given to the patients in appropriate dosages as the doctor would know the patient's genetic and how the body processes and metabolize the medicine.
3. One more benefit of pharmaceutical biotechnology is in the form of better vaccines. Biotech companies design and produce safer vaccines by organisms that are transformed through genetic engineering. These biotech vaccines minimize the risks of infection.

Biotechnology-based products:

In the future, biopharmaceuticals may be used against the AIDS, different types of cancer, asthma, Parkinson's and Alzheimer's disease. There are various classes of biotechnology based products that are produced for the treatment or prevention of different pathological conditions. There are different groups of biopharmaceuticals, including: antibiotics, blood factors, hormones, growth factors, cytokines, enzymes, vaccines and monoclonal antibodies. In the following sections, various classes of biotechnology based products are discussed along with their therapeutic applications.

Gene therapy:

Gene is a structural and functional unit of DNA. A heritable genetic change in the genetic material of an organism is called mutation [32]. Gene therapy is a technique for correcting this mutational gene. This is a technique aims to supplement a faulty gene with a working gene. The potential use of this therapy is to treat devastating inherited diseases [33]. Gene therapy may be Germ line gene therapy and Somatic cell gene therapy. Several approaches for nonfunctional genes are: Gene augmentation therapy, Gene replacement, Targeted mutation correction and the last is Targeted inhibition of gene expression [34].

Normally, a gene cannot be directly inserted into an organism's body which must be required a carrier, or vector. Two basic gene delivery systems are viral vectors and non-viral vectors. Viral vectors are highly efficient. In these systems, viruses attack their hosts to insert their genetic material into host cell and multiplied. Different viral vectors, including retroviruses, lentiviruses, adenoviruses and adeno associated viruses based on nucleic acid (DNA or RNA) of viruses are used [35]. As compared to viral vectors Non viral vectors are available for delivering drugs such as cancer reagents, antibodies, RNA and therapeutic genes. One is Electroporation which increases the permeability of the cell membrane with the help of exposure to an electric field to enable deliver the plasmid DNA into host cells However, the efficiency of Electroporation assisted gene delivery is used into the cells of skeletal muscles, tumours, brain, skin and other tissues [36]. Microinjection is another non viral approach transfers naked DNA into specific cellular compartments. In gene gun system, immunization through skin is currently receiving much attention as a way to increase DNA delivery which can be induced immune response against antigens. Another method is Ultrasound used to deliver an object by the help of ultrasound energy. In this method DNA is mixed with reagents (Optison and Levovist) and with the help of ultrasound cavitations is introduced [37]. Currently, gene therapy is an area that exists predominantly in research laboratories, and its application is still experimental used in developing countries like United States, Europe, and Australia, etc. It has the capacity to treatment of various diseases caused by recessive gene disorders (cystic fibrosis, haemophilia, muscular dystrophy, and sickle cell anaemia), acquired genetic diseases such as cancer, and certain viral infections, such as AIDS [38,39].

Biopharmaceuticals:

Biopharmaceuticals are related to medical drugs that are created with the help of biotechnology techniques. These are derived from living substances are proteins such as antibodies and nucleic acids such as DNA, RNA, antisense and oligonucleotide in nature. A biomedicine is a therapeutic substance used for treating and preventing disease. In the twentieth century Sir Alexander Fleming discovered penicillin from the mold penicillium. However, in 1976, the first biopharmaceutical company Genentech was founded by Herbert Boyer and Robert Swanson. This company produced human insulin invitro in 1982 and in 1977, the first human protein (somatostatin) in Escherichia coli on the basis of recombinant technology. It was the first biosynthetic biopharmaceutical products that entered the market. Some human growth hormones are also produced by biopharmaceutical companies [40]. For example, somatostatin and somatotropin to manage growth disorders, production of recombinant factors VIII and IX to treat haemophilia and Christmas disease respectively. Other examples include production of erythropoietin to control anaemia, relaxing to aid child birth, synthesis of serum and albumin protein used as plasma supplement, interferon α, β, ϒ and interleukins used in the management of cancers [41]. A large number of biotech medicines made through biotechnological processes (recombinant technology and monoclonal antibody technology) have been introduced throughout the world. On the other hand, they caused a great revolution in the treatment of malignant diseases, diabetes and other diseases. Due to biotechnology scientists are expand their research towards pharmaceutical drugs which can be treat severe and life threatening diseases like cancer, hepatitis and heart diseases [42].In children, growth failure occurs due to a lack of human growth hormone (hGH) production by the body. To solve these problem scientists used the hormone which was derived from human cadavers. Cadaver- derived hGH was susceptible to contamination with slow viruses that attack nerve tissue and cause fatal illnesses in some patients. Modern biotechnology is often associated with Recombinant hGH has greatly improved the long-term treatment of children whose bodies do not produce enough hGH [43]. Biotechnology equated with genetically modified microorganisms, are those that have been produced from a genetically engineered organism and are incorporated genes from another organism to produce the desired characteristics such as E. coli or yeast for the production of biosynthetic substances like insulin or antibiotics. It can also deals with 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 [44]. Plant biotechnology is another field of biotechnology which is used to the development of plant derived biopharmaceutical products includes monoclonal antibodies or other therapeutic proteins, or edible vaccines [45].

Monoclonal antibodies:

The discovery of Monoclonal antibodies (MAbs) is one of the greatest advances in the field of biotechnology. Monoclonal antibodies are extensively used in clinically to the diagnosis and therapy of an array of human disorders, including cancer and infectious diseases, and have been used for the modulation of immune responses [46].

Hybridoma technology is a method of forming hybrid cell lines which is called hybridomas by fusing a specific antibody producing B-cells with a myeloma cell (cancerous cell). The antibodies produced by the hybridoma are clones and therefore known as a monoclonal antibodies [47].The production of MAbs was discovered in 1975 by Georges Kohler of West Germany and Cesar Milstein of Argentina, who jointly with Niels Kaj Jerne of Denmark. They shared the Nobel Prize for Physiology and Medicine in 1984. In 1976, Kohler and Milstein developed that technique to fuse splenocyte cells (separated from the spleen of an immunized mouse) with immortal tumorous myeloma cells [48]. The hybrid cells, all of a single specificity were replicate of antibody producing cells against a desired antigen. The hybridomas are capable of dividing indefinitely like high secreting rates in myeloma cells, which can maintain the antibody genes of mouse spleen cells. The first humanized MAbs used to avoid reactions observed in patients injected with murine derived MAbs [49].The process of production of monoclonal antibody by hybridoma technology is demonstrated in the figure 2 [50].

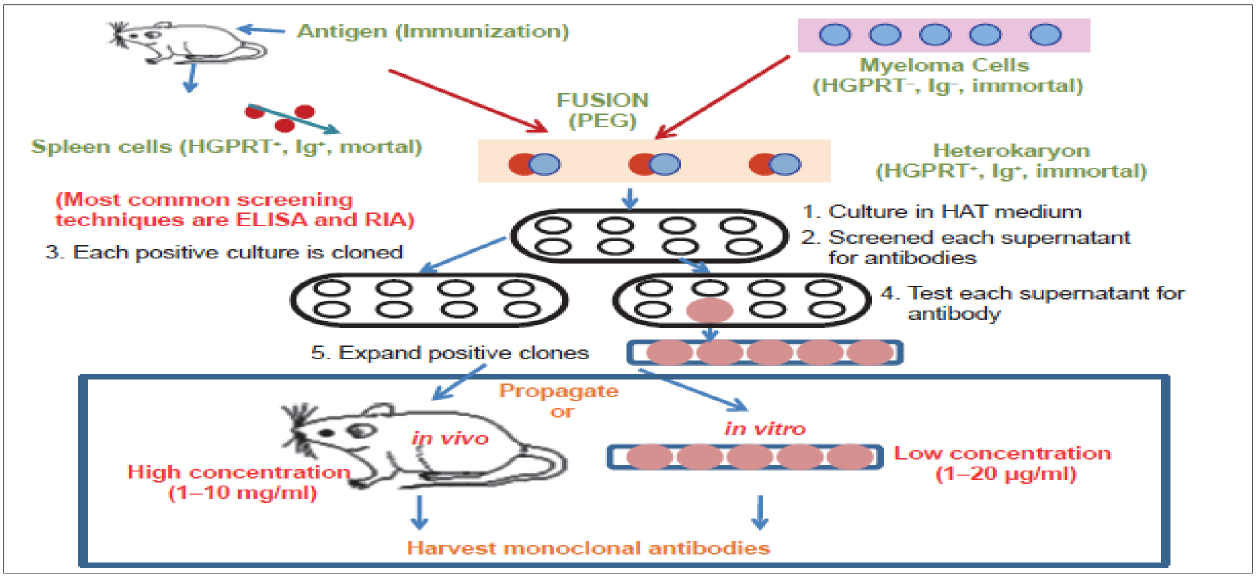

Figure 2: Production of monoclonal antibody by hybridoma technology.

MAbs can be used to detect the presence foreign antigen. Different technologies (Western blot, ELISA, radioimmunoassay (RIA), flow cytometry, immune histochemistry etc.) which are used in human therapy, commercial protein purification, suppressing immune response, diagnosis of diseases, cancer therapy, diagnosis of allergy, hormone test, purification of complex mixtures, structure of cell membrane, identification of specialized cells, preparation of vaccines, and increasing the effectiveness of medical substances [51]. The different monoclonal antibody based medicine with their therapeutic indications and mechanism are illustrated in table 3.

Table 3: Examples of monoclonal antibodies on the market and their therapeutic indications

Medicine	Active Substances	Therapeutic Indications	Mechanism
Leukoscan®	Sulesomab	Imaging of bone infection or inflammation	Antigranulocyte scintigraphy
Verluma®	Nofetumomab	Detection Kit for Lung Cancer	Directed against a 40-kilodalton(Kd)glycoprotein antigen expressed on the surface of numerous tumours
ProstaScint®	Diagnosisofprostatecancer	Diagnosis of prostate cancer	Recognizes a prostate specific membrane glycoprotein that is chiefly expressed by prostatic epithelial cells,(PSMA)
Rituxan®	Rituximab	B cells Non-Hodgkinlymphoma	Chimeric monoclonal antibody against the proteinCD20foundonthesurfaceofBcells
Mabthera®	Rituximab	Follicular lymphoma, diffuse non-Hodgkin lymphoma	Chimeric monoclonal antibody against the proteinCD20foundonthesurfaceof Bcells
Simulect®	Basiliximab	Reduces the incidence and severity of acute rejection in kidney transplantation	Blocks the receptor for IL-2,a protein that simulates proliferation of T-lymphocytes, which play a key role in organ transplant rejection
Remicade®	Infliximab	Rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriasis	Blocks the effects of tumornecrosis factor alpha(TNF-alpha)
Synagis®	Palivizumab	Against the Human respiratory syncytial virus (RSV)	Targets the fusion protein of RSV, inhibiting its entry into the cell thereby preventing infection
Zenapax®	Daclizumab	Reduces the incidence and severity of acute rejection in kidney transplantation	Binds specifically to the alpha subunit(p55alpha, CD25, or Tac subunit) of the human high-affinity interleukin-2 (IL-2) receptor that is expressed on the surface of activated lymphocytes
Herceptin®	Trastuzumab	Breast Cancer	AttachesitselftotheHER2receptorsonthesurface of breast cancer cells blocking them
MabCampath®	Alemtuzumab	Chronic Lymphocytic Leukemia	LocksontoaproteincalledCD52(lymphocytes)
Humira®	Adalimumab	Active rheumatoid arthritis moderate to severe, psoriatic arthritis in adults, severe active crohn's disease	TNF inhibitor
Trudexa®	Adalimumab	Rheumatoid arthritis	TNF inhibitor

ReoPro®	Abciximab	Antithrombotic	Inhibits platelet aggregation
Erbitux®	Cetuximab	Metastatic colorectal cancer	Binds specifically to the extracellular domain of the human epidermal growth factor receptor (EGFR).
Raptiva®	Efalizumab	Chronic and severe plaque psoriasis	BindstohumanCD11a
Zevalin®	Ibritumomabti uxetan	Non-Hodgkinlymphoma	CD20-directedradiotherapeuticantibody
Avastin®	Bevacizumab	Advanced cancer of the colon, breast and lung	Recognizes and blocks vascular endothelial growth factor A (VEGF-A)
Xolair®	Omalizumab	First humanized therapeutic antibody for the treatment of asthma and the first approved therapy designed to target the antibody IgE	Blocks immune globulin E (IgE)
Tysabri®	Natalizumab	Multiple sclerosis in adults	Bindstothecellsurfacereceptorsknown asalpha-4-beta 1(VLA-4)andalpha-4-beta-7
Vectibix®	Panitumumab	Metastatic colorectal cancer that has progressed after treatment with other chemotherapy	Specific to the epidermal growth factor receptor (alsoknownasEGFreceptor,EGFR,ErbB-1and HER1inhumans)
Lucentis®	Ranibizumab	Wetage-related macular degeneration(AMD)	Binds to and inhibits all subtypes of vascular endothelial growth factor A (VEGF-A)
Soliris®	Eculizumab	Paroxysmal no cturnalhemo globinemia (PNH)	Binds to the complement protein C5,thus inhibiting terminal complement mediated intravascular hemolysis in PNH patients
Cimzia®	Certolizumab Pegol	Active moderate to severe rheumatoid artithis	TNF inhibitor
Simponi®	Golimumab	Moderate to severe rheumatoid arthritis in adults, psoriatic arthritis in adults	TNF inhibitor
Ilaris®	Canakinumab	Treatment of children and adults with CAPS (Cryopyrin-Associated Periodic Syndromes)	Interleukin-1βblocker

Development of vaccines:

Public health is contemplated crucial in worldwide. Biotechnology has phenomenal role to catch out the problems regarding to human health. A vaccine is a biological preparation to establish a type of immunity known as artificial active immunity to a particular disease. The main objective used to improve immunity, the antigen is known as a vaccine [52].

It is a medical procedure of generating such an immune response that reduces the risk of contracting a targeted disease is thus referred to as vaccination. Vaccines used as one of the most active attainments against a number of infectious and death over any other medical advance of the 21th century [53]. The term "vaccine" derives from Latin word "vacca" which means cow was developed by Edward Jenner [54]. He was conducted experiment on an 8-year old boy, james Phipps. He scraped the skin of boy to introduce into his body fluid from a milkmaid, who was suffering from cowpox. Later the boy was exposed to smallpox, he did not get infection. It was the world's first vaccine against smallpox [55]. In vaccine, the principle behind this action obtained anything from whole organisms to smaller fragments can be used as antigen. Vaccines consist of whole organism which include live but attenuated organisms or killed organisms and purified vaccines. Four types of vaccines are currently available and each type is designed to boost your immune system. These are known as live attenuated vaccines, inactivated vaccines, subunit or recombinant or polysaccharide or conjugate vaccines and toxoid vaccines [56]. Recent developments in molecular biology provided two approaches of vaccines such DNA vaccines and therapeutic vaccines [57]. DNA vaccines also known as genetic vaccines contain DNA that encodes for specific proteins (antigen) from a pathogen injected directly into the host to produce an immune response. Hence in DNA vaccine, an immune response is made antagonist the protein encoded by the vaccine DNA. DNA vaccines are applicable in treatment or prevention of cancer, allergic diseases and autoimmunity [58]. On the other hand in therapeutic vaccine genes that encode antigens isolated from a pathogen can be inserted into nonvirulent viruses or bacteria. Such recombinant microorganisms serve as vectors, replicating within the host and expressing the gene product of the pathogen encoded antigenic proteins. For example therapeutic vaccine against HIV that will induce virus specific cyto-toxic T lymphocytes against HIV and activate T cells to destroy latently infected cells. Other efforts include developing therapeutic vaccines against *Helicobacter pylori*, mucosal candidiasis, herpes viruses, and human papillomavirus [59].Recent studies demonstrated that the use of recombinant vaccines from plants as attractive alternatives for the immunization of cattle against Foot and Mouth Disease (FMD) conventional FMD vaccines in Malaysia, Southeast Asia and Pakistan, South-western Asia [60,61].

Pharmacogenomics:

The human genome project (1990-2003), a collaborative project which determines the complete genome sequence of the human provided a new level of opportunity in the fields of medical research. The Pharmacogenomics is an emerging arena which aims to improve the therapeutic efficiency of a drug based on the genetic outline of an individual. This technology tries to detect connection between the genetic character of a person and the heterogeneous response to a drug [62]. The view of pharmogenomics is able to design and produce drugs that are customized according to an individual. Pharmacogenetics interlinks classical pharmaceutical science with single nucleotide polymorphisms (SNPs), which are most common variations in the human genome are continuously being uncovered and assembled into large SNP databases. The health care industry is clamoring for access to SNP databases for use in research in the hope of revolutionizing the drug development process and therapy. It is important to consider genetic diversity in all biological and pharmacological pathways to plan the treatment with reduced toxicity and better response [63]. Approximately 11 million SNPs in the human population with an average of one every 1,300 base pairs are estimated. Normally, genes are segment of DNA that code for particular enzymes and proteins. DNA variations in genes code for a class of liver enzymes known as the cytochrome P450 (CYP) family, which is responsible for breaking down more than 30 different classes of drugs. Some of enzymes are less active and inactive which unable to breakdown and eliminate drugs from the body can cause drug overdose in patients. Genetic test to screen and monitor for variations in cytochrome P450 in patients is an active solution. Now a day, pharmaceutical companies screen their compounds to see how they are broken down by different forms of CYP enzymes [64].Pharmaceutical companies can create drugs based on the proteins, enzymes and RNA molecules that are associated with specific genes and diseases. These drugs will not only to increase their therapeutic effects but also to decrease damage to nearby healthy cells. Genetic study of a patient will help doctors to detect the disease and metabolize with an appropriate medicine. It reduces the power of overdose. Most of genes are related with numerous diseases. Strong Potential therapies will be made easier using genome targets. The discovery of modern biotechnology, these genes can be used as targets for the development of effective new therapies, which could significantly shorten the drug discovery process [65].The disease prevention system is primarily based on a detailed description of the individual (e.g. clinical, molecular). Pharmacogenomics take part in personalized therapy, enhancement in efficacy and reduction in adverse drug reactions, less toxic drugs, correlation of genotype with clinical genotype, identification of novel targets for new drugs, and genome profiling of patients to predict disease susceptibility and drug response [66]. The general concept of pharmacogenomics is depicted in Figure 3 [11,67].

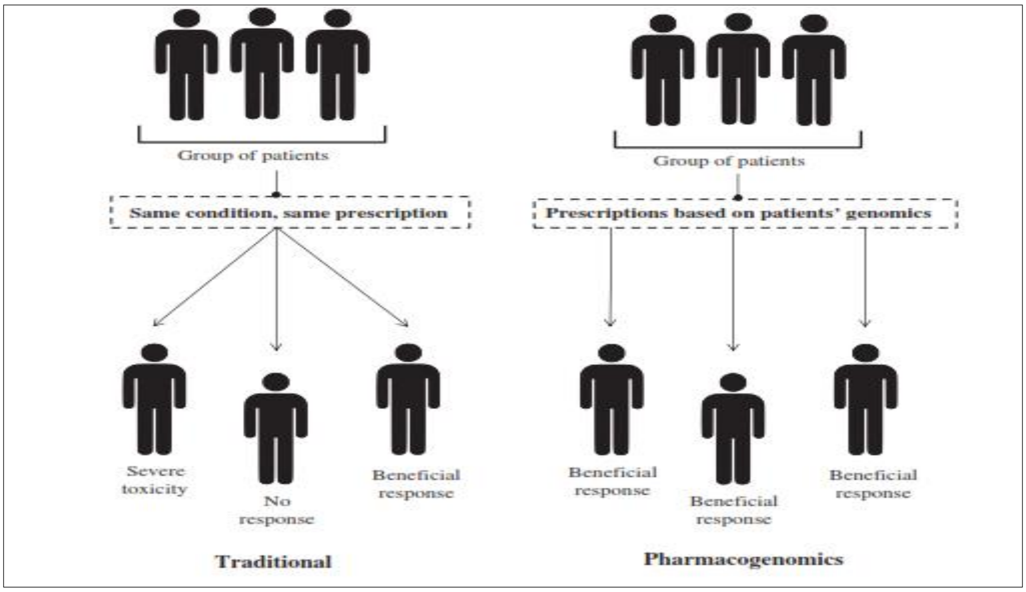

Figure 3: The general concept of pharmacogenomics.

DNA fingerprinting in forensic medicine:

DNA fingerprinting or DNA profiling is a forensic technique used to identify individuals on basis of their DNA [68]. In 1985, Sir Alec Jeffreys and his colleagues coined the term DNA fingerprinting. This laboratory technique can be used to trace the origin of human tissue samples such as blood, hair follicles, saliva, body tissue cells and semen. Forensic evidence of this type is now accepted in developing countries. Today, the application of DNA fingerprinting in the criminal justice system is an important issue for investigators [69]. Different steps involved in DNA fingerprinting are shown in the figure 4 [70].

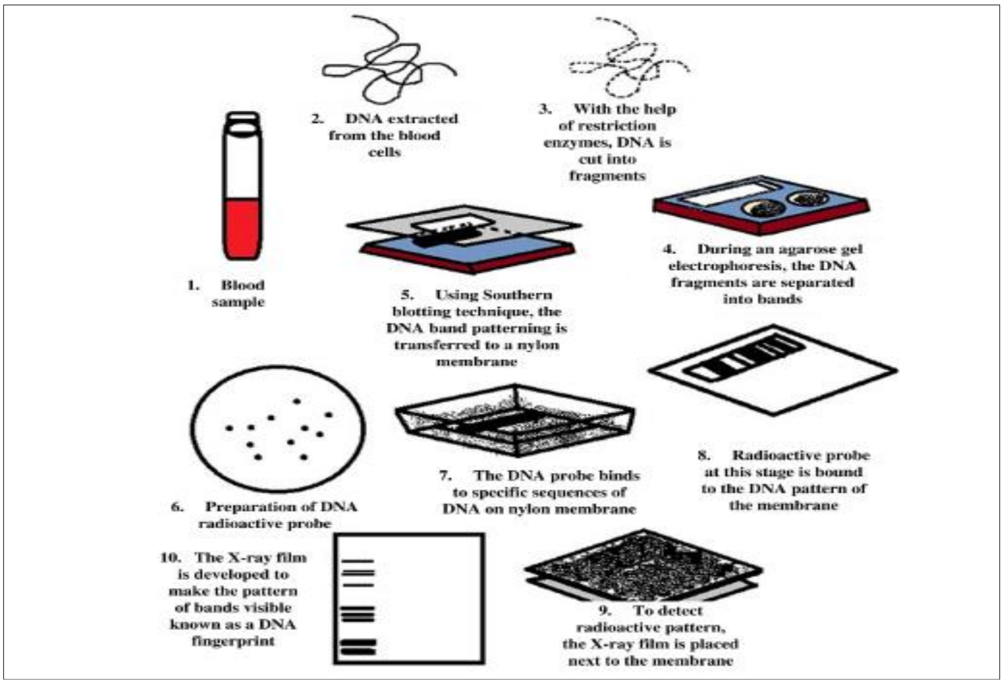

Figure 4: DNA fingerprinting process.

Stem Cell Therapy:
Stem cells are the undifferentiated type of cells that have the potential to differentiate into different types of cells depending on the chemical agents they are treated with. The clinical potential of stem cells lies in the possibility of using these cells for damaged tissue and even complete organ replacement. Stem cells taken from embryos involved in genetic diseases such as cystic fibrosis can also be used for achieving a better understanding of the mechanisms underlying these pathological conditions. The possibility to isolate human embryonic stem cells is an important advancement in the stem cell therapy field, as these cells can be induced to differentiate into various types of cells. For example, it is possible to obtain in vitro neural cells, hematopoietic cells, hepatocytes, and other types of cells from human embryonic stem cells [71].

Nanobiotechnology:
Nanobiotechnology has a wide range of applications in biomedicine including the treatment of pathological conditions, the design of drug delivery systems and in the diagnoses of various diseases. Nanobiotechnology also has applications in various stages of drug discovery and development such as in the target identification and validation, lead compound generation, and optimization. In addition, some nanomaterials have been investigated as drug candidates themselves such as dendrimers and carbon nanotubes (CNTs) [72].

An example of the application of nanobiotechnology is the development of cancer vaccines carriers. Cancer vaccines are used in tumor immunotherapy, which involves activation of the patient's immune system and allowing it to recognize the tumor cells and kill these cells, which are normally not recognized by the immune system. This method of treatment can be used as an alternative treatment to the other traditional methods of cancer treatment or adjuvant to them [73]. The main advantages of tumor immunotherapy over other methods such as chemotherapy include the selectivity for the cancer cells, which means a highly reduced toxicity to the normal cells. This advantage can be significant since the majority of the drugs used in chemotherapy are known for their severe toxic effects on normal healthy cells. Another advantage of this treatment method is that the activation of the immune system to recognize tumor cells will allow for the long-term prevalence of the immunity against these cells even in cases of the reappearance of the tumor.

The Future of Biotechnology in Medicine:
In the future, a key initiative will be the continued development of "personalized medicine," or pharmacogenomics, in which the genetics of the individual patient will indicate the likely response of the disease to the biologic treatment. This will allow prescribers to tailor individual treatment regiments to include medicines that have a high likelihood of offering a positive therapeutic outcome, while avoiding those treatments that might result in serious adverse events. For example, in aggressive metastatic breast cancer, trastuzumab's efficacy depends on the presence of the oncogene HER2/neu, which occurs in about 25 percent of patients, and they are the only group of breast cancer patients who will potentially respond to trastuzumab. A study involving nearly thirty companies indicated that 12–50 percent of the product pipelines [74].

Product development will continue to evolve into the next decade. The biopharmaceutical sector, now well established, continues to grow rapidly. While European figures are difficult to locate, the American association of pharmaceutical researchers and manufacturers (PhRMA) estimate that there are currently some 371 biotechnology medicines in development [75]. Well in excess of 300 of these are protein based, with recombinant vaccines and monoclonal/engineered antibodies representing the two most significant product categories According to a recent review, eighty-eight fully human monoclonal antibodies were in clinical development in 2010, along with a similar number of chimeric and humanized molecules. Cancer and immune disorders were the two predominant disease areas [76].Novel formulations are being evaluated to enhance product delivery via more efficacies and less toxicity. Over the coming decade, therefore, in the region of a dozen new therapeutic proteins should, on average, gain regulatory approval each year.

CONCLUSION:
The biotechnology-based products have created a great impact on the pharmaceutical industry and continue to show great success in the development of therapeutic agents. There is always a requirement of special oral delivery for biological products such as proteins or peptides that are intended for oral administration.

The pharma-based biotechnology products are highly unstable and always needs special attention and care. There are various other problems associated with biotechnology-based products, which include their unstable nature in pharmaceutical formulations as they are susceptible to both chemical and physical degradation. Immunogenicity of large molecules should also be considered since it may lead to fatal consequences.

In addition, there have been many ethical and regulatory concerns raised on biotechnology-based products such as patents on living organisms. Currently, various classes of therapeutic products are being produced through biotechnology such as antibiotics, enzymes, hormones, monoclonal antibodies, and vaccines. These products are used in treating and preventing different diseases that affect a large portion of the population.

There are many promising biotechnology-based approaches being developed for the improvement of medicine as well as for the treatment of various diseases. For example, gene therapy, pharmacogenomics, and stem cell therapy are biotechnology-based approaches that have the potential for highly improving the treatment process in different ways. Biotechnology has had an extraordinary impact on health care during the past years. This will continue into the foreseeable future, as understanding of the pathophysiology of many currently untreatable diseases grows. The governments around the world continue to advance initiatives that support biotech innovation; and business practices evolve to manage the expensive, time-consuming, and risky process of product development. The result will be a continuing stream of novel medicines, leading to breakthroughs in patient care.

REFERENCES:

1. Fári MG, Kralovánszky UP. The founding father of biotechnology: Károly (Karl) Ereky. International Journal of Horticultural Science, 2006;12(1):9-12.
2. Ereky K. 1919. Biotechnologie der Fleisch-, Fett-, und Milcherzeugung im landwirtschaftlichen Grossbetriebe: fu¨rnaturwissenschaftlichgebildeteLandwirteverfasst. Berlín: Parey.
3. Tonukari NJ. Fostering biotechnology entrepreneurship in developing countries. Afr. J. Biotechnol, 2004; 3(6):299-301.
4. Verma AS, Agrahari S, Rastogi S, Singh A. Biotechnology in the realm of history. Journal of Pharmacy and Bioallied Sciences, 2011; 3(3):321.
5. Raju P. World history of modern biotechnology and its applications. Biotechnology: an Indian journal, 2016; 12(11):107.
6. Adamu SM, Koki AY, Adamu S, Musa AM, Abdullahi A S. Biotechnology as a Cradle of Scientific Development: A Review on Historical Perspective. Journal of Advances in Biology & Biotechnology, 2016; 1-12.
7. Chekol C, Gebreyohannes M. Application and Current Trends of Biotechnology: a Brief Review. Austin Journal of Biotechnology & Bioengineering, 2018;5(1):1-8.
8. Mohammed BR, Malang SK, Mailafia S, Agbede RIS. Application of Biotechnology towards Diagnosis and Treatment in Veterinary Medicine in Africa: Potentials and Future Developments. J BiotechnolBiomater, 2016;6(245):2.
9. Therrien JP, Kim SM, Terunuma A, Qin Y, Tock CL, Pfu¨ tzner W, et al. A gene therapy approach for long-term normalization of blood pressure in hypertensive mice by ANP-secreting human skin grafts. Proc. Natl. Acad. Sci, 2010; 107 (3):1178-1183.
10. Wong MS, Hawthorne WJ, Manolios N. Gene therapy in diabetes. Self/nonself, 2010; 1(3):165-175.
11. Roy LH.2013. In: Betino, J.S., DeVane, C.L., Fuhr, U., Kashuba, A.D., Ma, J.D. (Eds.). Pharmacogenomics and Introduction and Clinical Perspective. McGraw Hill, New York, 1-8.
12. Kafarski P. Rainbow code of biotechnology. Chemik, 2012; 66(8):811-6.
13. Ribeiro BD, Coelho MAZ, Castro AM De. Principles of green chemistry and white biotechnology. Princ Green Chem White Biotechnol, 2015:1–8.
14. Barcelos MC, Lupki FB, Campolina GA, Nelson DL, Molina G. The colors of biotechnology: general overview and developments of white, green and blue areas. FEMS microbiology letters, 2018;365(21).
15. Burel C. Industrial or White Biotechnology - Research for Europe, 2000.
16. Singh RS. Industrial biotechnology: an overview, 2014.
17. Querellou J. Marine biotechnology. Introduction to Marine Genomics. Dordrecht: Springer, 2010; 287–313.
18. Kanwugu ON, Ivantsova MN, Chidumaga KD. Gold biotechnology: Development and advancements. InAIP Conference Proceedings, 2018;2015(1):020034.
19. Adepoju FO, Ivantsova MN, Kanwugu ON. Gray biotechnology: An overview. InAIP Conference Proceedings, 2019;2174(1):020199.
20. Jameel S. Ethics in biotechnology and biosecurity. Indian J. Med. Microbiol, 2011;29:331.
21. Riedel S. Biological warfare and bioterrorism: a historical review. In Baylor University Medical Center Proceedings, 2004;17(4):400-406.
22. Siró I, Kaplоná E, Kaplоná B, Lugasi A. Functional food. Product development, marketing and consumer. acceptance – A review. Appetite, 2008; 51:456.
23. Del Carmen Ortega-Navas M. Biotechnology in Health Education: Healthy

Lifestyles. Annals of Behavioural Science, 2016;,2(1).
24. Hsu LY, Teo FS, Chin TM. Medical biotechnology-modern development.
25. Shan M, Khan YA, Nazar H. Application of Biotechnology in Medicinal Field. Single Cell Biol, 2018;7:174.
26. Vijayakuma S, Sasikala M. Application of biotechnology: A current review. International Journal of Pharmacy, 2012;2:59-66.
27. Pineda C, Hernandez GC, Jacobs IA, Alvarez DF, Carini C. Assessing the immunogenicity of biopharmaceuticals.BioDrugs, 2016;30(3):195-206.
28. Nehal MM, Patel PM, Patel NM. A review on regulatory aspects of biotechnology derived product. Int.J. Res. Ayurveda Pharm, 2011;2(5):1495-1500.
29. Almeida H, Amaral MH, Lobão P. Drugs obtained by biotechnology processing. Brazilian Journal of Pharmaceutical Sciences, 2011;47(2).
30. Evens R, KaitinK.The Evolution of Biotechnology and Its Impact on Health Care health affairs, 2015;34(2): 210–219.
31. MALIK NN. Biotech acquisitions by big pharma: Why and What is next. Drug Discov. Today, 2009;14(17/18):818821.
32. Pearson H. Genetics: what is a gene? Nature, 2006;441(7092):398–401.
33. Kirn D, Niculescu DI, Hallden G, Springer CJ. The emerging fields of suicide gene therapy and virotherapy. Trends in Molecular Medicine, 2002;8(4): 68-73.
34. Cavazzana-Calvo M, Thrasher A, Mavilio F. The future of gene therapy. Nature, 2004;427(6977): 779–81.
35. Verma IM, Weitzman MD. Gene therapy: twenty-first century medicine. Annu Rev Biochem, 2005;74: 711-38.
36. Soofiyani SR, Baradaran B, Lotfipour F, Kazemi T, Mohammadnejad L. Gene therapy, early promises, subsequent problems, and recent breakthroughs. Advanced pharmaceutical bulletin, 2013;3(2): 249.
37. Kaneda Y, Tabata Y. Non-viral vectors for cancer therapy. Cancer Sci, 2006;97(5):348-54.
38. Misra S. Human gene therapy: a brief overview of the genetic revolution. J Assoc Physicians India, 2013;61(2):127-33.
39. Ginter EK. [Gene therapy of hereditary diseases]. Vopr Med Khim, 2000; 46(3):265-78.
40. Sharfstein ST. Biotechnology. Reference Module in Life Sciences. 2017.
41. Soetan KO, Abatan MO. Biotechnology: A key tool to breakthrough in Medical and Veterinary Research. Biotechnol. Mol. Biol. Rev, 2007;3(4): 084-094.
42. Valenzuela P, Rutter MA, AmmererWJ.Synthesis and assembly ofhepatitis B virus surface antigen particles in yeast. Nature, 1982;347-350.
43. FM Steinberg, J Raso. Biotech Pharmaceuticals and Biotherapy; Overview. USA: Georgia, 1998; 6.
44. D.A. Goldstein, J.A. Thomas. Biopharmaceuticals derived from genetically modified plants. QJM: An International Journal of Medicine, 2004;97(11):705–716.
45. Daniell H, Streatfield SJ, Wycoff K. Medical molecular farming: production of antibodies, biopharmaceuticals and edible vaccines in plants. Trends Plant Sci, 2001; 6:219–26.
46. Panchagnula R, Dey CS. Monoclonal antibodies in drug targeting. Journal of clinical pharmacy and therapeutics, 1997;22(1): 7-19.
47. Liu, Justin KH. The history of monoclonal antibody development–progress, remaining challenges and future innovations. Annals of Medicine and Surgery, 2014;3(4): 113-116.
48. Tyagi S, Sharma PK, Kumar N, Visht, S. Hybridoma technique in pharmaceutical science. International Journal of Pharm Tech Research,2011;*3*(1): 459-463.
49. Berger M, Shankar V, Vafai A. Therapeutic applications of monoclonal antibodies. The American journal of the medical sciences, 2002;*324*(1): 14-30.
50. Ansar W, Ghosh S. Monoclonal antibodies: a tool in clinical research. Indian Journal of Clinical Medicine, 2013.
51. Mahroof S, Pant G, Rafeek R. Monoclonal antibodies: an emerging immunotherapy technology. European Journal of Biomedical, 2016;*3*(4): 134-143.
52. Afzal H, Zahid K, Ali Q, Sarwar K, Shakoor S, Nasir U, et al. Role of Biotechnology in Improving Human Health. J Mol Biomark Diagn, 2016;8(309): 2.
53. Plotkin SA. Vaccines in the 21st century. Infect Dis Clin North Am, 2001;15: 307-27.
54. Lahariya C. A brief history of vaccines & vaccination in India. The Indian journal of medical research, 2014;139(4): 491.
55. Stern AM, Markel H. The history of vaccines and immunization: familiar patterns, new challenges. Health affairs, 2005;*24*(3): 611-621.
56. Dai X, Xiong Y, Li N, Jian C. Vaccine Types. In Vaccines. IntechOpen, 2019.
57. Poland GA, Murray D, Bonilla-Guerrero R. New vaccine development. Bmj, 2002;324(7349): 1315-1319.
58. Wahren B, Liu MA. DNA vaccines: Recent developments and the future, 2014.

59. Moingeon P, Almond J de Wilde M. Therapeutic vaccines against infectious diseases, 2003;*6*(5): 462-471.
60. Saeed A, Kanwal S, Arshad M, Ali M, Shaikh RS, et al. Foot-and-mouth disease: Overview of motives of disease spread and efficacy of available vaccines. Journal of animal science and technology, 2015;57: 10.
61. Laere E, Ling APK, Wong YP, Koh RY, Lila MAM, et al. Plant-based vaccines: Production and challenges. Journal of Botany, 2016; 11.
62. Adithan C. Pharmacogenomics:" The right drug for the right person". Indian Journal of Pharmacology, 2002;34(3): 155.
63. Moridani M. The pharmacogenetics of cytochrome P450 enzymes in personalized medicine, 2007.
64. Aneesh TP, Sekhar S, Jose A, Chandran L, Zachariah SM. Pharmacogenomics: the right drug to the right person. Journal of clinical medicine research,2009;1(4): 191.
65. Awais M, Pervez A, Yaqub A, Sarwar R, AlamF, Siraj S. Current status of biotechnology in health. American Eurasian J. Agric. & Environ. Sci, 2010;7(2): 210-220.
66. Xie HG, Frueh FW. Pharmacogenomics steps toward personalized medicine, 2005.
67. Beale JM. 2011. Biotechnology and drug discovery. In: Beale, J.M., Block, J.H. (Eds.), Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical chemistry., twelfth ed. Lippincott Williams &Wilkins,China, 119-155.
68. Sinha M, Arjun Rao I, Mitra M. Current Research, 9(01): 45542-45546.
69. Saad R. Discovery, development, and current applications of DNA identity testing. In Baylor University Medical Center Proceedings, 2005;18(2): 130-133.
70. Nizami SB, Kazmi SZH, Abid F, Babar MM, Noor A, Najam-us-Sahar SZ, et al. Omics Approaches in Forensic Biotechnology: Looking for Ancestry to Offence. In Omics Technologies and Bio-Engineering, 2018;111-129.
71. Barh D, Ahmed S, Bhattacharjee A. 2012. In silico and ultrahigh-throughput screening (uHTS) in drug discovery: an overview. In: Kayser, O., Warzecha, H. (Eds.), Pharmaceutical Biotechnology Drug Discovery and Clinical Applications. Wiley Blackwell, German,453-490.
72. Jain KK. The role of nanobiotechnology in drug discovery. Drug Discov. Today, 2005;10 (21): 1435-1442.
73. Peek LJ, Middaugh CR, Berkland C. Nanotechnology in vaccine delivery. Adv. Drug Deliv. Rev, 2008;60 (8): 915-928.
74. Tufts Center for the Study of Drug Development. Personalized medicine is playing a growing role in development pipelines. Medford (MA): The Center; 2010. (Impact Report)
75. New biotechnology medicines in development report. 2002. Avail- able at http://phrma.org
76. Nelson AL, Dhimolea E, Reichert JM. Development trends for human monoclonal antibody therapeutics. Nat Rev Drug Discov, 2010; 9(10): 767–74.