Brief Report

Medical Biotechnology Trends and Achievements in Iran

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Abstract

A healthcare system has been the most important priority for all governments worldwide. Biotechnology products have affected the promotion of health care over the last thirty years. During the last several decades, Iran has achieved significant success in extending healthcare to the rural areas and in reducing the rates of infant mortality and increasing population growth. Biomedical technology as a converging technology is considered a helpful tool to fulfill the Iranian healthcare missions. The number of biotechnology products has reached 148 in 2012. The total sales have increased to 98 billion USD without considering vaccines and plasma derived proteins in 2012. Iran is one of the leading countries in the Middle East and North Africa in the area of Medical biotechnology. The number of biotechnology medicines launched in Iran is 13 products until 2012. More than 15 products are in pipelines now. Manufacturers are expecting to receive the market release for more than 8 products by the end of 2012. Considering this information, Iran will lead the biotechnology products especially in area of biosimilars in Asia after India in next three years. The present review will discuss leading policy, decision makers' role, human resource developing system and industry development in medical biotechnology.

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Introduction

"Biotechnology" was defined in 1919 by Karl Ereky, a Hungarian engineer, to describe methods and techniques which produce substances from row materials with the aid of living organisms [(1)]. A standard definition of biotechnology was achieved in the Convention on Biological Diversity (1992) – "any technological application that uses biological systems, living organisms or derivatives there of, to make or modify products and processes for specific use" [(2)]. This definition was agreed by 168 member nations, and also accepted by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) [(2)]. According to this definition, medical biotechnology is applied living organisms to the diagnosis or treatment of a disease.

Modern Biotechnology or Molecular biotechnology was shaped in the early 1970 by the means of heterologous cloning in *E.coli* [(3)]. The first biopharmaceutical products, recombinant insulin and recombinant human growth hormone, were launched to the world market in 1980's [(4)]. In this decade, more than 10 biopharmaceutical products were approved by the regulatory offices in the United States and European countries [(4)]. From then, new and more affective vaccines, drugs and diagnostic tools have been developed by medical biotechnology for cancer, autoimmune disease, and infectious diseases such as tuberculosis,

malaria and HIV/AIDS. Figure 1 shows the new biopharmaceutical drugs approved by FDA since 1982 [5]. Biopharmaceutical approvals are expected to further increase in the coming years, with many applications pending or expected, including new classes of products, *e.g.*, gene therapies, stem and other cellular therapies, and cancer vaccines [5]. Due to its promising products, medical biotechnology is described as "technology of hope".

Therapeutic biotechnological products and vaccines that are currently being marketed have an annual market value of 98 billion USD, and benefiting over a hundred million people worldwide [6]. There are hundreds more of these products in clinical development. Medical biotechnology can deliver the next wave of technological change that can be as radical or even more pervasive than what brought about by other technology like Information Technology. Employment generation, intellectual wealth creation, expanding entrepreneurial opportunities, augmenting industrial growth are a few of the compelling factors that warrant a focused approach this technology. Therefore, Biotechnology is a powerful and enabling technology for a country like Iran which can revolutionize healthcare and pharmaceutical industry.

The Iranian biotechnology sector has, over the last two decades, taken shape through a number of scattered and sporadic academic and industrial initiatives. Trends of medical biotechnology in Iran are in the fields of biopharmaceutical, Diagnosis, Cell Therapy, and Regenerative Medicine. In recent years, Iran has registered achievements in this field for more than 12 products [7]. In this review, the leading policy for developing biotechnology, educational system and industries frontiers in Iran will be explored.

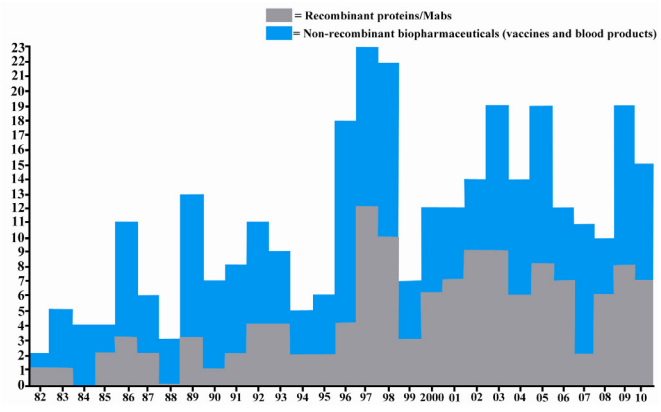

Figure 1. FDA approved biopharmaceutics 1982-2010 [5]

Policy

The advancement of biotechnology as a successful industry, confronts many challenges related to research and development, creation of investment capital, technology transfer and technology absorption, patentability and intellectual property, affordability in pricing, regulatory issues and public confidence. Central to this are two key factors: affordability and accessibility to the products of biotechnology. Policies that foster a balance between sustaining innovation and facilitating technology diffusion need to be put in place. The Ministry of Science, Research and Technology (MRS), The Ministry of Health and Medical Education, Deputy of Research and technology of Presidency, and Center for Cooperation of science and innovation of Presidency serves as the coordinating body for science and technology policy making.

The priorities of medical biotechnology involve molecular detection of infectious and genetic diseases, production of recombinant medicines and vaccines, and bioinformatics are defined by National Medical Biotechnology Network and National Molecular Medicine network. Based on these activities, different committees and working groups are assigned for these tasks. The most active task groups for policy making and priority setting are as follow:

- Biotechnology Committee under the supervision of Science and Technology Deputy of Presidency: The major tasks of this committee is setting policy and priority setting for research and development and grant the applied research and investment grant for biotechnology startup companies.
- Biotechnology Board for Medical Biotechnology at Ministry of Health and Medical Education: The task of this Board is helping to set up postgraduate studies and curriculum

development in Medical Universities and research centers.
- Biotechnology Committee at Environmental Department.
- Center for Cooperation of science, Technology and Innovation of Presidential office: The task of this center is to help for financial support and facilitate the rules and regulations that help start up companies to get into the market.
- High Tech Department at Ministry of Industry: This is an organization for supporting the financial status for production specially works such as Venture capitalist at the governmental level, in addition, to subsidize some portion of the Banking loans.
- National Medical Biotech Network: This network tries to bring the scientists together to work for a specific project at national level in areas of biopharmacutics and mega projects and also, to help increase national capacity building for centers and scientists. Priority setting and scientific advice are two major duties of this network.
- National Molecular Medicine Network: This network tries to bring the scientists together to work for a specific project at national level in areas of human genetics and genetic disorders, and mega projects. Also, helps to increase national capacity building for centers and scientists especially to establish national gene banks for different disorders.
- Eastern Mediterranean Health Genomics and Biotechnology Network, and Regional Network: This network was established in 2005 to bring the scientists of this region together. More than 8 countries are members of this network including Egypt, Pakistan, Oman, Bahrain, Iran, Morocco, Tunisia, Saudi Arabia, and Syria.

Human resource and education

Iran was involved with the imposed war from the Iraqi government for 8 years, 1980-1988. While most of the Iranian research centers and scientists were busy with problem raised during the war specially the chemical weapon that was used by the Iraqis, bioscience and biotechnology had the highest growth rates and research achievements in the world. Meanwhile, majority of the young students voluntarily were fighting and they were in front line of the battles. In addition to the war, a high number of senior scientists immigrated to the Western countries in this period. By the end of the war, research institutes had access to more scientific environments and money resources to develop new technologies like biotechnology. Nowadays, more than 15 biotechnology research centers and departments are operating in Medical Universities.

The first Iranian National Center for Biotechnology and Genetic Engineering (NCB GE) was established in 1989 under the supervision of the Ministry of Science, Research and Technology (MRST). Plant, animal, medical and marine, industrial and environmental biotechnologies are in the scope of NCBGE. Aims of this center are defined as research activities in the field of advanced molecular biology and biotechnology, promoting applied and basic research in science and technology.
Pasteur Institute of Iran, as the second biotechnology research center, started to work in this area in 1992. The first biotech and molecular biology departments started with 15 Ph.D., candidates in Pasteur institute. Pasteur medical biotechnology department has focused on recombinant production of different proteins used as biopharmaceutics, vaccine candidates or diagnostic kit components.

In collaboration with International Center for Biotechnology and genetic Engineering of Cuba, the production facility for Hepatitis vaccine and three recombinant pharmaceutical proteins, Erythropoietin, Interferon alpha, and Streptokinase was built. To assess the analytical characteristics of these recombinant proteins a protein chemistry unit was established in 1999. Further to recombinant pharmaceutics, a new drug discovery group has been recently established in Medical Biotechnology department to design and develop target based anti-infective compounds including new antifungal and also anticancer agents. The other important biotechnology institute is Razi, a vaccine and serum research institute.

It is one of the oldest and most important applied research and development organization in Iran. Razi produces over 2.5 billion doses of 55 different biological products, including human and veterinary vaccines and also diagnostic antigens, at an annual value of about 100 million USD. It has 28 different departments and 1250 staff, including 133 scientists.

Graduate programs for basic medical sciences related to biotechnology issues including immunology, microbiology, virology, mo lecular biology and chemical engineering were launched at state universities. At the moment, with not more than 1700, the number of senior researchers (with Ph.D.) seems to be very limited in the field of medical biotechnology, But, for Iran to build a competitive biopharmaceutical industry, it should increase the resources (human as well as financial) devoted to the field by several folds to build a critical mass of research and development activities. Table 1 shows the most important research centers and universities.

In addition to the above, there are several NGO's involved in biotechnology human resource organization. These NGO's are responsible to develop the Iranian science-matrix:

1. Iranian Society for Biotechnology (ISB), established 1997, 600 members, four branches in different provinces
2. Iranian Genetic Society (IGS), established 2001, 500 Members
3. Iranian Biosafety Society (IBS), established 2003, 150 members
4. Bioethics Society in Science and Technology (ESST), established 2004 industry.

Iran has a fairly well-developed pharmaceutical industry compared to others in the developing world. Iran has also been successful in extending healthcare to the entire population. Its origins date back about 80 years ago to the establishment of the Razi Vaccine Production Research Institute in 1925 and the Pasteur Institute in 1920. Both institutes began by producing vaccines through traditional biotechnology methods, first for veterinary applications and subsequently for human use. Pharmaceutical companies in Iran can be divided into two groups. One group develops the cell line and produce active raw materials in their facilities. There are 5 companies that can be categorized into this group.

The second group started their operations by licensing the products and processes from the Transnational Corporations (TNCs) and

Table 1. Universities and research centers involved in training of medical biotechnology

Centers and universities	Graduate programs
NCBGE	Molecular biology and medical biotechnology
Pasteur Institute of Iran	Basic medical sciences and biotechnology
Tehran University of Medical Sciences	Biopharmaceutic and basic medical sciences
Mashhad University of Medical Sciences	Biopharmaceutic and basic medical sciences
Gorgan University of Medical Sciences	Molecular Medicine
Zanjan University of Medical Sciences	Molecular medicine
Hamadan University of Medical Sciences	Molecular medicine and biotechnology
Shiraz University of Medical Sciences	Basic medical sciences
Semnan University of Medical Sciences	Medical Biotechnology
Sharif University	Chemical engineering
Tehran University	Chemical engineering
Tabriz University of Medical Sciences	Molecular Medicine and basic medical sciences
Shahid Beheshti University of Medical Sciences	Molecular Medicine and basic medical sciences
Royan Research Centers	Medical biology and biotechnology
Avacinna Research Centers	Molecular Medicine and biotechnology
Tarbiat Modares University	Genetic and medical biotechnology, chemical engineering, process development
Azad Islamic University	Genetic and medical biotechnology

manufacturing them locally. The operations mainly involved importing the raw material (bulk drugs) and formulating them locally.

Since 1980, more than 148 recombinant biopharmaceuticals have received approval and launched worldwide. Supporting the local manufacturing, biosimilar regulations have been approved in the Ministry of Health and Medical Education in Iran. More than 12 products have been approved and more than 15 are in the pipeline to be approved in the next three years for recombinant proteins and monoclonal antibodies. Table 2 shows the list of biopharmaceutical products in Iran. More than 15 recombinant pharmaceutical products are in the pipelines. It is expected to be released to the market in the next two to three years. Considering these products, Iran will be one of the biggest biosimilar producers in the world and will lead the countries in Asia in a numbers of products. Table 3 shows the number of biopharmaceutical products that are in different phase of development.

Table 2. List of biopharmaceuticals that have received approval from MOH as biosimilar

	Products	Name of company
1	IFN alpha	Pasteur Institute of Iran, Poyesh Daro
2	G-CSF	Poyesh Daro
3	EPO alpha	Pasteur Institute of Iran, Poyesh Daro, Notarkib
4	IFN beta 1a (CinnoVex)	CinnaGen,
5	IFN beta 1a (ReciGen)	CinnaGen
6	Epo beta	CinnaGen, Zahravi
7	PTH	CinnaGen
8	Buscerlin	CinnaGen
9	Interferon beta 1b	Zist daro Danesh
10	Interferon gamma	NoTarkib
11	Peg-Interferon alpha	Poyesh Daro
12	Antihaemophilic factor VII	AryoGen
13	HBS (Vaccine)	Pasteur Institute

There are also other companies involved in licensing biotechnology products. They are producing recombinant protein under the license using active raw materials as imported materials. Human Growth hormones and insulin are two major ones.

Biopharmaceutical products are among the most expensive medicines available in the market. Monoclonal antibodies and recombinant medicine for orphan drugs take most of the health care cost for all government. Iran has started to market its products outside its borders. Interferon beta 1a is one of the most expensive recombinant medicines in biopharmaceutics. Iranian brand for this medicine, CinnoVex, has been launched in three countries with annual sale of close to 18 million USD. Among the firms that are most active in the biotechnology industry are: Razi Vaccine and Serum Production Research Institute and the Pasteur Institute of Iran. Both institutes are publicly founded. The rest of the compa-

Table 3. List of biopharmaceutical products in different phase of development

	Products	Year expected to be launched
1	FSH	2012
2	PEG-G-CSF	2012
3	Human Growth Hormone	2013
4	Herceptin	2012
5	Enbrel	2012
6	Rituximab	2012
7	Cetuximab	2013
8	VIII	2012
9	LH	2013
10	Streptokinase	2012
11	t-PA	2013
12	Darbopoetin	2013
13	IL-2	2013
14	Infleximab	2013
15	Rabies Vaccine	2013

nies are private investments.

In order to build up a solid biopharmaceutical industry, a "big push" is needed by the government through the provision of substantial research funding in the national research institutes and the provision of seed and venture capital funding to start-up firms. This would stimulate entrepreneurship among the scientists. In some of developing countries such as India, the government-owned commercial banks have started their own venture capital operations. Iranian banks should be encouraged to do likewise.

Conclusion

Medical biotechnology is rapidly expanding world-wide and biotechnology-based diagnostics, vaccines and drugs offer very high added-value productions. Iran could enter profitably in this field, initially with generic products, since many important patents for such products have expired or are about to expire, and, conceivably, later, with novel products and processes more specific for the country and the region.

Advanced biotechnologies can offer interesting opportunities for the economic development of Iran, considering that biotechnology-based applications are not demanding in terms of capital investment or in requirements for raw materials, whereas they rely essentially on the availability of well-trained scientists and technicians. Iran can thus draw advantage from its appreciable human capital in different scientific fields.

In order to build up the biopharmaceutical sector, or the whole biotechnology sector for that matter, the government will need to adopt strategies of technology missions and technological roadmaps with clear long-term and short-term objectives and plans. Iran has established the long and short term plans for this sector. All the requirements, including human resources, capital investment, and rules and regulations that help to facilitate the production life cycle in the country are well defined. The only item that is needed is execution of the laws and regulations. Implementation of the both long and short term plans surely will put Iran in the first position in this technology in the region, third in Asia and 12 in the world. In some cases like biosimilar, it is noted that Iran can move to the first position in Asia and even in the world by launching more than 27 products by 2013. The total local market value will be close to 800 million USD with potential world-wide market value expected to be up to 2 billion USD annually. In terms of human resources, more than 3000 university graduates, with various degrees: BS, MS, Pharm. D., MD and Ph.D. will be hired and more that 9000 indirect jobs will be created for the university graduates.

Conflict of Interest

Authors declare no conflict of interest.

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