ROMANIAN BIOTECHNOLOGY THROUGHOUT TIME

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Abstract. *Although biotechnology is recognized as a separate branch of science and industry only of the late 20th century. Biotechnology through the oldest industrial processes has deep historical roots. Currently, as that the 20th century was the century of developing chemistry, in the 21st century biotechnology is one of the promoter sciences. In its history, Romania by known or anonymous researchers have contributed significantly to the development of modern biotechnology. This paper highlights Romania's contribution throughout time to the development of biotechnology*

Keywords: biotechnology, history, Romania

Introduction

The XXI century is the century of biotechnology, telecommunications and informatics as the twentieth century was dominated by the discoveries of physics, chemistry and biology. Although biotechnological processes are used from ancient times, the term "*biotechnology*" has been used according certain authors for the first time in 1910 by Thomas H. Morgan who proved that genes are carried by chromosoms and after others (the majority) by Karl Ereky in 1917 or 1919. Karl Ereky, defined biotechnology as "all lines of work by which products are produced from raw materials with the aid of living things" [2, 7].

Over the years, biotechnology has received various definitions, but currently is used mainly the definition adopted by the European Federation of Biotechnology and the European Commission, being as simple as just as comprehensive.

Thus, Biotechnology is the science that uses a live agent (microorganism, cellules, living part of the cell, enzymes.) to obtain products (antibiotics, dyes, enzymes, cheese, beer, wine, detergents, etc.) or services (pollution remediation, energy, metal mining,.) [22,23].

Biotechnology is extremely complex and covers virtually all areas of life. Today, as a result of intense industrial activity in the 19th and 20th centuries, as well as population growth has reached the point where mankind must solve a series of problems concerning the nature remediation and ensuring resources for human life. Consequently, at present is looking like through biotechnology,

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mankind to return to natural sources, to technologies which will be environmentally friendly.

From the historical perspective, biotechnologies are basically some of the oldest processes used by people to improve health, food and some services with deep roots in the most distant stages of development of human life on earth.

The main objective of this paper is to pursue the presence and development of biotechnologies along the Romanian history.

Biotechnology along the time

In this context the development of biotechnology can be divided into three main stages:

– Ancient Biotechnology
– Classical Biotechnology
– Modern biotechnology

Ancient Biotechnology

The longest period known in world history is the ancient one.It is comprised across thousands of years, from prehistory (over 10,000 î.e.n) until the early nineteenth century (≈1830).

Biotechnologies have begun with the first civilizations. The first sedentary populations, farmers and hunters realized empirically artificial selection, to obtain benefits such as larger fruit, resistant plants, larger animals, etc. or making products for health. The food processing is lost in the darkness of time. For example, old popullations were observved that fruits and fruit juices fermented into wine, that milk could be converted into yogurt, buttermilk or cheese [19].

Data recorded on biotechnologies in the ancient world are extremely few, mostly represented by various discoveries in archeology. Thus, the best known are papyruses, clay tablets and Bible Bible which provided evidence that Sumerians and Babylonians produced beer with thousands years before Christ.

Archaeological research and a series of world renowned archaeologists show that the geographic area that is today Romania, was more than 10,000 years ago, hearth of the world, where human civilization really began [25, 26, 27, 27].

In this context, it is evident that the ancestors of the Romanians developed different aspect of biotechnology.

In 1961, archaeologist Nicolae Vlassa, discovered three tablets, at a Neolithic site in the village of Tărtăria, Romania. The tablets are inscribed on only one side, and the inscriptions resemble a horned animal, a vegetal motif and a variety of mainly abstract symbols. Tablets dating is uncertain even if they were tested with carbon 14 due to contradictory stratigraphic evidence.

So, the tablets have been dated from around 6500 years ago, 5500 or even earlier at 7300 years old. Hovewer is wiser as a precaution to date the stones to6000-5800 years ago. In any case, through images presented can conclude that

at that time lived in Romania farmers growing animals and plants (figure 1) [6, 12, 13, 17, 18].

Figure 1. Tărtăria tablets

The use of microorganisms in food processing is lost in the mists of time (bread, cheese, wine, beer). For example, Romanian ancestors grown vines in order to obtain the wine, at least 2000 years before Christ. De asememea, istoria arata ca vita de vie, originara din Romania, a fost introdusa in cultivation in the valley of the Rhine and Moselle rivers between 276 and 282 after Christ by the emperor Probus Marcus Aurellius [11].

Using the gifts of nature in Dacia there were most outstanding known physicians of antiquity. Thus, Plato (427 B.C. – 347 B.C.), reveals a discussion between Socrates and Carmides, where Socraates explains that he had learned from a 'Thracian' doctor [9, 15].

Plant and animal sources have been used by humans for making clothing from time immemorial. In Romania, of textile fibers and animal material transmitted over millennia are found today in popular creations and newest creations in the fashion world. Thus, the renowned national blouses are now highly coveted worldwide. The original blouses are made from fine flax textile.

Over the thousand years, and continuing today, traditional pieces of folkloric art (from carpets to clothes) are being produced using flax fibers, hemp fibers or wool.

To obtain the desired textiles, hemp and flax were placed to melt in small pools landscaped alongside of the flowing water fords where specific microorganisms destroyed the pectin substances leaving available long cellulose fibers [3, 5].

Figure 2. The flax melting in small ponds near a river ford [29].

In the Middle Ages scientific development has entered into obscurity. Religious restrictions wars also, virtually permanents, made that development of science and hence of biotechnology to be an extremely low level.

However, during this period were mentioned some finds. For example in the China of the years 100 BC, chrysanthemum powder was used as insecticides. But, have to specify that such a preparation, although it was not mentioned in the documents, but was transmitted orally, was used by our ancestors for the same purpose.

The term "Ethanol" coined for the first time around the year 1150 by Paracelsus for the beverage obtained from distillation of beverages produced by fermentation.

It were attempted the first vaccinations against smallpox (1701, 1797), it was concluded that plants and animals alike reproduce in a sexual manner (1630), were described protozoa and bacteria and were recognized that such microorganisms might play a role in fermentation, it was used microscope to describe protozoa and bacteria and were recognized that such microorganisms might play a role in fermentation and was studied blood circulation in capillaries, described the nervous system as bundles of fibers connected to the brain by the spinal cord.

Advancements in the aspects concerning biotechnology in the Romania during the Middle Ages, are not registered. This is understandable if it is take into

account that this tumultuous period is marked by conflicts, wars and invasions of various nomadic peoples. Being on the eastern edge of Europe, Romania was the first country to which was kicked the invaders, against which the the country was forced to stand up to, to fight to protect the country and prevent their movement towards Western Europe.

Classical Biotechnology

Classical technology began to develop with the industrial revolution in the mid-1800s and it covered a large part of the nineteenth century, being carried on until the 1970s. This period is marked by adapting the known methods from all areas to industrial production. There are produced large quantities of food products and other materials in short amount of time. It developed various industries and intensive agriculture, processes that led to a large part of the problems facing mankind today. Many methods developed through classical biotech are widely used today. Biotechnology must find appropriate solutions to transform these traditional methods in the environmentally friendly means or at least with reduced pollution degree.

However the classical period is rich in numerous discoveries which are the basis for progresses of our days. Thus, it are achieved: advanced fermentation processes that allow better control, the use of predictable yeasts which led to modern baking industry; are discovered proteins, enzymes, penicillin, the structure of chromosomes and structure of nucleic acids; are developed methods for the production of ethanol by fermentation; acetone, acetic acid, butane, solvent dyes, etc. at level industrial; was introduced crop rotation; the first hybrid maize is performed; the discovery of the double helix structure of DNA resulted in an explosion of research in molecular biology and genetics, paving the way for the biotechnology revolution; the genetic code was "cracked" and was demonstrated that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids and many others very important descoveries.

A large part of Romanian contributions to the development of biotechnology during this period are not known or are given a low importance. However, from the Romanian broad category of inventions, there are a number of discoveries / inventions that may be included in biotechnology.

So, the natural scientist Grigore Antipa, biologist, zoologist, ecologist and university professor, was the first who presented biological dioramas, a form of the framing nature in the cityscape (1907).

Ioan Cantacuzino, academician, doctor, microbiologist, university professor, has developed a cholera vaccination method, called "Method Cantacuzino", used today in countries where cholera cases can be observed, and in 1912 creates antityphique vaccine. He created the notion of immunity by contact. In the First World War he led the first massive cholera vaccination in the outbreaks of

infectious, saving many thousands of lives [30, 31]. As a result of his activity, the Professor Cantacuzino created, from legal point of view in 1921: « Serums and vaccines Institute "Dr. I. Cantacuzino"». But this will function as a state institute from 1924 and will have different sources of revenues such as those from the State budget, through the sale of vaccines and serums or donations [32].

Dr. Nicolae Paulescu discovered the insulin (1921), the hormone secreted by the pancreas that regulates the metabolism of carbohydrates, lipids, protids and minerals from the body. Dr. Paulescu is the one who has demonstrated efficacy of this substance in reducing the hyperglycemia and who used the insulin to treat diabetes. Unfortunately, due in part to historical conditions, after 8 months of publication in a Belgian specialized journal by Dr. Paulescu the results of his research under the title Recherches sur le rôle du pancréas dans l'assimilation nutritive", two Canadians, who had taken notice of the Romanian work from the publications of the time, were able to isolate the insulin and use it to treat a patient, such as in 1922, so that in the 1922 they received the Nobel Prize for this discovery at the expense of Paulescu. In 1969, the Nobel Committee recognizes the merits and priority of N.C. Paulescu in the discovery diabetic treatment, but ruled out official repairing. "Oficial Repair" would have required significant material compensation [14, 30, 31].

Figure 3. Dr.Paulescu and insulin [32]

Emil Racoviță is the first biologist in the world who has studied life in Antarctica, he is the founder of biospeleology and discovered the beaked whale 8].

A spectacular discovery is *Gerovital*. Dr. Ana Aslan prepared this product in 1952 and it was patented in over 30 countries.

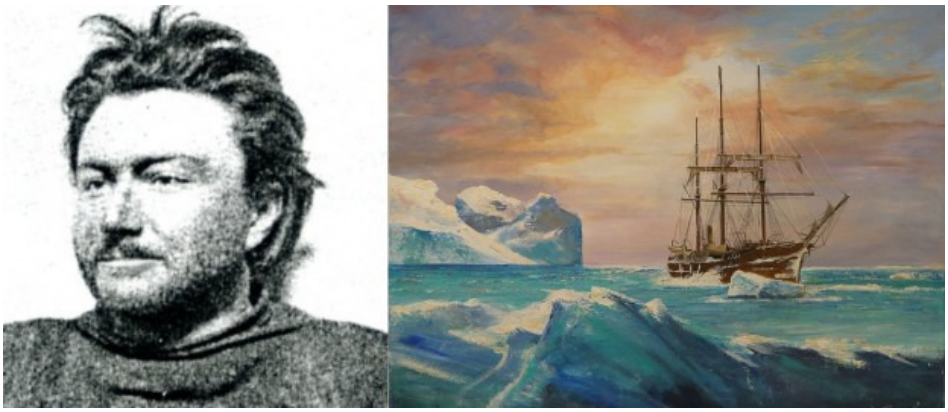

Figure 4. Emil Racovita and the Belgica ship [8]

In the same year she founded the *National Institute of Gerontology & Geriatrics* „Ana Aslan".

Together with the pharmacist Elena Polovrageanu, Dr.Ana Aslan invents the geriatric *Aslavital* product too. Aslan therapy effects on aging were convinced from the start. Many famous patients (Tito de Gaulle, Pinochet, Chaplin, Claudia Cardinale, princesses, comtes, managers of the world's largest banks, etc.) came to treatment at *National Institute of Gerontology & Geriatrics* „Ana Aslan" from Otopeni.

Figure 5. Dr. Ana Aslan and Gerovital [30, 31]

Reputation of "Aslan" products known around the world, led to the worldwide setting up of clinics, hospitals and institutes specialized in using of Gerovital and derived products [30, 31].

In 1928/1929, Alexander Fleming discovered penicillin produced by *Penicillium* mould. However, industrial production of penicillin was developed only after the Second World War. With the help of chemical engineering processes were established methods of sterilization, cultivation, purification, concentration and conditioning of this first antibiotic. The discovery of penicillin led to the discovery and production of many antibiotics and other metabolites such as vitamins, hormones, enzymes, polyglucides, vaccines, monoclonal antibodies, alkaloids, gasoline, etc by using different kinds of microorganisms (bacteria, yeasts, moulds) [1, 4].

Thus, the period 1945 - 1970 is marked by the development and characterizing of microorganism's growth processes to produce at level industrial in the bioreactors whose capacity can reach values of 250,000 l.

In these circumstancesin Iasi was built and opened in 1955, the first factory in Romania and South-Eastern Europe that has produced penicillin, had called the Chemical Factory nr. 2, Iasi. Four years later, as a result of diversifying the production of antibiotics and other medicines, the factory received the name of Antibiotics Factory. This factory is subsequently expanding its traditional portfolio becoming the most important producer of generic drugs and a brand with tradition (over 148 items), recognized in Romania with exports to over 73 countries worldwide [34].

Medical practice was developed as a result of the dedication of some doctors. For example Dr.Ioan Pop Popa is the first physician who performed open heart surgery from Romania, Dr. Marian Ionescu invented surgical equipment and artificial heart valves and Dr.Radu Deac invented as well artificial heart valves [35].

Develops wastewater treatment processes using microorganisms. For example Eng. George Volocvinschi is famous for inventing numerous technologies and systems with favorably impact through utility whereon it shows in terms of protecting the environment and their usefulness in everyday life [35].

In the period before 1990, Romania was difficult to have access to news published in scientific journals from developed countries such as those in Western Europe or the USA.

However, passionate scientists have published books foccussed on biotechnology. For example, there were three Romanian reference books on obtaining enzymatic preparations, namely: Industrial Microbiology - D. Motoc, 1962; Technology and industrial applications of enzymes - I.Vasilescu 1963 and Bioengineering of microbial enzymatic preparations - G.Zarnea, Gh.Mencinicopschi, St. Bragarea, 1980.

Modern Biotechnology

Modern biotechnology is often considered as genetic engineering whose foundations were laid in 1800 with the first investigations on genes.

Genetic discoveries made in the nineteenth century made that biotechnology to develop accelerated after the 1970s. Scientific knowledges are becoming more thorough and advancements in their use and application are growing at least exponentially.

Practically, modern biotechnology is the fund for genetic engineering and development processes using enzymes or immobilized cells, enzymatic or cell bioreactors, bioreactors optimization, development of new bioreactors according to the needs of cell cultures or microorganisms, improve control, mathematical modeling, and process control through computers.

Modern biotechnology has applications in all areas of life: agriculture, bioremediation, light industry, chemical industry, food processing, health, food security and social development, energy, etc.

Since the 1980s, by manipulating genetic informattilor and using advanced microscopy and information technology are made stunning advances in the treatment of some genetic diseases, gene transfer is accomplished in mammals, human insulin is obtained using the bacterium *Escherichia coli* (E. coli) genetically modified, was cloned the first mammal (Dolly the sheep, 1996), technology developed Polymerase chain reaction (PCR), there was the first drug to treat a form of leukemia through genetic engineering - interferon (Roche, 1986), are obtained genetically modified crops (tomatoes, corn, soybeans .. - leader biotech firm Monsanto), the human genome is achieved through an international project, it establishes the method to create stem cell lines, was creates a recombinant vaccine for human papillomavirus (2006) and many others.

Many scientists worldwide have contributed to the amazing development of biotechnology of the last four decades. Romanian scientists' contribution, though not always mentioned, is appreciable. The causes of the lack of visibility of the contribution of Romania in biotechnology are mainly due to political regimes before and after 1990 which have given little real interest in research. As a result, a high number of Romanian scientists including biotechnologists, are working in various renowned institutions worldwide (ex: NASA, Cambridge) participating to important discoveries. It is important to note that annually tens of pupils, students win first places in international competitions and most are invited to attend renowned universities abroad and unfortunately most of them remain abroad.

However, despite the difficulties encountered, biotechnologists of different specialties have outstanding achievements, appreciated worldwide.

The best known example are the medals won by Romanian wines obtained through green technologies (Feteasca Neagra Egregio, Floare de Luna, Feteasca Neagra, Feteasca Alba, Grasa de Cotnari, Mosia de la Tohani, Origini Cabernet

Sauvignon, Sable Noble Alb, Solo Quinta White).

The discovery of the telocytes – a world first, made by a team of Romanian medical researchers from the Victor Babes National Institute of Pathology of Bucharest headed by Academician Laurentiu Mircea Popescu, who is the President of the Romanian Academy of Medical Sciences has been recognised in the United States too [20, 24].

A group of Romanian researchers have developed a technology for rapid regeneration of peripheral nerves (M. Albu, Professor I. Lascar, PhD. D. Zamfirescu, Acad. M. Simionescu, dr. I. Zegrea, dr. M. Popescu, I.D. Titorencu and G.Bumbeneci) for which at Trade Fair Innovations - Innova in Brussels in 2013, they received the gold medal [36].

Figure 6. The young researchers who represented the team and received their medal technology for rapid regeneration of peripheral nerves [37].

Doctors at the Institute Fundeni working on an artificial pancreas device (the size of a powder compacts, in which are implanted pancreatic cells). This objective is the attention of many researchers around the world but it is expected that this tool will be available only in the years 2017 - 2018 as it raises a number of issues concerning the speed of insulin action forms that will be used, reliability, convenience and accuracy of glucose monitors plus cybersecurity to protect devices from hacking [21].

Artificial blood, obtained by doctors at the "Babes-Bolyai" University of Cluj could get the Nobel Prize. Researchers who have conducted are skeptical about its realization in Romania [10].

Rodica-Mariana Ion - university professor and researcher at the Valahia University, specialist in porphyrin chemistry, and her team is the inventor of a new method of treatment of pre-malignant skin cancers [16].

The list could continue with other researchers from biotechnology, but the most remarkable are those who are involved in medical biotechnology as mentioned above.

Unfortunately, although Romania has enough smart minds able to meet the new challenges arising from population growth, antibiotic resistance or climate change, the real research is very little sustained. The funds are mainly for other than for applications in science, so in biotechnology. So if something does not change, inventions such as artificial blood or other will be taken, developed and promoted by interested institutions worldwide, and Romania will lose, like lost, for example Nobel Prize for the discovery of insulin.

Conclusions

Biotechnology is the science of today, of the future and it has its roots in the distant history. This science with its ramifications and roots in all exact sciences is meant to find solutions to the current problems of the world: healthy and safe food for the entire world population, non-invasive medical treatments, environmental pollution, green energy sources, climate change and many others.

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