

The role of scientific research in the field of medicines and the development of the pharmaceutical industry

*Victor Ghicavii, MD, PhD, Professor, Corresponding Academician;

Ecaterina Stratu, MD, PhD, Associate Professor; Ianos Coretchi, MD, PhD, Associate Professor

Department of Pharmacology and Clinical Pharmacology

Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova

*Corresponding author: victor.ghicavii@usmf.md. Received April 02, 2018; accepted October 01, 2018

Abstract

Background: Approximately 91% of drugs are imported, some of which are quite expensive and unaffordable for the majority of the population. The process of drug development, i. e. the pathway from synthesis of active substance to drug, its implementation in the clinic, is quite complicated and long-lasting, of great responsibility and particularly costly, requires enormous investment. The manufacture and implementation of the medicine in the medical practice creates great difficulties in starting it. Pharmaceutical manufacturing companies from the country with modest profitability are unable or unwilling to invest financial resources in scientific research – an important stage in the development of medicines and in ensuring the beneficial activity of the concerned institutions.

Conclusions: National industry must be focused on the modern manufacturing medicine, competitive and effective medicines from local raw material and first of all on the needs of the health system in the country. The situation requires insistence and can only be improved by a joint activity of specialists in many fields (production, distribution and rational use) and strengthening the research-development and coordination forces of the scientific activities in the country for research, development and implementation of new native original drugs, mainly based on local raw materials. Thus, in finalizing the analysis of the role of the pharmaceutical industry in the economic development of the state, it is necessary to mention the important social aspect of it, the close interrelation with other branches of industry, as well as the high innovation and investment capability.

Key words: drug development, implementation, investments, pharmaceutical companies, scientific support.

Introduction

The contemporary pharmaceutical industry is the nucleus of the pharmaceutical branch and one of the strategically important and strategically developed economic segments of each state [1, 2, 3]. Generally, high and stable production growth rates are characteristic of the branch, little dependent on economic ups and downs [4].

It is well known that in the 21st century medicine came in with a vigorous arsenal of medicines and that the world pharmaceutical industry is currently producing tens of thousands of pharmaceutical preparations. More than 5 thousand of them are registered in the Republic of Moldova and authorized for use in medical practice in the country. The nomenclature of medicines used in medical practice has been renewed by 62-75%, so the contemporary physician has an enormous number of drugs for the prophylaxis and treatment of the most diverse conditions [5, 6, 7, 8].

Supplying quality, effective, safe and affordable medicines greatly determines the viability of the healthcare system of the country. The state of the pharmaceutical field has a clear influence on the health, insurance, financing, employment and other spheres, and also contributes to the development of mutual cooperation with other fields of industry (chemical, machine building, agriculture, biotechnology, military industry complex and others) [4].

In addition, the pharmaceutical industry invites contributions to research and development, to the development

of innovative potential, trade relations and the creation of technological infrastructure [9].

Domestic pharmaceutical production by 10 authorized manufacturers in 2015 of 804 authorizations, 13% or 104 were indigenous products, in 2016 of 1028 authorizations, only 9% or 92 were autochthonous products [10].

Thus, about 91% of drugs are imported, some of which are quite expensive and unaffordable for the majority of the population. 9% of the pharmaceutical products in the country are generic (reproduced) and only 14 names of drugs proposed by the country's researchers are native, previously registered, with antiviral, anti-inflammatory, antihypertensive, and antiseptic actions, etc., but unfortunately not all are produced.

In this situation, the lack of essential medicines, of course, is compensated by expensive imports, through expensive drugs, less accessible to the population. Today we import medicines from 62 countries (343 companies). In 2013, pharmaceuticals and parapharmaceutical products were imported in the amount of \$241.74 million, \$271.95 million in 2014, \$339.39 million in 2015, and in the Republic of Moldova during this period were manufactured drugs amounting to 12.3-32.7 million dollars (fig. 1).

The volume of sales (external) amounted in 2013 to 13.75 million dollars, in 2014 – 11.95 million dollars, in 2015 – 26.47 million dollars. This has demonstrated the low level of national pharmaceutical industry and directly con-

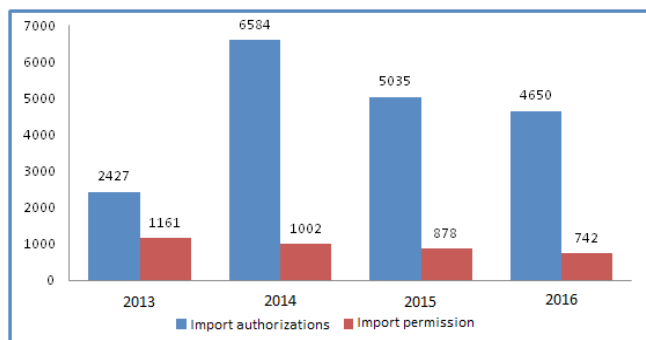


Fig. 1. The dynamics of the import of medicines for 2013-2016.

tributed to the development of other countries' pharmaceutical industries [10].

According to the volume of imports on the names of medicines, the first 10 places are: medicinal coal, sodium chloride, Valeriana officinalis extract, acetylsalicylic acid, citramon, sea buckthorn oil, mucaltin, injectable water, naphthasin, etc., less essential preparations, when certain requirements are advanced to medicinal products presented on the pharmaceutical market: to be effective, safe, quality and affordable. We import a lot and expensive, we produce less, not totally according to GMP and production is not required for export - we produce for us.

The pharmaceutical industry includes science and production enterprises specializing in the synthesis of synthetic drugs, preparations of vegetable raw materials, vitamins, enzymes, antibiotics, endocrine preparations, blood substitutes, galenical preparations and bacterial medicinal products [11]. It is well known that no country in the world produces the whole arsenal of drugs; at the same time any country tends to develop its own pharmaceutical industry, for the following reasons:

- Guaranteeing the population with essential medicines;
- Creating new jobs;
- Improving the economy of the country, because the pharmaceutical industry around the world is one of the most cost-effective.

The pharmaceutical industry is one of the most science-intensive and high-tech sectors of the economy. Worldwide pharmaceutical manufacturers' spending on research and development in this field is 15-20% of the profit [12]. Thus, the USA pharmaceutical research spending represents 25% of the overall costs for research and development, England – 24%, France – 13.8%, Japan – 7.5% [13, 14]. The pharmaceutical industry is characterized by the technical and economical particularities that influence its functionality: high labor productivity, small volume of production, systematic renovation of the nomenclature of manufactured medicinal preparations, lasting production cycle, completeness of technological products, high requirements for quality of production [11].

The drug development process, i.e. the pathway from

drug-to-drug synthesis, to its implementation in the clinic, is quite complicated and long-lasting (10-12 years), of great responsibility and costly, requires enormous investment. The total cost of the research project exceeds US \$ 350 million (fig. 2).

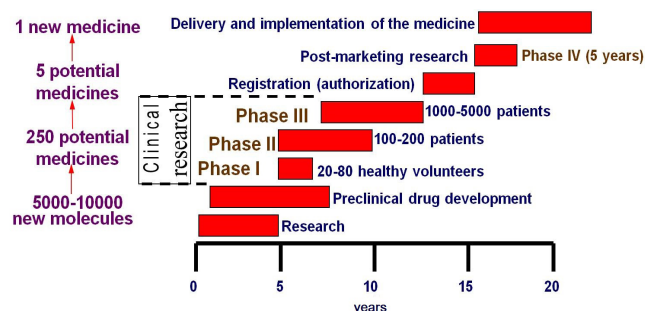


Fig. 2. The process of clinical research of new drugs (typically exceeding 10 years).

This process includes several stages of preclinical and clinical assessments, requires the participation and collaboration of specialists (chemists, pharmacists, pharmacists and clinicians) in many fields, the application of quite sophisticated contemporary methodologies and technologies.

A special role belongs to the pharmacological research, the idea as such and the detection of the actions and the basic effects of the new substances, which subsequently generate the pharmaceutical activities, the clinical research, and the manufacturing and implementation technologies.

Manufacture and implementation in medical practice are two final stages of the complicated drug development process, which creates great difficulties in starting it.

The contemporary pharmaceutical industry relies on a considerable volume of fundamental scientific research, using chemical synthesis, biotechnology, genetic engineering and others in its arsenal. For these reasons, drug companies invest in developing synthesis, performing preclinical and clinical assessments, improving technology, and implementing new quality control methods around 20-25% of revenue.

State-owned pharmaceutical companies, all joint-stock companies, LLCs, manufacturing companies in the country are currently involved, as far as possible, in the reproduction of less important drugs, approved and used many years ago, especially from imported raw material, cheap, suspected to be valid and not local (e. g. hydrogen peroxide, iodine solution, brilliant green, ascorbic acid, analgin, nistatin, novocaine etc). We found that no native enterprise is working with scientific researchers to develop new drugs.

Drug-producing companies in the country with modest profitability are unable or unwilling to invest financial resources in scientific research – an important stage in the development of medicines and ensuring the beneficial activity of the institutions concerned.

The national industry must be geared towards develop-

ing modern, competitive and efficient medicinal products from local raw material and the main one to the needs of the health system of the country.

However, we will try to bring to the attention of specialists trained in drug development, collaborators of institutions interested in and involved in solving the problem of developing and implementing pharmaceutical preparations for ensuring the health system with essential medicines and accessible to the population, finding ways of significantly reducing the import monopoly of medicines and developing the national pharmaceutical market.

During the last few years, in several institutions of the Academy of Sciences of Moldova (ASM) and in the Nicolae Testemitsanu State University of Medicine and Pharmacy were researched various active biological substances, possessing antidepressive, antihypertensive, hepatoprotective, immunomodulating and biostimulating, antimicrobial and antifungal, regenerative and cytoprotective, used in the treatment of cardiovascular, gastrointestinal, infectious, immunodeficiency diseases, etc. But unfortunately these scientific achievements are slowly evolving into the stage of microproduction (experimental pilot) and mass production with subsequent implementation in practice. For our country, the issue of using existing natural sources and the implementation of domestic pharmaceutical products in medical practice is extremely important.

The Republic of Moldova has a considerable potential of scientists in the field of scientific, academic and university institutions, local raw materials necessary for the development and implementation of new medicines. This is confirmed by the results of the scientific researches carried out under the State Program «Elaboration and implementation of new pharmaceutical preparations based on the use of local raw materials for the years 2007-2010» [15] elaborated by the ASM, and continued in subsequent periods, which determined the necessity of:

- Forming the scientific basis of development of the national pharmaceutical industry by implementing in the production of new original medicinal, vegetal, animal, entomological and synthetic medicinal preparations based on local raw materials and creation of new jobs;
- By technologies of synthesis and obtaining biologically active substances from the local vegetal, animal, entomological and synthetic raw material from industrial waste present in enormous quantities in the country (seeds, kernels etc.) to develop and research antibacterial and antifungal drugs of new generations, anti-atherogenic preparations of algal origin, various types of oils (with regenerative and cytoprotective properties), dyes, astringent and adsorbing substances, lipo- and water-soluble antioxidants, antiviral, immunomodulatory and hepatoprotective products: all necessary for the treatment of diseases and pathological conditions (immunodeficiency, etc.);

- The expansion of preclinical and clinical scientific research in the field of medicine with the rational use of the intellectual potential of the country and the endowment of the bases and scientific research centers with modern and efficient equipment;
- Rational alignment to the strategy for the development of scientific research in the field of medicines and the pharmaceutical industry with respect to the requirements and good practice rules (GLP, GCP, GMP etc) established by international bodies in the field and timing of actions using rational and well-grounded human, financial and material resources available;
- Centralizing research and development activity of the pharmaceutical industry by setting up an accreditation center for all (state and private) manufacturing companies, coordinating their work (including state order), implementing GMP, protecting and supporting the manufacturer, accomplishing production inside and outside the country.

All that is mentioned is only one measure – how could science, including scientific research in the field, contribute to the expansion of the domestic drugs problem in our country?

The elaboration and approval of the National Program of Scientific Research in the field of medicine and the continuous development of the pharmaceutical industry in Moldova will contribute to:

- Strengthening the research and development forces and coordinating the scientific activities in the country in order to research, develop and implement new native drugs, mainly based on local raw materials;
- Excluding the unwanted distances between scientists and producers (pharmaceutical industry) – working in the interests of the health system;
- Increasing the range of less expensive (indigenous) medicines and providing medical institutions and population, including socially vulnerable, with first quality, harmless, effective and affordable medicines;
- A significant reduction in the cost of purchased medicines and the cost of treatment – import control, producer support;
- Improving the country's economy, because the pharmaceutical industry is one of the most cost-effective;
- Orientation towards the production of competitive and efficient products at the necessity of the health system in the country [5, 6, 7, 10].

But the healthcare situation in the country is far more difficult (immense, but unstable and irresponsible import of drugs, less accessible to the population, lack of effective native medicines, irrational and ungainly use of medicines, poorly developed national pharmaceutical industry, lack of scientific basis for manufacturing enterprises and other problems).

This situation requires insistence and can only be improved by a joint activity of specialists in many fields (pro-

duction, distribution and rational use), concurrent activity - what today needs to be well organized, essentially restructured and strengthened. In order to help to remedy the situation in the field of domestic medicine and the national pharmaceutical industry, some scientific opportunities for improvement have been resorted to, and have been supported by ASM and P.I. The Expert Advisory Council of the ASM adopted the project for young researchers – «New Autochthonous Drugs in Optimizing the Treatment» (2018-2021), the technology transfer project, »Autochthonous Antihypertensives – New Emergency Medicines (Production and Implementation)» (2018-2019) and others.

Conclusions

Supplying quality, effective, safe and affordable medicines greatly determines the viability of the healthcare system in the country. The accessibility, quality, efficacy and harmlessness of drugs is the priority policy of the State in the social sphere, contributing to increasing the life of the population and enhancing its well-being. The national industry must be oriented towards the manufacture of modern, competitive and efficient medicines from the local raw material and mainly to the needs of the health system in the country. The situation requires insistence and can only be improved by a joint activity of specialists in many fields (production, distribution and rational use) and strengthening the research-development and coordination forces of the scientific activities in the country for research, development and implementation new native original drugs, mainly based on local raw materials. Thus, in finalizing the analysis of the role of the pharmaceutical industry in the economic development of the state, it is necessary to mention the important social aspect of it, the close interrelation with other branches of industry, as well as the high innovation and investment capability.

References

- Ivashchenko A, Kravchenko D. Kontsepsiia innovatsionnogo razvitiia otechestvennoi farmatsevticheskoi otrasli [Concept of innovative development of domestic pharmaceutical industry]. In: [Pharma 2020: Problems and perspectives]. Moscow; 2009. p. 19-26. Russian.
- Petrov VI, Lutsevich AN, Reshet'ko OV. Novye tekhnologii, regulirovanie, standartizatsiia i farmakoekonomika v sfere obrashcheniia lekarstvennykh sredstv [New technologies, regulation, standardization and pharmacoconomics in the field of drug circulation]. Moscow: Meditsina; 2006. 456 p. Russian.
- Kholn TA. Regulirovanie farmatsevticheskogo rynka: sushchestvuet li pochva dlia razvitiia innovatsionnykh farmatsevticheskikh preparatov v Rossii? [Regulation of the pharmaceutical market: is there a possibility for the development of innovative pharmaceutical products in Russia?] Problemy ucheta i finansov. 2012;4(8):73-5. Russian.
- Iurgel' NV, Tel'nova EA. Sostoianie farmatsevticheskogo rynka Rossiiskoi Federatsii i vozdeistvie na nego mirovogo finansovogo i ekonomicheskogo krizisa [The Russian pharmaceutical market in the time of the global financial and economic crisis.]. Vestnik Roszdravnadzora. 2009;(1):46-56. Russian.
- Ghicavii V, et al. Farmacologie clinică [Clinical pharmacology]. Chisinau: Medicina; 2009. 1068 p. Romanian.
- Ghicavii V, Bacinschi N, Gusuila G. Farmacologie [Pharmacology]. Chisinau; 2012. 996 p. Romanian.
- Belousov YuB, Leonova MV, editors. Osnovy klinicheskoi farmakologii i ratsional'noi farmakoterapii [Basics of clinical pharmacology and rational pharmacotherapy]. Moscow: Bionika; 2002. 368 p. Russian.
- Belousov IuB, Kukes VG, Lepakhin VK, Petrov VI. Klinicheskaiia farmakologii: natsional'noe rukovodstvo [Clinical pharmacology: national guide]. Moscow: Geotar-Media; 2009. 965 p. Russian.
- DSM Group. Farmatsevticheskii rynek Rossii 2013 [Pharmaceutical market of Russia 2013]. Moscow: DSM Group; 2013 [cited 2018 Jul 9]. Available from: www.dsm.ru/docs/analytics/dsm_report2013.pdf. Russian.
- Agenția Medicamentului și Dispozitivelor Medicale a Republicii Moldova [Medicines and Medical Devices Agency of the Republic of Moldova]. Raport de activitate 2016 [Annual activity report 2016]. Chisinau: The Agency; 2016 [cited 2018 Jan 15]. Available from: <http://amed.md/sites/default/files/Despre%20Agentie/Raport%20%20AMDM%202016%20general.pdf>. Romanian.
- Balashov AI. Formirovanie mekhanizma ustoichivogo razvitiia farmatsevticheskoi otrasli: teoriia i metodologii [Formation of the mechanism of sustainable development of the pharmaceutical industry: theory and methodology]. St. Petersburg: SPbGUEF; 2012. 161 p. Russian.
- Tishchenko AN, Dorovskoi AV. Sotsial'no-ekonomicheskoe znachenie i kharakternye cherty farmatsii [Socio-economic significance and characteristic features of pharmacy]. Problemi ekonomiki (Ukraine). 2013;(3):13-20. Russian.
- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). Farmatsevticheskaiia promyshlennost' i global'noe zdavookhranenie: fakty i tsifry = The pharmaceutical industry and global health: facts and figures]. Moscow: IFPMA; 2013. 208 p. [cited 2018 Jul 19]. Available from: www.ifpma.org/fileadmin/content/Publication/2013/Facts_and_figures_2013_Russia__web.pdf. Russian, English.
- OECD Science, Technology and R&D Statistics. [cited 2018 Jun 5]. Available from: www.oecd-ilibrary.org/science-and-technology/oecd-science-technology-and-industry-scoreboard_20725345.
- Academy of Sciences of Moldova; Ghicavii V, coord. Elaborarea și implementarea noilor preparate farmaceutice în baza utilizării materiei prime locale: Program de stat [Elaboration and implementation of new pharmaceutical preparations based on the use of local raw materials: State program] [cited 2018 Jan 15]. Available from: <http://www.asm.md/administrator/fisiere/programe/f3.pdf>. Romanian.