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STATUS AND ANALYSIS OF TRENDS IN THE METFORMIN-BASED DRUG DEVELOPMENT: FORMATION OF THE LOGISTIC SYSTEM OF SCIENTIFIC RESEARCH

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The aim *of the work is analysis of the current state and trends in the metformin-based drug development with the subsequent formation of the logistics system of scientific research.*
Materials and methods. *Studies were conducted using databases on the Internet (2015–2022): PubMed; U.S. Food and Drug Administration, European Medicines Agency, the State Expert Center of the Ministry of Health of Ukraine, scientific and metric databases – Scopus, Cochrane Database, US Patent Office. It has used retrospective, logical, graphic research methods, content analysis, modelling.*
Results*. The model of the logistic system of metformin scientific research has developed. It represents the set of elements that are interconnected through information communication, its composition and features, which are associated with the pharmacological action of metformin, are determined.*
Logistic system of metformin scientific research allows: to demonstrate the uniqueness of the drug, to reveal its potential and new opportunities for medical use, prospects for the development of new types of dosage forms and new combined drugs; to identify the threat of patent infringement, to identify opportunities for establishing partnerships; to present scientific products in the form of a drug on the pharmaceutical market, optimizing the research time, reducing the development stages due to the available information and documentation, ensuring the synchronization of innovative information flows; to optimize the total costs of scientific research and receive at the expense of the specified profit.
Logistic system of metformin scientific research is recommended for implementation in scientific organizations and pharmaceutical companies that perform R&D to achieve concentration of information search in solving logistics problems in the field of creating medicines based on metformin.
Conclusions*. Thus, the management of scientific research in pharmacy using the logistic approach ensures the time reduction of the medicine to entry into the market, reduces the cost of its creation, prevents duplication of research, and promotes optimization of solutions. The analysis revealed that the creation of medicines based on metformin should be aimed at the search and development of combined sugar-reducing drugs with mutually complementary mechanisms of action*
Keywords*: logistic system of scientific research, metformin, dipeptidyl peptidase-4 inhibitors, SGLT2 inhibitors*

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1. Introduction

Diabetes mellitus (DM) is a serious medical and social problem in almost all countries of the world. The number of patients with DM in the world over the last 10 years has increased more than 2 times, and by the end of 2019 year exceeded 463 million people. According to the forecasts of the International Diabetic Federation by 2030, the DM will suffer 578 million people and by 2045 – 700 million [1, 2].

Metformin is a basic medicine in the treatment of type 2 diabetes mellitus (DM2), which has the most powerful evidence base. It is a unique antidiabetic medicine, because it has a minimal risk of hypoglycemia, a pronounced sugar-lowering effect and the potential to reduce the risk of cardiovascular complications. Metformin acts in three ways: reduces glucose production in the liver by inhibiting gluconeogenesis and glycogenolysis; increases insulin sensitivity in muscles, enhancing glucose capture and disposal in peripheral tissues; reduces glucose absorption in the intestine [3, 4]. Research data suggest that metformin interacts with various intestinal bacteria [5, 6].

Metformin is one of the most widely used antidiabetic medicines. Since 2005, it has been referred to the medicines of the first line of pharmacotherapy of DM2 in the recommendations of the International Diabetes Federation (IDF), since 2006 – first-line medicines together with non-pharmacological treatment of DM2 in the framework of the recommendations of American Diabetes Association (ADA) and European Association for the

Study of Diabetes (EASD). Since 2007, metformin is the only medicine in the drug prevention of the development of DM2 in the recommendations of ADA. ADA Standards 2020 preserved metformin as a first-line medicine in DM2 therapy. Therefore, ADA in its updated guidelines continues to recommend metformin as the best medicine to start therapy DM2 [7, 8].

Metformin is included in the British National Formulary (2020–2021), British National Formulary for children (2019–2020), which contains the basic provisions of the system for ensuring effective and safe pharmacotherapy, as well as in the State Formulary of Ukraine (issue 13). Metformin is included in the 21st edition of the WHO prescribed list of essential medicines and the 7th edition of the WHO's list of essential medicines for children.

Even though metformin has been used in clinical practice for more than 60 years and has been well studied, studies of recent years have discovered its new facets, thereby confirming its exclusivity [9]. Metformin is called an old drug with new tricks in your pocket [10], which is incorporated into the modern strategy of profiting existing drugs used to treat other diseases.

In order to optimize scientific research of medicines, including metformin, the use of a logistic approach is promising. The specificity of scientific research is the predominance of the information component at all stages. The variety of circulating flows, as well as subjects of individual stages, causes the need for their systemic research and further coordination. Implementation of the logistic approach will ensure the consistency of the study; allow considering objective and subjective uncertainties, risks, to present scientific research not with a set of individual operations, but systematically [11].

In recent decades, studies have been conducted demonstrating the effect of metformin not only on carbohydrate metabolism, but also on various organs and systems, an evidence base of its preventive impact on the development of many diseases has been formed. At the same time, several issues related to the peculiarities of efficacy and safety of medicines based on metformin and its dosage forms need to be clarified.

The aim of the work is analysis of the current state and trends in the metformin-based drug development with the subsequent formation of the logistics system of scientific research.

2. Planning (methodology) of research

The following research plan has developed:

– theoretical and scientific-practical approaches to the use of logistic approach during scientific research were analyzed and summarized.

There are the following main possibilities when using the logistics system of open type research in pharmacy: reducing the cost of research and development of medicines; reduction of the development cycle and preparation for the introduction of science-intensive products into production; increasing differentiation in the market; creation of new sources of income for pharmaceutical companies;

– the composition, peculiarities of the model of the logistic system of scientific research of metformin was determined.

When creating high-tech products in pharmacy, scientists [12] are guided by the "funnel" model. The input of the model is represented by many ideas that are further processed and evaluated, so that less information flow (the most promising ideas) reaches the next stage of development. There are two main tasks of logistics in managing the information flows of this model: the maximum expansion of the entrance of the "funnel" by increasing the intensity and magnitude of the information flow to create science-intensive products (increasing the internal knowledge base of the pharmaceutical companies and expanding access to internal and external sources of information); narrowing the "base of the funnel", that is, the magnitude and intensity of the information flow by optimizing the choice of ideas in conditions of limited resources;

– general analysis of controlled clinical trials of new pharmacological effects and indications for the use of metformin;

– data analysis of more than one study, including any complex analyses, meta-analyses, joint research analyses;

– general analysis of dosage forms of metformin, as well as its combined medicines registered in Ukraine and U.S. Food and Drug Administration, their patent protection;

– determination of the prospects for practical medical application of systematic results and directed further research on the topic;

– formation of a logistic system of metformin scientific research, analysis of its components and development on its basis directions of improvement of research metformin using a logistic approach in order to increase the level of effectiveness of metformin promotion to the final consumer in the pharmaceutical market.

3. Materials and methods

Studies were conducted using databases on the Internet (2015–2022): PubMed; U. S. Food and Drug Administration, European Medicines Agency, the State Expert Center of the Ministry of Health of Ukraine, scientific and metric databases – Scopus, Cochrane Database, US Patent Office. Search was conducted by key words: metformin, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter (SGLT) 2 inhibitors, clinical trial/ trials, and their combinations. It has used retrospective, logical, graphic research methods, content analysis, modelling. The study of registration of domestic and foreign medicines containing metformin in Ukraine is given as of November 2021 according to the website of the State Expert Center of the Ministry of Health of Ukraine.

The use of logistics models and information support allows you to model R&D processes, reflect the state and dynamics of development of the creating process, identify potential difficulties and potential reserves in the development process, reducing the element of uncertainty.

The application of the system allows you to optimize the research time, will contribute to maximum minimization of all necessary flows, reducing the cost of creating medicines.

Logistics of scientific research will also reduce the time of development and implementation of medicines in production, optimize the cost of work, including by excluding their duplication, improve the quality of forecasting, planning, validity of solutions at all stages of R&D.

Effective managerial decision-making is possible only when the flows of information are optimized, standardized, which can be provided through the application of logistic approach and modern information technologies. With the help of information logistics, coordinated work of all links of the logistics system of scientific research is ensured.

4. Results of the research

Covering the whole set of processes, logistics is a methodology for optimizing any flows, rationalizing, and harmonizing them, including information flows in scientific research.

The analysis of the studies shows that the experience of clinical use of metformin confirmed its high therapeutic effectiveness, a beneficial safety profile and the ability to significantly improve the quality of life of DM2 patients. Modern research reveals more and more pharmacological effects of metformin in clinical practice. A feature of this medicine is the presence of dosage forms with a variety of releases. In addition, in recent years, the effectiveness and safety of a combination of metformin with *sulfonylureas*, sodium-glucose co-transporter 2 inhibitors, glucagon-like peptide-1 agonists, etc.

The above-mentioned was a justification for the allocation of 4 components of the logistic information system of metformin scientific research: 1) evaluation of the effectiveness of diabetes treatment; 2) new pharmacological effects and indications for use; 3) new dosage forms; 4) new combinations. They, as follows from the literary review below, are relevant and priority for the current situation in the pharmaceutical sector of Ukraine.

The first component of metformin research, which is associated with the assessment of its effectiveness in patients with DM2, is thoroughly and fully presented in the United Kingdom Prospective Diabetes Study (UKPDS, *n*=5102). UKPDS has proven that metformin is as effective in controlling glycemia as sulfonyl derivatives and insulin, at a lower risk of developing hypoglycemia [13]. The international, multi-center randomized double blind study ADAPT is a serious addition to the study UKPDS (*n*=4360) [14].

The second component of the logistic information system of metformin scientific research is associated with new pharmacological effects and new indications for its medical use. A number of experimental studies of metformin are devoted to various aspects of its effect on organs and tissues. Along with the well-known antihyperglycemic action, metformin has several favourable cardiovascular and metabolic effects, allowing a positive effect on various components of metabolic syndrome.

In patients with DM2 leading cause of death are cardiovascular diseases. In view of this, it is important that antidiabetic medicines not only reduce blood glucose levels, but also protect against cardiac and vascular events. In recent years, there is increasing evidence that this medicine is metformin [15].

It has been found that a significant initial decrease in HbA1c and achieving low HbA1c levels within 6 months after the start of metformin administration are associated with a lower risk of cardiovascular events and death in patients (*n*=24752) with DM2 [16].

Data from 17 studies indicate that the use of metformin in patients with chronic kidney disease, congestive heart failure or chronic liver disease is associated with the improvement of basic clinical results (reduction of the risk of hospitalization by 13 %, total mortality by 22 %) [17].

Several meta-analyses state that metformin is largely associated with a lower risk of developing serious adverse cardiovascular events and generally, a lower mortality from all causes compared to placebo or other antihyperglycemic medicines [18, 19].

Analysis of 40 studies involving 1,066,408 patients found that metformin better reduces the rate of cardiovascular events than sulfonylureas medicines [20].

A recent analysis of observational studies involving 12,156 patients showed that the use of metformin was associated with a significantly lower mortality rate from all causes [21].

Against the background of treatment with metformin, there is a decrease in lipid spectrum disorders that are associated with insulin resistance [22].

There are studies on the effects of metformin on overweight and obesity. Thus, in a one-center prospective randomized placebo-controlled study of the use of metformin in patients with mental disorders receiving antipsychotics, it is possible to achieve a decrease or stabilization of body weight in 80 % of cases, in 44 % of patients, a decrease in body weight is 5 % or more from the initial size [23].

The effectiveness of metformin to reduce body weight in patients with simple obesity (exclusion criteria: DM, polycystic ovary syndrome) is also shown, while the medicine does not cause hypoglycemia as a side effect [24].

It should be noted that in the elderly, additional unintentional weight loss could be considered as an adverse treatment effect. A meta-analysis of 6 randomized placebo-controlled studies (*n*=1541) showed a slight decrease in body weight (by 2.23 kg) along with improved lipid blood profile in patients older than 60 years. The authors conclude that metformin is a safe remedy for patients older than 60 years [25].

Patients with obesity and DM2 have an increased risk of cancer. To date, metformin is the antidiabetic medicine, on the background of therapy, which has been demonstrated a decrease in mortality from cancer [26].

The study of the effectiveness of the use of metformin to reduce the risk of development and improve overall survival in certain types of cancer was conducted. The authors conclude that metformin can be a useful adjuvant agent, with the greatest benefits observed in colorectal cancer and prostate cancer [27, 28]. In case of

chest and urothelium oncopathology, there were no significant advantages [29].

There are a few studies demonstrating the effect of metformin on the aging process, the action as a *geroprotector*. It is reported that additional metformin during progressive workouts with burdens can have a positive effect on aging-related metabolic pathways in the muscles of the elderly [30].

The analysis of the effect of metformin on dementia, Alzheimer's disease or any indicator of cognitive impairment in 14 studies has carried out. A meta-analysis of three studies showed that cognitive impairment was significantly less common in metformin diabetics, while six studies showed that dementia incidence also decreased significantly [31].

Diabetes is one of the most common concomitant diseases, and it is associated with worse outcomes in patients with Covid-19. A meta-analysis of 9 studies involving 10233 people showed that metformin is associated with lower mortality [32]. Randomized controlled trials are required to confirm this conclusion.

Studies in 2021 have shown a strong signal that metformin should be used to treat COVID-19 in patients with concomitant diabetes to reduce the risk of mortality [33].

It is assumed that metformin provides protection against COVID-19 in patients with DM using effects affecting the level of FNF-alpha [34]. Prospective research is needed to understand the mechanisms and causal connections of this impact.

Thus, the results of clinical studies indicate the possible expansion of the spectrum of pharmacological action of the drug.

The third component of the logistic information system of metformin scientific research is associated with the development of dosage forms on its basis.

According to the results of the studies, it has established that in Ukraine registered metformin medicines for immediate release and extended-release; however, medicines with delayed-release are absent.

Available in the pharmaceutical market and registered in Ukraine metformin *monotherapy* medicines are *film-coated tablets,* immediate release, and extended-release tablets. Among *film-coated tablets,* immediate release, in the pharmaceutical market of Ukraine there are 8 domestic (Arterium LTD, Farmak JSC, Kievmedpreparat, Astrapharm LLC, Kusum Pharm LLC, Kyiv Vitamin Plant JSC, Private Joint-Stock Company "On the production of insulin "Indar", Universal Agency "Pro-Pharma" LLC) and 9 foreign (including Merck Sante, France; Sandoz Pharmaceuticals D.D., Slovenia; Berlin-Chemie AG, Germany; M. Biotech Limited, UK, etc.) medicines in doses 500, 850, 1000 mg. Extended-release tablets are represented by 3 medicines of domestic pharmaceutical companies (Farmak JSC, Arterium LTD, Kyiv Vitamin Plant JSC) and Glucophage XR (Merck Sante S.A., France) in doses of 500 or 1000 mg. Thus, Ukrainian metformin medicines mainly cover dosage forms with immediate release.

In accordance with the principles of DM2 treatment outlined in the ADA/EASD Consensus (2018), treatment of primary patients must begin with metformin immediate release medicines [35].

According to the results of studies, the use of extended-release metformin tablets could increase compliance and improve long-term effects [36, 37].

It has established the advantages of creating delayed-release metformin medicines, to enhance its intestinal mechanisms of action while minimizing the systemic impact [38]. The prerequisites for the development of a dosage form with delayed release are publications that convincingly prove that the mechanism of action of metformin is manifested mainly in the lower intestine [3, 4].

The fourth important component of the logistics information system of metformin research is aimed at creating combined dosage forms based on it.

The global goal of treating patients with DM2 is to influence cardiovascular risks considering the assessment of heart failure and renal function. The combination of metformin and sulfonylureas medicines has cardiac and nephroprotective effects and is therefore the most frequent combination in the world, which is recommended for appointment as the first or second stage of treatment of patients with DM2.

In Ukraine, medicines based on metformin and sulfonylureas are represented by 2 domestic drugs (metformin and glibenclamide, Farmak JSC; metformin and glimepiride, Kusum Pharm LLC) and 5 foreign medicines (metformin and glibenclamide, Merck Sante, France, Laboratori Guidotti S.p.A., Italy; metformin and glimepiride, Sanofi-Aventis LLC, Ukraine; metformin and gliclazide, Micro Labs Limited, India; metformin and glipizide, Micro Labs Limited, India). It should be noted that patent protection of most of the combined forms of metformin with sulfonylureas has expired.

ESC and EASD recommended in case of high risk or presence of cardiovascular diseases, the prescription of sodium-glucose cotransporter 2 inhibitor (SGLT2: dapagliflozin, canagliflozin, empagliflozin) and glucagon-like peptide-1 agonists (GLP-1: liraglutide, lixisenatide etc.).

In Ukraine, medicines based on metformin and sodium-glucose cotransporter 2 inhibitors are represented by 2 foreign drugs (metformin and empagliflozin, Boehringer Ingelheim International GmbH, Germany; metformin and dapagliflozin, extended-release tablets, AstraZeneca AB, Sweden).

In recent years, the efficacy and safety of a combination of metformin with dipeptidyl peptidase 4 inhibitors (DPP-4: sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin) has been studied. Thus, in the study VERIFY has established that early combined vildagliptin therapy with metformin by 49 % reduces the risk of loss of glycemic control, exceeds the strategy of phased intensification, provides stable control of glycated hemoglobin (HbA1c) for 5 years, provides a stable lower level of HbA1c [39].

In Ukraine, medicines based on metformin with dipeptidyl peptidase 4 inhibitors are represented by 1 domestic drug (metformin and vildagliptin, Farmak JSC) and 2 foreign medicines (metformin and saxagliptin, AstraZeneca AB, Sweden; metformin and sitagliptin, Merck Sharpe & Dohme Idea, Switzerland).

Considering the logistic approach in order to improve scientific and practical approaches to the management of scientific research in the process of creating combined forms of metformin (with dipeptidyl peptidase 4 inhibitors, sodium-glucose cotransporter 2 inhibitors) and registration of the FDA, we analyzed and systematized the terms of their patent protection (Table 1).

Table 1

Analysis of the state of patent protection of registered combined forms of metformin with dipeptidyl peptidase 4 (*DPP-4*) *inhibitors*, s*odium-glucose cotransporter* (SGLT) *2 inhibitors*

Active ingredient	Trademark	Pharmaceutical company	Patent No.	Expiration date actions
Dipeptidyl peptidase 4 inhibitors (DPP-4)				
Alogliptin, metformin	Kazano	Takeda Pharmaceuticals USA Inc.	7807689 8173663 8288539 8900638	06/27/2028 03/15/2025 06/24/2025 05/24/2029
Linagliptin; metformin	Jentadueto	Boehringer Ingelheim Pharmaceuticals Inc.	7407955 8119648 8178541 8673927 8846695 8883805 9155705 9415016 10022379 10973827	05/02/2025 08/12/2023 08/12/2023 05/04/2027 06/04/2030 11/26/2025 05/21/2030 04/02/2029 04/02/2029 04/02/2029
Saxagliptin, metformin	Kombiglyze Xr	Astrazeneca ab	8628799 9339472	07/13/2025 07/13/2025
Sitagliptin, metformin	Janumet	Merck Sharp and Dohme Corp.	6699871 7125873 7326708 8414921	07/26/2022 07/26/2022 11/24/2026 07/21/2028
Sodium-glucose cotransporter (SGLT) 2 inhibitors				
Canagliflozin; metformin	Invokamet	Janssen pharmaceuticals Inc.	7943582 7943788 8222219 8513202 8785403	02/26/2029 07/14/2027 04/11/2025 12/03/2027 07/30/2024
Dapagliflozin; metformin	Xigduo XR	Astrazeneca ab	6515117 7919598 8501698 8685934 9616028	10/04/2025 12/16/2029 06/20/2027 05/26/2030 11/12/2030
Empagliflozin; metformin	Synjardy	Boehringer ingelheim pharmaceuticals Inc.	7579449 7713938 10258637 10610489 11090323	08/01/2028 04/15/2027 04/03/2034 09/30/2030 04/03/2034
Ertugliflozin; metformin	Segluromet	Merck Sharp and Dohme Corp.	8080580 9308204 9439902	07/13/2030 10/21/2030 10/21/2030
Sodium-glucose cotransporter (SGLT) 2 inhibitor +Dipeptidyl peptidase 4 inhibitor (DPP-4)				
Empagliflozin; linagliptin; metformin	Trijardy XR	Boehringer Ingelheim Pharmaceuticals Inc.	7407955 7579449 7713938 8119648 8178541 8551957 8883805 9155705 9415016 9949998 10022379 10258637 10406172 10596120 11090323	05/02/2025 08/01/2028 04/15/2027 08/12/2023 08/12/2023 10/14/2029 11/26/2025 05/21/2030 04/02/2029 06/11/2034 04/02/2029 04/03/2034 06/15/2030 03/07/2032 04/03/2034

The obtained results indicate that combined medicines of metformin with dipeptidyl peptidase 4 (*DPP-4*) *inhibitors*, s*odium-glucose cotransporter* (SGLT) *2 inhibitors* are under patent protection up to 2030–2034 years. Licensing, which provides information about the technological process, is one of the ways to scale and accelerate the global production of combined forms of metformin in the long term. At the same time, it is extremely important that patent holders could control the efficiency and quality of the medicines.

5. Discussion of the results

The global burden of disease is expected to change by 2030. A significant increase in the global mortality rate from non-infectious diseases, such as cancer and cardiovascular diseases, DM, due to aging of the population, is projected. Their share by 2030 will account for 75 % of deaths.

According to the results of the analysis and systematization of data, it is proved that metformin currently occupies a leading position in the treatment of DM2. The accumulated experimental and clinical data revealed new aspects of the pharmacological action of metformin, enabled a wider assessment of its clinical significance. In many studies of the last decade, devoted to various aspects of the use of metformin, the uniqueness of the metformin demonstrates, its potential and new opportunities for medical use reveals. Along with the hypoglycemic action of metformin, additional positive effects are established: normalization of the level of lipids, cardiac and geroprotective action, anticancerogenic effect, influence on the level of TNF-alpha on the background of COVID-19. Metformin reduces the risk of general mortality and cardiovascular disease.

The state of metformin scientific research indicates the need to strengthen the coordination of resource flows as a prerequisite for improving the quality of management, planning, forecasting, validity of solutions at all stages of R&D, as well as ensuring the production of high-quality and competitive domestic medicines.

Scientific research is associated with a certain risk due to the presence of the uncertainty factor. The lack of a rational approach to R&D leads to an unforeseen increase in material, information, labor, financial flows, and in the worst case – to the futility of research results. In this regard, it is necessary to ensure the parallelity of the work performed.

The example of scientific research of metformin shows the peculiarity of information flows in the logistics system R&D when creating any medicine, which consists in the fact that the flows act as: a direct product of intellectual activity; one of the types of resources; integrator of all stages of R&D; a link between the R&D system and the macro environment that contributes to the formation of the logistics chain: "research – production – sales".

With the late arrival of information flows, the cycle of "research – production" is lengthened, as a result, the cost of scientific research increases.

The analysis of inter-functional and interorganization interactions of structural elements of scientific research served as the basis for the development of a model of the logistic system of metformin scientific research as a set of complex modules, economic flows, subsystems, step-by-step R&D processes, modular and informational communications that ensure the implementation of the R&D process (Fig. 1).

The input information flow determines the promising directions of metformin R&D, namely, investigates the effectiveness in the treatment of diabetes mellitus, the appointment of new indications, and offers new dosages, new dosage forms, as well as new combinations with other medicines. It should be noted the prospects for the creation of delayed-release metformin medicines, in order to strengthen its intestinal mechanisms of action while minimizing the systemic impact, which is absent in the Ukrainian market.

Internal material and financial flows connect with each other and allow to effectively interacting with all structural subdivisions of the organization – participants of the creation of metformin, should be formed as a system of direct and feedback, the common goal of which is the registration and launch of a new medicine.

The effectiveness of the logistic system of metformin scientific research is ensured through resource, information, production and technological subsystems.

It should be noted the need for patent research at the stage of choosing a topic for establishing the possibility of developing and implementing the medicine without violating the rights of patents of third parties. The analysis shows patent protection of several combined forms of metformin. At the stages of pharmaceutical development, preclinical research, legal protection of development is necessary, namely the acquisition of exclusive property rights to inventions, utility models, trademarks. The result of the logistics system is the creation of a scientific development product for the pharmaceutical market, which will allow pharmaceutical companies to expand the production of metformin based on one active substance, increase revenues, and save finances for the promotion of the medicine, reduce the timing of its development.

Within the framework of the proposed system, the following main ways of optimization and rationalization of the logistic flow of scientific research of metformin medicines can be distinguished: finding new indications for the medical use of existing medicine, developing new modifications, and improving the existing science product. This will improve the availability and effectiveness of medicinal supplies to the population of Ukraine of medicines for the treatment of DM2 with a wider spectrum of pharmacological action. The use of the proposed model allows identifying reserves of growth, development and increase of competitiveness of the pharmaceutical companies, as well as in the future to substantiate and timely implement appropriate measures to improve the efficiency of innovative activities of the companies.

In connection with this, the management of scientific research in the field of drug development for the treatment of DM2 based on metformin should be aimed at the search and development of combined sugar-reducing medicines with mutually complementary mechanisms of action, as well as the creation of new types of dosage forms, the expansion of the spectrum of pharmacological action of the medicine.

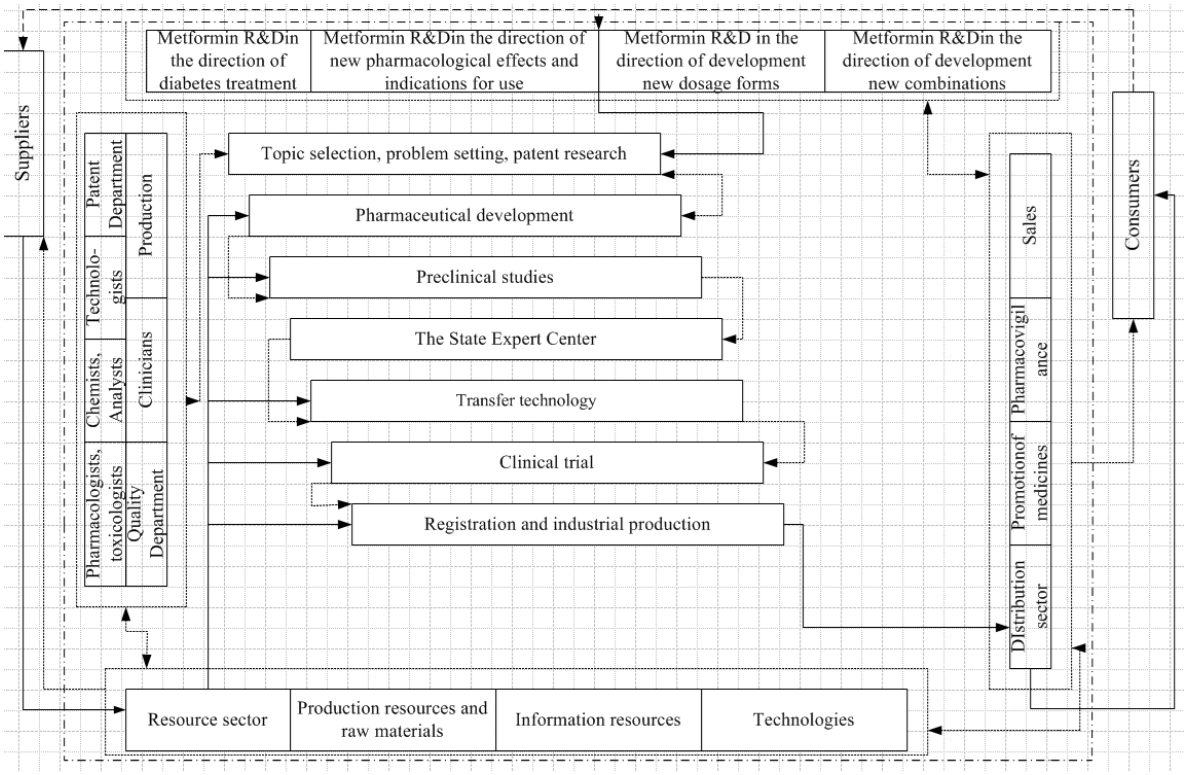

Fig. 1. Logistic system of metformin scientific research: ..... – information flow, — – material flow,--► – financial flow, _____ – modular communications, — • — – logistics system contour

Study limitations. The article does not consider the pharmacological effects of combined forms of metformin. This is the subject of further research.

Prospects for further development of this field. Perspective is the use of the proposed logistics information system in scientific studies of medicines of different pharmacotherapeutic groups.

6. Conclusions

1. Based on the analysis of clinical studies of metformin, its high efficacy, additional positive pharmacological effects of metformin were established: normalization of lipid levels, cardioprotective and geroprotective action, anticancerogenic effect, influence on the level of TNF-alpha on the background of COVID-19. The possibility of using three types of dosage forms is substantiated: immediate release, extended-release, delayed-release medicines. The prospect of creating new modern combined medicines with an interoperable mechanism of action, as well as delayed-release medicines (these forms are not registered in Ukraine) is shown.

2. A logistic system of scientific research of metformin has established. It is representing a set of elements interconnected through information communication, defined its composition and features, which are due to the pharmacological action of metformin

2. Created logistic system of scientific research of metformin allows:

– to demonstrate the uniqueness of the medicine, reveal its potential and new opportunities for medical use, prospects for the development of new types of dosage forms and new combined medicines;

– to identify the threat of patent infringement, to identify opportunities for establishing partnerships;

– to present scientific products in the form of the medicine on the pharmaceutical market, optimizing the research time, reducing the development stages due to the available information and documentation, ensuring the synchronization of innovative information flows; to optimize the total costs of scientific research and receiving at the expense of this profit.

3. The logistics system of scientific research of metformin is recommended for implementation in scientific organizations and pharmaceutical companies that perform R&D to achieve concentration of information search when solving logistics tasks in the field of drug development based on metformin: “the required amount of information, necessary content, at the right time, with minimal cost”.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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