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The beautiful thing about learning is nobody can take it away from you—B. B. King

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TABLE OF CONTENTS

ISSN: 2613-5817; E-ISSN: 2613-5825
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ISSN: 2613-5817; E-ISSN: 2613-5825
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IMPROVING THE MANAGEMENT SYSTEM OF HOLDING COMPANIES AND FINANCIAL-INDUSTRIAL GROUPS IN AZERBAIJAN

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Introduction

Holdings first appeared in world practice at the end of the 19th century and the beginning of the 20th century as a result of the prohibition of the trust system in the United States with "antitrust laws". In Azerbaijan, it can be said that the holding system began to gain importance after gaining independence in the 1990s. Recently, the constantly occurring processes of creation of new companies in Azerbaijan, organizational and legal restructuring of existing companies (mergers, joints, separation of independent companies), their destruction, and bankruptcy are accompanied by directing capital to such a sphere of the economy where its more profitable use is expected.

One of the effective forms of capital centralization is the creation and functioning of complex economic systems that represent a group of interconnected organizations with a certain internal structure. That is why in the economic environment of Azerbaijan, the spread of consolidation of enterprises in the form of consolidated (holding) groups in large, medium, and small businesses has expanded. There are many reasons for this: the multi-profile business of the majority of medium and small enterprises, territorial and field divisions of enterprises, and trying to appear as a consolidated taxpayer. On the one hand, operational activity related to the market (marketing policy, market strategy) and financial independence is the need of the period. On the other hand, a single center of general management is still required [1,79].

Principles of classification of holding companies

1. Holding companies are divided into 2 parts in terms of their activity: financial and mixed. A holding company whose capital is more than 50% of securities of other companies, enterprises and other financial assets is considered a financial holding. In the financial holding, only the capital of the enterprises is combined, and therefore the parent company performs the tasks related to the financial activities of the subsidiary enterprises.

2. In a mixed holding company, the parent company can engage in independent economic activity. Holding companies of this type are useful for scientific and technical, and technologically connected business subjects. Because those organizations are engaged in complex scientific and technical, production and other types of activities. Mixed holding companies also have the right to perform the function of the general contractor, to carry out scientific-technical and commercial work, to engage in foreign economic activity on behalf of industrial groups [2,90]

In terms they control of the companies, holdings are divided into 2 types: single-story and multi-story. Single-story holdings include the parent company and its directly affiliated subsidiaries. Subsidiary companies are directly under the control and management of the parent company.

In multi-story holdings, the parent company itself has connections with other parent holding companies. There are subsidiary companies on the lower floor. Therefore, the subsidiary companies are first merged into the parent holding company and later into one parent holding company.

3. Taking into account different holding relationships, holding companies are divided into 2 types: "hard" and "soft" holding. "Hard" holding is based on the ownership of the property of industrial groups, and soft holding is based on the agreement on the regulation of joint activities and other relations. Effective operation of holding companies depends on choosing the right management model.

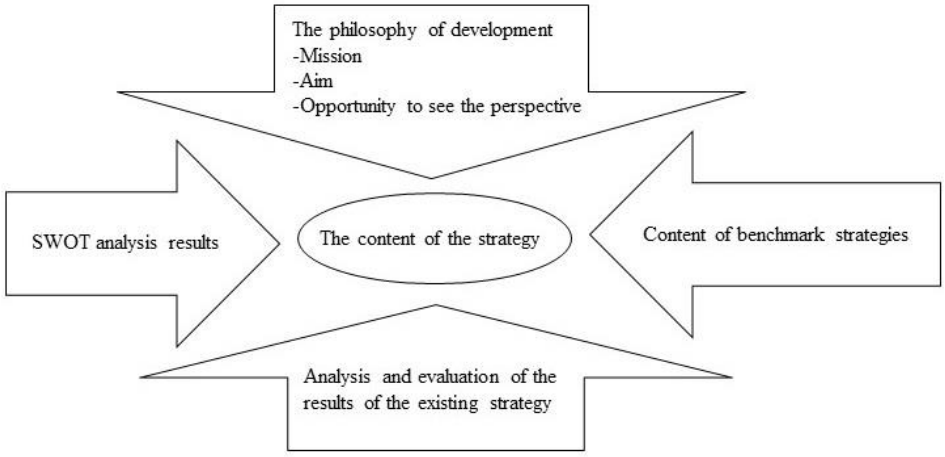

Figure 1. Content of the strategy

Holding structures operating in Azerbaijan

World experience shows that the structure that combines these features is the holding structure. Thus, the fast-moving socio-economic and political processes accompanying the integration of Azerbaijan into the world economic society create an opportunity for the creation of integrated-universal holdings that organically combine both synergy and diversification. In Azerbaijan, today, holding structures function in a large number of important areas of the economy: banking and financial spheres, industry, construction, transport, and other areas.

It is possible to centralize a number of functions in the holding and thereby save costs. The functional division of responsibilities between the main and industrial groups occurs in such a way that the main organization focuses on planning, organizing financial flows, centralized accounting, legal protection, personnel policy, data provision, statistics, marketing, and sales organization. stands Highly qualified specialists working in these spheres are concentrated in the main organization and perform their functions not in relation to a legal entity, but in relation to all or a group of participants of the holding association. In this case, the high salary of such managers is justified, and the functions they perform are in demand [4, 79].

Cost savings also result from, for example, simultaneous large wholesale purchases of materials and raw materials for several participants of the holding, exclusion of duplication of functions, as well as the distribution of resource savings. The holding ensures the concentration of technical, technological, management experience, and scientific work within one economic entity. By combining the technology, organizational, and investment capabilities of various participants, the holding can reduce the investment cost of any project as a whole. Holding allows ensuring the necessary rationalization of production, so that certain items are not made in different factories at certain costs, but are required to be sent to places where costs are low.

Inefficient production sites may be dissolved, which lowers the cost per unit of the produced unit. Reducing the costs of product (work, service) development is especially effective in a vertically integrated holding, where all operations from the acquisition of raw materials to the release of the finished product are combined under single technological conditions. The main goal of a vertically integrated business organization is to minimize the concentration of product production and the costs of its production and realization in order to maximize the supply. Holdings realize their own property by providing appropriate financial and tax planning.

Corporate schemes of tax planning aimed at reducing tax losses can be based, in a special case, on the rational distribution of functions between holding participants, and on internal (transfer) assessment. Management of financial flows within the holding is less important, but in any case, the use of privileges for business associations in the tax legislation allows the company's entrepreneurs and managers to obtain certain effects from the holding form of the business organization. However, it should be noted that the legislation does not consider a special tax regime for holdings. Many companies obtain a special tax regime by registering their participants in "tax havens" or offshore zones [6, 98].

Holdings provide confidentiality of control to business owners. According to the principle of confidentiality, the possibility of using information about the actual purpose and results of the work carried out in the direction of optimizing tax payments should be limited to the maximum. Individuals participating in the optimization process should not imagine the process in general but should be based only on certain instructions of a local nature. At the top of the "holding pyramid" in a holding system may be an organization formed by individuals, thereby carried out by the governing bodies of the parent organization, and can only be detected through the system of qualified persons.

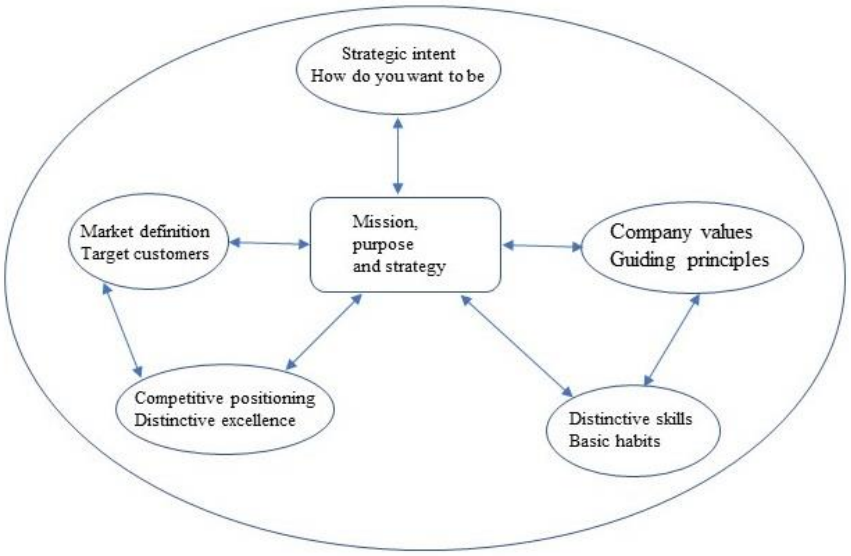

Figure 2. Principles of management in holding

In describing the advantages of holdings, matching certain characteristics, let's note that, firstly, not every holding ensures the realization of all the listed advantages at the same time. Secondly,

some of the listed advantages of the holding concern disadvantages for other subjects (the state, citizens, other entrepreneurs, for example, contractual counterparties) from the point of view of realizing their interests. For example, anti-competitive policies, monopolization of individual market segments, and minimization of tax payments due to internal adjustment of transfer prices between holding participants can have a negative impact on the entire economy. In particular, the practical solution is more important and complex. These problems are the protection of the interests of the minority of shareholders in dependent organizations; protection of the rights of creditors of partners included in the group; protection of the interests of the state in the territory where the holding operates; is to provide a guarantee to the workers working in his enterprises.

According to the constitutional laws, the existence of human and citizen rights and freedoms should not violate the rights and freedoms of other people. According to the citizenship code of the Republic of Azerbaijan, the actions of citizens and legal entities who deliberately harm another person, as well as abuse their rights in other forms, are inadmissible and cannot be protected. The citizenship code of the Republic prohibits the use of citizenship rights in order to limit competition, as well as the abuse of a dominant position in the market. In addition to the obvious advantages of the holding form of business organization, there are also certain disadvantages. One of the reasons for such shortcomings is the lack of competition within the holding, which requires constant improvement of product (work, service) quality [4, 89].

Artificial retention of unprofitable production may take place in the holding, which lowers the economic efficiency of the association as a whole. Although the entire organizational structure of the holding has been optimized, decision-making procedures have been formed and ensured, the holding remains a complex hierarchical system with significant internal bureaucratic apparatus with often repetitive functions. Here, the apparatus tends to expand in order to justify its existence, trying to strengthen its organizational and managerial effects. As a result, the main organization sometimes begins to abuse its supervisory functions, depriving industrial groups of the necessary operational economic independence.

Taxation of holdings

There is an insufficiently optimal mode of taxation of holdings. Any exit from the "border" of a legal entity entails the creation of taxation markets. In addition, in a legal entity, the loss of one product can be offset by the income of another, thus a fair balance of income and expenses is corrected. Holdings are actually double-taxed. Industrial groups earn income, pay tax on income and pass this income on to the parent entity in the form of dividends, which are also taxed as unrealized income of the parent entity. These conditions force holdings to find ways to optimize intra-holding flows, some of which are not approved by the state for known reasons (offshores, transfer prices) and are even outside the limits of legal activity [3, 90].

If the holding in an entrepreneurial activity does not get proper management, the "uniform tax" of these entrepreneurial associations will remain an unrealized idea. Other disadvantages accompanying the holding form of business organization include: - the lack of adequate legal management of this entrepreneurial association; there are agreements related to a large number of interests in holdings in the absence of a simplified regime for the execution of agreements between holding participants in the legislation; the need to comply with a significant number of restrictions imposed by antitrust legislation, while still not taking into account the nature of the characteristics of the holding combination.

Separately mentioned shortcomings of the holding form of business organization can be eliminated only by legislation, but the correction of others depends on the entrepreneurs. The skillful combination of positives and negatives of integration at the same time as neutralization (establishment of the optimal management structure, fight against the expansion of the bureaucratic apparatus, simplification of management decision-making procedures, effective management system in the holding, etc.) allows the holding to be adjusted as an effective form of entrepreneurial activity.

Consolidation of the accounting, monitoring, and control computer system in the holding structures allows to significantly reduce costs, consistently, and increase the income and profitability of the group as a whole. Construction and development of holding structures, increasing the effectiveness of management and control, and determining the features of the functioning of the holding structure, as well as their classification, are necessary for more effective use of capital in the group. The complexity of the classification of holding structures arises from the great variety of characteristics by type.

These symptoms allow them to differentiate or unite in a group, depending on one or other qualities that enter into their company, determining the motivation of their movement in the market [6, 89].

At this time, it is necessary to note that any classification of holding structures is conditional. Business experience, as a rule, can rule out any ideal variant of the division of related organizations by type. Many of their types are characteristic only for certain countries and do not occur in others. Let us distinguish the following as classification signs:

1. Methods of determining control over industrial groups: In real estate holding, the parent company exercises control by having a control package of shares in the capital of industrial groups, but in contract holding, when there are no control packages of shares of industrial groups, management is carried out on the basis of an agreement concluded between them.

2. One of the more important signs is the presence of a share of the parent company in the ownership of capital of industrial groups. At this time, the following options are possible in the holding structures: the main company owns 100% of the capital of industrial groups; the main company owns 50% of the capital of industrial groups and one or more shares; has share packages that exceed the size of the company's shares. It should be noted that usually, the group's industrial groups include elements of the parent company's name in their names and trademarks. This phenomenon, as part of the system of intangible assets, seems attractive to medium and small companies, which see of the possibilities of "survival" by entering the holding structure.

3. According to the motivation of the holding company's actions in the securities market, three types of holding structures are distinguished: portfolio holding (However, it owns controlling packages of shares of other companies.); investment holding (owns and manages packages of shares of other companies); portfolio-investment holding (represents the combination of the 1st and 2nd types in itself.)

Result

Accompanied by Azerbaijan's integration into the world economic community, the fast-moving socio-economic and political processes have created an opportunity for the creation of integrated and universal holdings that organically combine both synergy and diversification. Holding structures in Azerbaijan currently operate in a large number of important sectors of the economy: banking and finance, industry, construction, tourism, insurance, transport, etc. The multiplicity of

holding structures is quite natural: business is expanding, many companies are opening foreign branches. So, the more dependent companies there are within the holding, the more complex tax payments, financial flows, and risks for the company can be.

In the article, as a result of the description of the theoretical basis of the management of large holding structures, the features of financial management in holding structures, and the mechanism of organizing financial planning, it was determined that at the present time, quite a large amount of experience in the operative organization of management in holding structures has been collected.

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THE OIL FACTOR IN ECONOMIC GROWTH

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ABSTRACT

The article evaluates the role of the oil factor in the development of the economy of Azerbaijan in the last 20-25 years. The structuring importance of the oil factor at different stages in the formation and rapid growth of the national economy and its role in the sustainability of growth are interpreted with reasonable arguments. One of the most important conclusions drawn by the author in the article is that the economic potential created by the realization of a well-thought-out oil strategy eliminates the possibility of negative trends in the national economy in the near future.
Keywords: oil, economic growth, sustainable development, investment, real sector

Introduction

In our opinion, the main group of carriers of economic growth in Azerbaijan is made up of production areas that play the role of a locomotive in the recovery and expansion of the economic cycle. If we look at the development path of our country from this point of view, we will be sure that the first of the most important influencing elements in the organization and expansion of the national economic cycle is the energy sector, which includes the production and transportation of hydrocarbon resources to the world market. The main factors determining the choice of this area are primarily its structural and creative features. Thus, the energy sector, in addition to its wide and complex nature, is actually distinguished by its investment attraction, and at the same time, it has accelerating properties for the development of other areas.

As it is known, the oil sector has had a serious structuring role in the economy of Azerbaijan since the middle of the 19th century. For more than 150 years, Azerbaijan, despite being a small territorial component, has always played the role of an "energy driver" for the economy of such giant countries as Tsarist Russia and the USSR as an important oil producer, producer of petroleum and chemical products. However, in 1991, at the moment of the restoration of state independence, Azerbaijan's capabilities as an oil country were extremely low. The profitability of the main economic source was extremely low in the country, which was turned into a military-political and socio-economic collapse, and the danger of the existing extraction and processing industry being completely stopped due to lack of investment became a reality.

Such conditions continued until the signing of the "Contract of the Century" in 1994, a phenomenal event - a war and deep socio-political crisis in the country. As a result of the joint effort of the investment and technology, management and professional experts of the world's leading countries and large multinational companies, the revival of Azerbaijan's oil industry was actually achieved in a short period of time. It is possible to evaluate the effects of the "Contract of the Century" on the economy of Azerbaijan from different perspectives and with different parameters, and such evaluations have been sufficiently placed on scientific-economic, geopolitical and geoeconomic platforms.

The structuring role of oil in the national economy

As the most concise indicator of the importance of this agreement in the approximately 180-year

history of oil production in Azerbaijan, we consider it important to pay attention to the speech of President Ilham Aliyev at the meeting held in 2017 on the occasion of the production of 2 billion tons of oil in our country. "... of the 2 billion tons of oil produced as a whole, about 700 million tons were produced during the period of independence, and 460 million tons of it were produced by the consortium. Therefore, let our public know once again what a great role foreign partners have played in the development of Azerbaijan, in strengthening the economic potential of Azerbaijan."

On the whole, during the period of independence, Heydar Aliyev's oil strategy is rightfully considered the engine of our national development. According to experts, the keystone of this strategy is the involvement of the country's energy resources in the economic cycle, and on the basis of this, ensuring the national security of our newly independent state, giving sustainable character to socio-economic development, and forming a material base for the prosperous life of future generations by solving the problems faced by our country. can be (2)

As a logical continuation of the successful implementation of the oil strategy, on September 14, 2017, a new international agreement was signed on the development of the Azeri-Chirag-Gunashli oil and gas field until 2050. At the signing ceremony, President Ilham Aliyev emphasized the great importance of the new contract for our country. emphasizing that the contract is even more favorable for Azerbaijan: after signing the contract, foreign investors will pay a bonus of 3.6 billion dollars to our country; "AzACG" company of SOCAR will participate in the execution of the contract as a contractor; SOCAR's share is increased from 11.6 percent to 25 percent, and the level of profit oil that will reach Azerbaijan will be 75 percent. ... The main conditions already show that this contract is of great importance for the future development of Azerbaijan and the expansion of financial opportunities."

The oil and gas sector and the fuel and energy complex as a whole have a stable and continuous driving force in the structure of the national economy. It is true, at the same time, we support the expert's note that, despite the great potential, the resources for the improvement of oil conversion in the economy of Azerbaijan still remain quite high. Increasing the processing volume and processing depth of oil and gas resources, further diversification of the industry's activity is the barometer and main indicator of the modern national economy even today, to a sufficient extent, is related to the oil and gas sector. One of the conditions that strengthens the relevance of the issue is that the oil and gas industry is actually the main resource component of national and economic security. 60-70% of the country's budget is formed at the expense of its funds. All this makes the study of the oil and gas sector in a broader economic aspect necessary, which is determined in the interests of the nation state, and also fundamental in terms of its global character. (2)

An important sign of the importance of the oil and gas sector for our economy can be considered that this field traditionally occupies an important place in national development programs. In the "Strategic Road Map of the National Economy Perspective of the Republic of Azerbaijan" and the "Strategic Road Map of the Development of the Oil and Gas Industry (including Chemical Products) of the Republic of Azerbaijan" (4) a free market that is further improved with modern conceptual approaches in line with global economic challenges, in line with strategic goals relations and the role of the oil sector among the tasks of forming a socially oriented, diversified national economy with the ability of self-development.

As a whole, the oil and gas sector is considered an important determinant in justifying the high rates of GDP production in developing countries in general, especially in countries where serious reforms are being implemented, due to a number of reasons, especially due to its dynamism and

volatility as a structurer of the conjuncture. In most cases, in the example of this sector, the radical change itself is considered a supporting component of rapid growth. In the world experience, it is possible to confirm the correctness of the hypotheses that the oil and gas sector is one of the preconditions for achieving rapid growth in transitional countries, by determining the impact of the national socio-economic model on institutional growth.

According to the well-known economists Acemoglu S. and C. Robinson, it is appropriate to compare the development model between the era of oil revenues and the previous one based on the quality of economic and political institutions and the conditions created for natural growth. Therefore, first of all, it is necessary to carry out a justified identification of institutional factors. It is considered that in order to form a more adequate scheme of the influence of institutional factors on economic growth, it is appropriate to approach from the perspective of social conflict theories. According to this approach, the choice of economic (political) institutions is determined not by the society as a whole, but by the groups in power, and not by the society, but by the goals of enriching the group to which they belong. (5)

At the same time, one of the trends observed in the world experience is that at certain stages of development, for various reasons, the specific weight of energy resources and related services in GDP decreases. It is true that during these stages, the dynamics of the GDP is usually observed to deteriorate. According to well-known experts, the main determinant of GDP growth in those moments is characterized by other parameters. For example, the impact of energy prices on the growth rate of GDP is not considered so serious in countries where the raw materials economy is the leader. (6) In our opinion, such parameters should be sought first among institutional factors, taking into account the price factor.

According to expert assessments, in world experience, the share of this sector in the structure of GDP in developed countries with oil and gas producers usually exceeds 20-30%. In general, 20-25% of the relevant standard is considered optimal for such countries where the oil and gas industry is the leader. Here, it is also necessary that the volume of GDP per capita is above 20-25 thousand dollars. (1)

The successful implementation of the oil strategy in Azerbaijan in the last 20-25 years has led to the generation of revenues that allow financing the development of areas that ensure the sustainability of economic growth. Due to the rapid growth of the oil sector during this period, the share of the mining industry in the structure of industrial production was traditionally high, and in 2019 it was 69.9%. The share of the oil and gas sector in GDP increased to 50.8 percent in 2018. Researches show that in 2010, compared to 2000, 43.4 percent of the growth of the country's gross domestic product, and approximately 50 percent in 2019, was due to the oil and gas sector.

As it can be seen, the effects of the oil and gas sector in the overall development dynamics of the country remain decisive during the analysis period. Although, starting from 2004, in macroeconomic development programs and economic policy documents, with the aim of strengthening the style and stability of national economic development, the development priority of the non-oil sector was identified as an important target.

According to official statistics, 94.3% of foreign investment in the amount of 155.5 billion dinars that entered the country's economy in 1995-2019 took place in the period of 2003-2019. In the period of 2003-2019, 37.5 billion of all foreign investment entered the country. dollars (or 24.1%) of the financial loans of the government of Azerbaijan and individual state and private institutions from international financial and credit organizations, 100.4 bln. dollars (64.5%) of direct investments, 217.7 mln. dollar (0.2%) oil bonus, the remaining 17.2 bln. dollars (11.1%) were

other investments (mainly portfolio investments). 100.4 billion directed to the economy of Azerbaijan in 2000-2019. 86.2 billion dollars of direct foreign investments. dollars or 85.9% in the oil sector, the remaining 14.6 bln. USD (14.1%) was realized in non-oil fields. The ratio of attracted foreign direct investments to annual GDP in the oil sector was always over 20% until 2007 (it even exceeded 150% in 2004), in the range of 10-20% in the period of 2008-2013. changed, and after 2015 it settled again at 30%.

The main macroeconomic indicators of the oil-gas sector

Indicators	2006	2008	2010	2015	2016	2017	2018	2019
GDP volume mln, AZN	18746,2	32665,2	41574,7	54380.0	60425.2	70337.8	79797.3	81681.0
growth rate %	134,5	120,5	105,0	101.1	96.9	100.1	101.4	102.2
Oil sector GDP, mln AZN	10091,7	18673,0	20165,0	19879.1	24474.0	30325.5	38208.7	37209.2
growth rate %	163,2	128,9	101,8	98.6	123.1	123.9	125.9	97.4
Oil sector GDP payı%	53,8	57,2	48,5	36.6	40.5	53.1	47.9	45.6
Oil sector World Bank share %	59.3	67.8	68.8	58.4	52.7	47.9	60.3	56.2
Oil fund transfers World Bank share	15.1	10.2	51.9	46.5	43.5	36.8	49.5	46.9
Oil sector foreign investment share	59.5	34.5	35.2	46.5	42.3	53.8	38.1	46.9
Export share %	92.2	95.2	94.8	88.7	61.6	90.3	82.7	90.1
Import share %	20.4	14.1	12.4	24.6	25.9	14.9	16.4	15.8

Table The State Statistics Committee (https://www.stat.gov.az/menu/6/) Central bank (https://www.cbar.az/page-43/), The Chamber Of Accounts (http://sai.gov.az) and SOFAR (https://www.oilfund.az/report/) were compiled by the author based on data

According to the information of the State Security Council, 8.2 billion manats (72.6 percent) of all 12.1 billion manats of foreign investment (including FDI) directed to fixed capital in Azerbaijan's economy in 2019 were in the mining industry (mainly oil and gas production), and the remaining 3.9 billion manats were in other sectors of the economy. carried out in the fields. 45% of the foreign capital investment in non-oil/gas fields was for construction, 22.8% for transport and storage, 19.5% for water supply, and approximately 8.3% for electricity and steam production.

The place of the oil factor in economic policy

One of the interesting trends observed in this period can be considered the decrease of oil production between 2010 and 2015. Studies show that the role of external factors was decisive in the emergence of such a situation. Thus, thanks to the global economic crisis that started in 2008, the members of the Neft consortium, our main partners, and primarily the BP company, did not fully comply with their contractual obligations due to their personal problems. Foreign partners have blamed delays in the commissioning of new production wells under the contract due to the crisis. At the same time, it should be noted that this tendency is also reflected in the dynamics of

the share of the oil sector in the GDP and the share of direct investments directed to this sector in the total investment. At the same time, with the joint efforts of the Government and foreign partners, unfavorable trends were prevented in time. This is evident in the dynamics of recent years. Of course, as explained above, the new agreement signed in 2017, which included the extension of the "Contract of the Century" to 2050, had a strong impact.

When evaluating the effects of the oil sector on the growth process of the national economy, at least in the last 10-12 years, in our opinion, the "transfer" of the State Oil Fund, which has become the main "driver" in our national development, plays a decisive role in expanding the income potential of the State budget and thus the circulation of the non-oil sector in the country. it is important to take into account the role of politics. Starting from 2008, the implementation of the experience of the implementation of the mission of the Oil Fund, which is essentially characterized as supporting the improvement of well-being, in the budget policy, has undoubtedly paid off. Opinions of scientists and specialists about the efficiency and necessity of such an experiment, as well as the lessons of world experience, have a wide dispersion and are not of one value. Taking into account that such an approach applied in Azerbaijan, by comparing it with theoretical considerations and experiences that took place in different conditions, researching and evaluating the conclusions and "hypothetical" considerations is not within the scope of our research, we believe that the issue should not be approached from the perspective of "hypothetical possible options", but real requirements and it is more appropriate to evaluate at the level of results. The real development requirements and goals of our country and the achieved general development results prove that the use of the Oil Fund funds, as in our experience, should be evaluated positively. It is true that it is extremely important in economic policy to take into account the possible unpleasant effects of extreme "enthusiasm" in the use of funds of welfare funds, with the aim of ensuring stimulating, encouraging and at the same time strategic effectiveness. Therefore, the formation of the medium-term expenditure framework provided for in the SYX adopted in 2016, the creation of the "result-based" model of the State budget, and the determination of the "golden rule" norms of funds from the Oil Fund, etc. We believe that such requirements are correct.

Thus, there is no doubt that Azerbaijan has been among the leaders among the countries of the world in terms of the growth rate of GDP in the last 15 years. Since 1995, investments in offshore oil and gas fields, the construction of the Baku-Tbilisi-Ceyhan oil and South Caucasus Gas corridor, world oil - dynamic price trends in the gas market, economic policy that ensures the multiple growth of the oil and gas sector itself and the realization of all opportunities under more favorable conditions. When we look at the impact of the development of the national oil and gas sector on economic growth in the country in different contexts, we see that this sector is among the main drivers of growth in all directions and has the potential for stable and sustainable development.

What was mentioned above about the effects of the oil factor on economic development in Azerbaijan actually reflects the direct manifestation of those effects. Considering that the national economy consists of a complex system of social and economic relations, we can confirm that the effects of the oil factor are even wider. The fact is that the added value created in the field of oil and gas production in Azerbaijan constitutes the main part of the gross domestic product, and the spending of a part of these revenues has ensured their development by creating demand for the products of other fields. In particular, a significant part of the added value created in education, health and other fields was generated by spending oil revenues. Researches show that the total

demand generated only from the part of the State budget formed on the basis of oil revenues constituted more than 30.0 percent of the domestic demand in 2008-2019. If we take into account the multiplier effect of the mentioned expenses, then we come to the conclusion that the role of the spending of oil revenues in the formation of domestic demand is greater. Thus, it is proven once again that the incomes obtained due to oil and gas production are one of the main factors determining economic growth in our country.

On the other hand, studies show that the share of profit in the total output of the oil and gas production industry is significantly higher than in other areas. In 2019, the share of intermediate consumption in the total output of this field in our country was 5.6%, the share of wages was 2.3%, the share of consumption of fixed assets was 0.8%, and the share of net profit was 91.3%. was. Although such high profitability essentially has a positive effect on the stability of economic growth, it limits the impact on the growth of demand for products produced in other areas of the national economy, as well as aggregate demand. In this regard, based on some assumptions of the economic theory, it can be said that having such indicators in one area of the economy can have certain negative effects on national development. However, it is important to take into account that based on the nature of aggregate demand and accumulation in Azerbaijan, which has been formed over the years and, the experience of the last 30 years, we can say that there is no serious danger. Thus, while the share of oil and gas production in the total output of products and services was 33.6% in 2019, its share in intermediate consumption was 5.6%, and its share in paid labor was equal to 10.0%. Thus, it can be concluded that, as some "experts" claim, in the conditions of high economic growth mainly due to oil and gas production in Azerbaijan, a significant disruption of the macroeconomic balance is unlikely. (3)

The result

Conducted researches and lessons of world experience prove that the "driver" role of the oil factor in the modern economy of Azerbaijan, while being sufficiently fundamental, has the characteristics of flexible and efficient management. Therefore, it is considered that the probability of the oil factor remaining as one of the main drivers of sustainable growth in the national economy in the near and medium term should be highly evaluated.

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FEATURES OF THE MANIFESTATION OF THE INFLUENCE OF DIABETES MELLITUS ON THE MUCOUS MEMBRANES AND SKIN OF THE MOUTH

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ABSTRACT

Aim of the research was to study and analyzed the effects of diabetes on the skin and mucous membranes of the mouth. Skin pathology is registered in vast majority of patients with diabetes mellitus (DM). Despite the abundance of publications on dermatological problems in DM, there is still a number of gaps to be discussed in terms of pathophysiological mechanisms. The goal of this review was to assess the mechanisms of development of different skin pathologies under DM. One of the key pathogenic mechanisms of skin lesions in diabetes is hyperglycemia and the effects of the advanced glycation end products, inducing oxidative stress, endothelial dysfunction and inflammation; that in its turn can accelerate the mechanisms of skin aging, the development of diabetic dermopathy and scleroderma diabeticorum. Imbalance of growth factors, cytokines and hormones under insulin resistance, is associated with increased proliferation of keratinocytes, fibroblasts and sebocytes, mast cell dysfunction and melanogenesis disorders in acanthosis nigricans, acrochordons, acne and inflammatory dermatitis in diabetic patients. In addition, authors discuss the role of dendritic cells and macro- phages dysfunction in impairment of peripheral tolerance and diabetic wounds pathogenesis in patients with DM.

Keywords: diabetes mellitus, hyperglycemia, advanced glycation end products, insulin resistance, skin.

Introduction

The effect of diabetes mellitus on the dynamics of the intensity of apoptosis of neurocytes and gliacytes in the cortex of the frontal, parietal and temporal lobes of the cerebral hemispheres under conditions of ischemia injury -reperfusion has been studied. It has been established that the level of apoptotic processes in the neuro- and gliacytes of the frontal cortex does not change after a 20-minute carotid ischemia followed by a 1-hour reperfusion according to the parameters studied in animals without diabetes mellitus. Neurocyte apoptosis is activated in the parietal lobe cortex, while neuro- and gliacyte apoptosis is activated in the temporal lobe cortex. Three-month diabetes mellitus enhances apoptosis of neurons and glial cells in the cortex of the frontal and temporal lobes, neurons in the cortex of the parietal lobe, and reduces the apoptosis of gliacytes.

At the beginning of the ischemia-reperfusion period, the activity of apoptotic processes in the cortex of the frontal and temporal lobes does not change in animals with diabetes mellitus, but decreases in the cortex of the parietal lobe due to glial cells. On the 12th day of observation, the activity of apoptotic processes in the neurocytes of the cortex of the temporal lobe in rats without diabetes mellitus increases, while it decreases in glial cells. Reduced p53 protein content in neurons and increased density of p53+ cells were revealed. During this period of observation, in rats with diabetes mellitus, the activity of apoptotic processes in neurons and glial cells of all lobes generally decreases. The results obtained indicate the presence of regional differences in the dynamics of the reaction of the lobes of the cerebral hemispheres in response to an ischemia-reperfusion injury, characterized by the intensity of apoptosis of neurons and glial cells.

According to the data of the World Health Organization (WHO) for 2014, the number of patients with diabetes mellitus (DM) among the adult population of the planet was about 422 million [5]. Among the complications of DM, diabetic angiopathy, polyneuropathy, retinopathy, nephropathy, and diabetic foot syndrome have clinical and social significance. [5,16]. Diabetic dermopathy also plays an important role, which clinicians should pay attention to. According to different authors, dermatological problems are observed in 40-70% of patients with DM [8,14]. Moreover, the risk of developing skin pathology in DM inversely correlates with the efficiency of correction of metabolic disorders, varying within 30-60% with adequate glycemic control, up to 94% with its inefficiency [9].

When discussing the clinical aspects of skin pathology in DM, it is worth noting some dualism: on the one hand, dermatological changes can be the first clinical manifestation of DM [14], on the other hand, the skin, as the largest organ, is the springboard for the implementation of key pathogenetic mechanisms for the development of diabetes [15].

As is known, DM can lead to the development of diabetes-specific skin lesions (diabetic dermopathy, diabetic scleroderma, diabetic bullae, diabetic wounds) [8]. On the other hand, the presence of DM predetermines a higher incidence of other dermatological lesions (infections of the skin and appendages, inflammatory dermatoses, benign and malignant neoplasms, etc.) [12,14]. Dermatological problems in DM are based on key systemic disorders, including microangiopathy, polyneuropathy, metabolic disorders (hyperglycemia, glycosylation end products, dyslipidemia), impaired immunological reactivity [3,9,15]. One of the earliest and most frequent nonspecific manifestations of skin involvement in the pathological process in DM is the development of xerosis and pruritus, the appearance of which is considered to be a consequence of microangiopathy, leading to impaired trophism and hydration of the skin, dysfunction of mast cells, and also linear pathology [1,8,12,24]. The latter is associated not only with impaired sensory function of the skin and regulation of vascular tone, but also with changes in the balance of neurotransmitters and neurotrophic factors that modulate microcirculation, proliferation, and differentiation of epidermal and dermal cells [14,15,18]. No less typical variant of skin lesions in DM are skin infections (bacterial or fungal), which are detected, according to different authors, in 30-42% of patients, and are a reflection of a violation of the barrier properties of the skin and immunological reactivity in DM [8 ,21]. Although the modern literature presents a sufficient number of works devoted to the study of dermatological problems in DM, it should be noted that they are more focused on describing the epidemiology and clinical picture of skin lesions in DM [9,14,19]. But at the same time, there are a number of gaps in the interpretation of the pathogenetic mechanisms that determine the development of skin pathology in DM.

Aim of the research

The purpose of this review is to analyze the mechanisms of development of various types of skin pathology in diabetes mellitus.

Results and Discussion

Prevention of the development of these changes- the effects of diabetes on the skin and mucous membranes of the mouth, is based on the knowledge of the key pathophysiological mechanisms, which are given below.

Hyperglycemia and the effects of glycosylation end products (AGEs) underlie the development of most variants of skin lesions in DM. Hyperglycemia inhibits the proliferation and migration of keratinocytes, protein synthesis, causes apoptosis of endothelial cells, stimulates the synthesis of nitric oxide in phagocytes, leads to impaired chemotaxis and phagocytic activity of neutrophils [4,21]. The result of these changes is a decrease in the number of cells in the basal layer, smoothing of the epidermal-dermal border, restriction of the expression of the corresponding keratins, and a decrease in the total concentration of DNA in the epidermis [21,27]. However, at the same time, opposite changes can be observed in the skin of patients with DM - increased proliferation of keratocytes and the development of acanthosis, which is associated with the effects of hyperinsulinemia and insulin resistance (IR) [11,16]. In addition, in the epidermis of the skin of patients with DM, a violation of the keratinization process is determined, accompanied by an increase in the number and area of corneocytes - terminally differentiated keratinocytes [12]. The consequence of this is the development of hyperkeratosis, which is recorded in the early stages of diabetic dermopathy, with acanthosis nigricans, etc. [14,19]. In the stratum corneum of the epidermis of diabetic skin, a change in the lipid composition was also noted: a decrease in the level of triglycerides and an increase in the level of ceramides, cholesterol, and fatty acids, compared with the control [21].

Hyperglycemia also leads to the development of significant morphological and biochemical changes in the dermis, which are largely associated with an imbalance in the processes of synthesis and degradation of the extracellular matrix, followed by a violation of histoarchitectonics [27]. As recently as 40 years ago, Moczar et al. [18] demonstrated a violation of the ultrastructure of fibroblasts isolated from diabetic skin biopsies. AGEs directly change the properties of collagen, reducing its solubility and elasticity, increasing rigidity and resistance to enzymatic degradation during remodeling [28]. The latter may explain the role of AGEs in the development of fibrosis in diabetic dermopathy and scleroderma. An equally important mechanism of sclerotic changes in diabetic skin is a change in the differentiation of subcutaneous fat adipocytes into myofibroblasts, followed by the production and accumulation of collagen in the deep layers of the skin, which leads to an increase in its thickness and rigidity, for example, in diabetic scleroderma. [17]. In a number of patients with DM, these changes lead to impaired mobility of the joints of the hands and feet. On the other hand, diabetes is accompanied by fragmentation and disappearance of elastic fibers in the subepithelial zone of the dermis, a change in the thickness, quantity, and architectonics of collagen fibers, which is caused by an increase in the amount of matrix metalloproteinases (MMPs), which ensure the degradation of the components of the intercellular substance of the dermis [10.28]. The latter fact (in particular, an increase in the levels of MMP2 and MMP9 in the skin with DM) plays a critical role in reducing the volume of hyaluronic acid and remodeling the microvasculature, especially in the thin skin of

the face, scalp and forearms [17,27]. These changes are largely similar to those during aging, and therefore DM is considered one of the key promoters of skin aging [10].

Another mechanism for promoting skin aging in DM2 is the development of pro-inflammatory events [3]. The end products of glycosylation formed as a result of glycation of proteins, lipids and nucleic acids [10] are powerful stimulators of the formation of active oxygen radicals (AOR), while they disrupt the functioning of antioxidant systems, inhibiting the elimination of ARC [10,21]. This ultimately leads to disruption of the functioning of intracellular and extracellular proteins that induce the activation of inflammatory cytokines through the pathway triggered by nuclear factor κβ (NF-κβ) [21]. Receptors for AGEs (RAGEs) belong to the multiligand receptors of the immunoglobulin family encoded by a gene located on chromosome 6 near the genes of the major histocompatibility complex class I and II [6], i.e. pattern-recognition receptors that bind, in addition to AGEs, a number of other molecules, including S-100/calgrnulin, amphoterin (high motility group protein B1 – HMGP-B1), and β-amyloid peptides. In the skin, this type of receptor is expressed by various cells, including: keratinocytes, dendritic cells, endotheliocytes, fibroblasts, macrophages [2,6,14]. This determines the pro-inflammatory activation of both immune cells (macrophages, lymphocytes) and skin residents - keratinocytes and fibroblasts, in which the expression of pro-inflammatory factors and chemokines that stimulate the recruitment of leukocytes is enhanced [8,24]. The binding of RAGE to the ligand involves several signaling cascades, in particular, mitogen-activated protein kinases (MAPKs), extracellular signal-regulated kinases (ERKs) 1 and 2, phosphatidyl inositol 3 kinase, p21Ras, stress-activated kinase/c-Jun- N-terminal kinase and Janus-kinases involved in the regulation of cell growth and death [10]. In addition, stimulation of RAGE in cells leads to the activation of the transcription factor NF-κB, followed by transcription of a number of pro-inflammatory genes [10,28]. The consequence of this is an increase in the number of cells in the dermis that initiate inflammation - macrophages with a predominance of the M1 phenotype [3,29].

Despite the fact that hyperglycemia and AGE are a common pathogenetic mechanism of type 1 and 2 DM, a certain specificity of dermatological disorders in different types of DM has been identified. So, lipoid necrosis, vitiligo and diabetic bullae are considered specific for type 1 diabetes [18]. Although these variants of skin lesions are also described in type 2 diabetes [1,9]. For the latter, acrochordons (fibroepithelial polyps), black acanthosis (acanthosis nigricans), eruptive xanthomas, diabetic scleroderma, androgenetic alopecia, acne, psoriasis, etc. are more characteristic [12,16]. This association is due to the presence of systemic changes due to the metabolic syndrome (dyslipidemia, IR) in patients with DM2. The main part of patients with obesity and DM2 suffer from secondary IR, which is characterized by combined variants of changes in the functioning of insulin receptors and post-receptor signal transmission. It is believed that IR is the result of the accumulation and dysfunction of visceral adipose tissue [6]. Adipocyte hypertrophy is accompanied by a change in the spectrum of secreted adipokines, accumulation of M1 macrophages and lymphocytes [4]. The consequence of these disorders is a systemic increase in the levels of monocyte chemotaxis factor (MCP-1), tumor necrosis factor (TNF-α), interleukins (IL-6, IL-8 and IL-18), leptin, activator inhibitor plasminogen (PAI)-1 [16]. At the same time, skin cells are in conditions of a double imbalance: insulin deficiency and an excess of inflammatory cytokines [28]. Insulin plays an important role in maintaining homeostasis and skin function. Normally, insulin regulates the balance between the processes of proliferation and differentiation of keratinocytes [11]. Insulin receptors belong to the family of receptor tyrosine kinases. This family also includes receptors for numerous growth factors, including insulin-like

growth factor (IGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and colony-stimulating factor receptors. and some cytokines [25]. It has been shown that hyperinsulinemia increases the production of IGF-1 and 2 in the liver, which leads to an increase in the systemic level of these growth factors [16]. In addition, the possibility of insulin cross-activation of IGF-1 receptors, which are expressed by keratinocytes and fibroblasts, has been proven, which leads to an increase in the proliferation of these cells [25]. IGF-1 activity is regulated by the level of IGF-binding proteins (IGFBPs), which increase the half-life of IGF-1 and regulate the pool of metabolically "free" IGF-1. In obese patients with hyperinsulinemia, the levels of IGFBP-1 and IGFBP-2 are reduced, which contributes to an increase in the plasma concentration of free IGF-1. An increase in bioactive IGF-1 stimulates cell growth and differentiation [14]. This explains hyperkeratosis, papillomatosis in acanthosis nigricans, as well as the formation of benign skin neoplasms - acrochordons [11]. Often, intensification of proliferative processes in the skin is accompanied by a violation of pigment metabolism, usually with hyperpigmentation [7,30]. This phenomenon is associated with the effect of activation of E3 receptors for prostaglandin E2 [30]. The production of the latter increases due to increased expression in keratinocytes and dermal cells of NF-kB and COX-2 (cyclooxygenase) [15]. Activation of the E3 receptors of melanocytes is associated with an increase in their proliferation, an increase in the local formation of MSH from the precursor, proopiomelanocortin, which ultimately leads to the accumulation of melanin [7,22,30].

An equally significant mechanism of association between IR and skin pathology in T2DM is the effects of insulin on the production of sex hormones. Insulin and IGF-1 have a powerful stimulating effect on the activity of 17-hydroxylase in the ovaries, which determines the excessive production of androgens, especially 17-hydroxyprogesterone [11]. In addition, an increase in insulin levels contributes to a decrease in the production of SHBG (sex hormone-binding globulin) in the liver, which determines more pronounced effects of free testosterone on target cells [25]. In the skin, the target of androgens is the pilosebaceous unit. An increase in the level and intensity of androgen signal transduction leads to an increase in the proliferation of sebo cytes, an increase in lipogenesis and their secretory activity, cell proliferation in the area of the funnel of the hair root, hyperplasia of the sebaceous glands, promoting the development of acne [11]. IGF-1 has a similar effect on the sebaceous glands [25]. IGF-1 is a potent growth promoter during puberty and plays a central role in the development of acne and the induction of hyperandrogenism [19] and, in fact, is a factor in signaling the relationship between insulin resistance and the development of acne vulgaris. In addition, in vitro studies have shown that insulin and IGF-1 can also stimulate the growth of hair follicles, which, in all likelihood, leads to the development of hirsutism [21,35]. However, an alternative effect of excessive insulin levels on hair growth is also possible. Thus, it has been shown that hyperinsulinemia leads to an increase in the activity of 5-alpha-reductase in the cells of the hair papilla, which leads to an increase in the conversion of testosterone to dihydrotestosterone, resulting in the development of androgenetic alopecia [8].

The spectrum of dermatological problems in patients with DM has a certain paradox - on the one hand, patients with DM are more susceptible to the development of an opportunistic infection, and on the other hand, they are more likely to develop hypersensitivity reactions, various types of inflammatory dermatosis and autoimmune pathology [11, 16]. This is associated with a dysfunction of one of the key moderators of maintaining the immunological homeostasis of the skin - dendritic cells (DC). Today, among the skin DCs, it is customary to distinguish between

typical (stable) DCs that are normally present in the skin, and plasmacytoid DCs (pDCs), which appear in the skin only during inflammation [2]. According to localization, typical DCs are divided into epidermal Langerhans cells and dermal DCs (dDCs). After receiving a signal about damage, DCs are activated, capture the antigen, and its process is accompanied by cell migration through the system of lymphatic vessels of the skin to regional lymph nodes [2]. At the same time, the activation of different DCs has different consequences. It is assumed that the main effect of activation of Langerhans cells is the development of tolerance to antigens through stimulation of Treg (T-suppressor cells) [20]. Whereas the maturation of dermal DCs can lead to the activation of various variants of the immune response through the activation of Th1, Th2, or Th17 [2,35]. It is assumed that different dDC subtypes are capable of activating different types of immune response. The most important factor in the activation and determination of the DC phenotype is the microenvironment in which these antigen-presenting cells are located [20]. The latter fact is of particular importance in the conditions of DM, which provides a combination of a complex of pathogenetic factors in the skin, including: hyperglycemia, endothelial dysfunction, oxidative stress, cytokine imbalance, mast cell dysfunction [10,24].

The study of the DC status in DM showed very conflicting data. On the one hand, it has been found that the number of both myeloid and plasmacytoid DCs decreases in the peripheral blood of patients with DM [23]. However, experimental studies revealed the parallelism of the processes of peripheral nerve degeneration and the development of polyneuropathy, the accumulation of mature DCs in the cornea of the eye [13]. Similar results were obtained by other authors who proved the association between diabetic neuropathy and DC dysfunction in peripheral tissues and organs in DM, reflecting the specifics of neuro-immune relationships in DM in different tissues. Similarly, in the skin of patients with diabetic foot syndrome, an increase in the number of DCs, primarily Langerhans cells, was revealed. At the same time, the authors showed a direct relationship between the number of Langerhans cells and the likelihood of developing diabetic wounds [25,33].

Factors stimulating DC activation, in addition to the classical stimulant, bacterial lipopolysaccharide, include reactive oxygen radicals, the formation of which, as already mentioned, is increased under conditions of hyperglycemia. It has been shown that ARCs stimulate myeloid DCs, stimulate their activation and maturation, which can contribute to the promotion of inflammatory events. In addition, insulin and IGF-1 are also stimulators of DC maturation, activating the expression of scavenger receptors (SR-A) in them and the uptake of oxidized low-density lipoproteins [20]. This determines the enhanced activation of dendritic cells, including those in the skin, under T2DM conditions. DC activation can stimulate the recruitment of monocytes and the accumulation of macrophages [2,26], which is associated with the development of diabetic complications. Previous studies have shown that a similar pattern is also characteristic of the skin - an increase in the number of macrophages is associated with the development of diabetic wounds and impaired healing [4,29]. This phenomenon is determined by a violation of metabolic processes in cells: dyslipidemia is associated with the accumulation of lipids in macrophages, which leads to special variants of inflammation, for example, in eruptive xanthoma and granuloma annulare, associated with accumulation of lipids in histiocytes, a delay in the mechanisms of resolution of inflammation and chronic inflammation [20,32]. In addition, there was a violation of the metabolism of L-arginine with enhanced activation of iNOS with the development of pro-inflammatory events, oxidative and nitroxyl stress, impaired mechanisms for resolving inflammation, progressive alteration and fibrosis [3,17,29]. An increase in the number

and dysfunction of DCs and macrophages in diabetic skin may explain the higher likelihood of developing inflammatory dermatoses, such as psoriasis, although to this day the interpretation of the association between psoriasis and DM is based mainly on the role of IR. First, the skin manifestations of IR are in many respects similar to the disorders in the epidermis observed in psoriasis (hyperproliferation with impaired differentiation of keratinocytes). Secondly, the revealed close association of the development of psoriasis and metabolic syndrome with IR can be explained by the already discussed factor of chronic inflammation that develops as a result of dysfunction of visceral adipose tissue [14]. Thus, in patients with psoriasis, a decrease in the level of anti-inflammatory adiponectin was shown with an increase in such pro-inflammatory agents as omentin, resistin, vasfatin, interleukin-6, and TNF-α [11]. The latter is considered one of the most significant cytokines involved in the development of psoriasis [15]. On the other hand, the role of TNF-α in impaired insulin sensitivity through inhibition of the tyrosine kinase activity of insulin receptors is no less known [11,25].

Conclusion

Thus, DM2 is characterized by a high frequency and variability of skin lesions. The key mechanisms for the development of skin pathology in T2DM are hyperglycemia, microangiopathy, insulin resistance, changes in the balance of growth factors and sex hormones, as well as dysfunction of antigen-presenting cells and skin macrophages. The complex of these factors determines the violation of the barrier function of the skin, the imbalance of the processes of proliferation, differentiation and cell death, the change in the skin aging program, the violation of peripheral mechanisms of tolerance to antigens, which is accompanied by an increased risk of developing infections, inflammatory dermatosis and neoplasia.

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LEXICAL FEATURES OF BRITISH SLANG AND DESCRIPTION OF ITS WORD FORMATION

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ABSTRACT

Clarification of all aspects of the social differentiation of language is one of the urgent problems of modern linguistics. An in-depth study of this problem is especially important in terms of clearly showing the direction of language development and its causes, revealing the relationship between people's living conditions and language options. British slang needs to be studied in terms of studying the specifics of linguistic, cultural and social groups. Opinions on the classification, analysis, lexical and semantic features of slang in linguistic researches are different. The research topic is approached from the point of view of lexical-semantic linguistics and lexical factors influencing its development are noted. The main goal of the article is to identify the lexical features of modern British slang and for this purpose, examples from English literature, dictionaries, and articles in periodicals were selected.
The article can be useful in the in the teaching of lexicology courses and in the preparation of lectures on lexicography. The lexical features and word formation of slang were researched with the use of general scientific methods, descriptive, linguistic analysis, and historical-comparative research methods in the article.
Keywords: Slang, semantics, stereotype, informal layer, marginal, grammatical canons.

Introduction: Slang is a type of informal layer used by certain social groups and professions (teachers, students, military, youth, gamblers, prisoners, etc.) as well as people living in different geographical areas. Slang acts as a kind of code. The use of this type of informal layer creates a sense of belonging among group members and effectively excludes outsiders. People outside the group are reluctant to use such words in general contexts because they do not understand or misinterpret them. Slang is a complex phenomenon that combines processes such as semantic change and enrichment, as well as uncertain moments in the lexicology.
Main text: Slang generally does not conform to grammatical stereotypes. The lexical features and word-formation ways of this type of informal layer, which has its own word-formation methods, have been studied in the article and its conformity to grammatical canons has been clarified along with its marginal features. British slang needs to be studied in terms of studying the specifics of linguistic, cultural and social groups. Opinions on the classification, analysis and lexical features of slang in linguistic researches are different. A study of British slang reveals that one of the most controversial issues is the lexical characteristics of slang. Slang lexicology is a complex subject that combines processes such as lexical change and enrichment, as well as uncertain moments.
The slang lexicon expands by giving new meanings to existing words. These words become part of the technical dictionary used within a certain group and expressing them. The lexical structure of some slang words is in accordance with the laws of standard language and grammatical rules. For example, the suffix "y", which is formed adjectives by adding to the end of nouns, is also used

in the formation of slang: words such as moody-being in a bad mood, gobby-explict are examples. With the adding "ette" suffix some nouns, the feminine slang words are formed. Such as punkette–a punk woman [7, p. 112].

Some slang words have morphological features outside the grammatical rules. Instead of the standard English productive suffixes "er, ed, s", slang expressions were created using non-productive suffixes "o / oo, eroo, ers" in the slang lexicon. For example, dumbo is used to denote a stupid person,thicko is a squeezing person, or people who are distinguished by a certain habit or characteristic. The words saddo-poor or disrespectful, sicko-disturbing and unpleasant are words of the same kind. This suffix also appears to be effective in correcting adjective forms and words with onomotopic (names given to words according to the sounds they make) colors. Words like kiddo-child, yobbo-boy, doo doo-ruin are examples of this. The suffix “eroo”, which is formed with the participation of both the suffixes “o/oo” and “er”, is also involved in the formation of slang words. The word Smackeroo-dollar is a good example of this. The suffix “ers” (a combination of the noun-forming “er” and the plural suffix “s”) is added to even nouns to form the plural form of words. In addition to cobblers, conkers, knackers, nadgers, knockers, milkers slang expressions used for women's breasts, choopers-teeth, trousers-drawers. This suffix are also added to some words used for some uncountable nouns: ackers-money, uppers-anfitamine(drug substance) [6] can be shown as samples.

In some expressions, the plural suffix “s” loses its properties and can take on the meaning of creating new meanings: afters – sweets (desserts), flicks – movies, readies / spends – money (especially cash) expressions are the samples of it. Unlike its standard English function, the suffix “er” is added to the end of nouns in the slang lexicon to express a new meaning: belter–a person who refuses easily or does not have the courage to cope with a task. This feature is observed in slang as a ghoster–night shift. The suffix “ed” also contributes to the enrichment of the slang lexicon. The suffix at the end of slang words, such as boxed, brained, hammered, ratted, stoned, trousered, which means drunk or drug-addicted, is the adjective suffix "ed" and is added to the end of nouns to form adjective slang.

Complex slangs: Some complex slang wordsand expressions are formed by combining the word ache–pain with various simple words. Examples of such complex slang as ballache–a laborious and irrelevant task, earache–a talkative person, face-ache–a person with a mischievous appearance. Many complex slang words are formed by adding new meanings to words that exist in the standard language. For example, with the addition of the word “head”, slang expressions meaning bubblehead, fat-head, bone head–stupid were formed. The terms crackhead, smackhed, and hash-head, which mean drug addicts, are similar. Some complex slang expressions are formed by adding words such as brain, face, and mouth. Words such as bollock-brain–stupid, crater face–ragged face, big mouth–garrulous can be shown an example of such complex slang expressions [5, p. 33].

A number of complex slang expressions formed by infixes that are not very common in standard English have entered the British slang lexicon. The humorous expression of the word absobloodylutely–absolutely and the enhanced expression of the word fanfuckingtastic–legend, and other similar expressions can shown as examples of such complex slangs [6].

There are a number of assimilated complex expressions in the slang lexicon. These expressions are morphotactically complex and morphosemantically opaque. For example, dimbowhich means minded one who pretends to be intelligent, is formed from an asymptomatic combination of dim–minded and bimbo–attractive but foolish. Looksee–inspection is a complex slang and formed with

the combination of the words look and inspection and two words have been assimilated to achieve simplification during speech [5, p. 35].

There are also new expressions in the slang lexicon created by adding metaphorical meanings to the adjectives in accordance with the lexical meanings they express. Examples of such slang can be an expression high–intoxication, an expression massive used in the sense of people united by social interests, an expression previous–criminal record. Another atypical formation in the slang lexicon is the prepositions that express or create new slang expressions. An example of an atypical formation of a word included in the slang lexicon is out, which means someone who does not hide his homosexual identity, and up, which means to be under the influence of high doze drugs.

A number of expressions that are widely used in the slang lexicon are the result of the abbreviation and the processes involved in it (clipping, blending, abbreviations). Slang words formed by the process of clipping are mainly found in Cockney rhythmic slang. In this case, the second element of the slang is preserved to maintain the rhythm. Piddle slang expression was created by cutting the jimmy riddle rhythmic slang. In another example, we see that the jam tart slang derived from the word sweetheart is simply clip in the form of a tart-woman. In some slang expressions, the first side is protected and the second side is clipping more: dig–shaving slang derived from the expression dig the grave, tom–jewel slang derived from the expression Tom Foolery means stupidity, naughtiness [7, p. 123-126].

Blending slang is the process of taking a part of an existing word and combining it with another word: Edutainment slang is a mixture of the words education and entertainment and means educational entertainment. Let's pay attention to the meaning of the slang in the following sentence: In the four years since the Kickstarter campaign, Rebel Girls has become a global multi-platform edutainment brand [1]. Another expression in the slang lexicon, the word hoolivan–police caravan, is a mixture of the words hooligans and van. Some expressions in the slang lexicon are formed by abbreviations (acronyms) and the use of capital letters (initialism). 24/7–24 hours a day, 7 days a week, IMO–in my opinion, lulz–just for laugh and other slang words and expressions are used widely, especially by Internet and social media users [7, p. 128-129].

In the British slang lexicon, a number of slang expressions have been used under the influence of an event known as Back-slang and are used among various social groups. These expressions are slang words that are formed by reversing words. Most of these expressions are words that exist in the standard language and whose lexical meaning is clear to everyone. Yob–boy, riah–hair and other slang words can be an example of this.

Conclusion

From the approaches of various linguists and lexicographers, it can be concluded that slang word and expressions differ from the vernacular in terms of vocabulary and they have a completely new (more metaphorical) meaning, or these words are taken from other languages. The phonetic, morphological and syntactic features of such words do not differ much from those of the common language. As a result of expanding the scope of slang, it can be included in the active vocabulary of the English language and be certified. Therefore, slang can be one of the main means of enriching the language. These expressions, which are widely used in oral language, give a noticeable stylistic effect when used in written language and add a characteristic feature to that speech. Slang generally does not conform to grammatical stereotypes and has its own word formation methods. Slang has marginal features due to its nature, but it is incorrect to call it a

completely marginal linguistic phenomenon and there is a need to expand the analysis parameters in the morphological field.

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THE SCIENTIFIC BULLETIN OF SPECIFICITIES OF TRENDS, DIVERSITY, INCLUSION, AND DISTINCTIVE OF THE CLINICAL PHARMACISTS IN MONDIAL

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ABSTRACT

Aims of the study was to analyze and determine the peculiarities of specificities of invocation, outlook and character of the clinical pharmacists globally. Clinical pharmacists ensure a consistent patient care process that ensures the relevance, efficiency and safety of patient care. The clinical pharmacist consults with the patient's physicians and other health care providers to develop and implement a treatment plan that can meet the patient's overall goals of care set by the medical team. Clinical Pharmacist Applies specialized knowledge of the scientific and clinical use of drugs, including drug action, dosage, side effects and drug interactions, in the performance of their patient care activities in collaboration with d 'other members of the health care team. Clinical pharmacists look to their clinical experience to address health problems through the rational use of drugs. Clinical Pharmacist Rely on your professional relationship with patients to tailor their recommendations to better meet the individual patient's needs and wants. Clinical pharmacists are licensed physicians with advanced education and training who practice in all types of healthcare settings with an emphasis on integrated medication management. These specialist pharmacists focus on optimal medication use with an emphasis on dosing, monitoring, side effect detection, and cost effectiveness to achieve optimal patient outcomes. Increasingly, clinical pharmacists around the world are gaining attention as important members of the ambulatory and emergency care team. This article describes the real and potential scope of practice of clinical pharmacists around the world.

Keywords: Specificities, invocation, outlook, character, clinical, pharmacists, globally.

Introduction

Clinical pharmacists work directly with physicians, other healthcare professionals, and patients to ensure that medications prescribed to patients contribute to the best possible health outcomes.

Clinical pharmacists work in healthcare settings, where they communicate frequently and regularly with physicians and other healthcare professionals, which contributes to better coordination of care. Clinical pharmacists are educated and trained in many direct patient care settings, including medical centers, clinics, and many other healthcare facilities. Clinical pharmacists are often granted patient care privileges by collaborating physicians and / or healthcare systems, which allows them to perform the full range of drug decision-making functions within the team. medical condition of a patient. These privileges are based on the clinical pharmacist's demonstrated knowledge in pharmacotherapy and on his clinical experience record. This specialist knowledge and clinical experience is usually acquired through residency training and specialist certification.

Aims of the study

Aims of the study was to analyze and determine the peculiarities of specificities of invocation, outlook and character of the clinical pharmacists globally.

Research methodology

The main question of this article was to research and analyses the specificities of invocation, outlook and character of the clinical pharmacists globally. We have searched and analyzed PubMed, Web of Sciences, Clinical key, Tomson Routers and Google Scholar mostly, using search terms bases, including the words to research and analyses specificities of invocation, outlook and character of the clinical pharmacists globally. In addition to the desired subject understanding. Then, each article was discussed and an abstract of the total information gathered during the process was provided, aiming at easy understanding of the public. To establish these outcomes, over two hundred articles were investigated. We brought together all published data to comprehensively examine the effects in a systematic review, to define the roll out of the study of the research and analyses of specificities of invocation, outlook and character of the clinical pharmacists globally.

Results and discussion

Clinical pharmacists often apply their knowledge of drugs to a patient-specific treatment plan and evaluate dosage suitability, side effects, efficacy, and drug interactions. If necessary, the clinical pharmacist can discuss any issue and advise the physician, who is primarily responsible for prescribing drugs to patients, to ensure optimal use of the drugs. To practice, clinical pharmacists must graduate in a recognized area of qualification. The specific requirements for these degrees may differ depending on the country of operation. Subjects that are commonly found in the university's clinical pharmacist program include biology, chemistry, pathology, pharmacology, and socio-behavioral sciences. Most clinical pharmacists in the United States hold a Ph.D. in Pharmacy (Phar.D.) in addition to several years of postgraduate education such as a pharmaceutical residency. They can be certified as a clinical pharmacist through the Pharmaceutical Specialties Council, which is independent of the American Pharmacists Association. Education and certification requirements in other countries may differ depending on the guidelines set by the regulatory authorities. Clinical pharmacists are responsible for providing safe, effective, and timely drug therapy. Through various tasks in the department, they provide support for centralized and decentralized drug use systems, as well as optimal drug therapy for patients with a wide range of medical conditions. Clinical specialist pharmacists are competent in

delivering direct patient-centered medical care and integrated operational pharmacy services in a decentralized practice with the participation of doctors, nurses and other hospital staff. These physicians are aligned with targeted multidisciplinary programs and specialized services to ensure drug therapy management within specialized patient care services and to ensure that pharmaceutical care programs are properly integrated across the facility. In these clinical roles, clinical pharmacists are involved in all necessary aspects of the drug use system, while providing comprehensive and personalized pharmaceutical care to patients in their assigned areas [1-2].

Pharmaceutical care services include, but are not limited to, assessing patient needs, integrating age and disease characteristics into drug therapy and patient education, adjusting patient care, and providing clinical interventions to identify, mitigate and prevent adverse drug reactions. Specialist clinical pharmacists serve as department resources and liaison with other departments, hospital staff, or external groups. They also lead clinical research and practice improvement projects as well as quality patient care and compliance initiatives to improve drug use or pharmaceutical practice. Specialist clinical pharmacists provide education and training related to medicines and practice and actively act as mentors for doctoral students and pharmacy residents. Where appropriate, participation in a quality management program is expected to improve services by monitoring processes, analyzing data, implementing interventions to improve and evaluating the effectiveness of those interventions. The responsibilities of a clinical pharmacist may include setting and maintaining long- and short-term goals for a quality management program; track and document quality improvement projects to make progress towards quality improvement goals; as well as consulting and training of personnel on priorities and plans of quality management [3-4].

Clinical pharmacists ensure a consistent patient care process that ensures the relevance, efficiency and safety of patient care. The clinical pharmacist consults with the patient's physicians and other health care providers to develop and implement a treatment plan that can meet the patient's overall goals of care set by the medical team. Clinical pharmacist applies specialized knowledge of the scientific and clinical use of drugs, including drug action, dosage, side effects and drug interactions, in the performance of their patient care activities in collaboration with d 'other members of the health care team. Clinical pharmacists look to their clinical experience to address health problems through the rational use of drugs. Clinical Pharmacist Rely on your professional relationship with patients to tailor their recommendations to better meet the individual patient's needs and wants. Clinical pharmacists are licensed physicians with advanced education and training who practice in all types of healthcare settings with an emphasis on integrated medication management. These specialist pharmacists focus on optimal medication use with an emphasis on dosing, monitoring, side effect detection, and cost effectiveness to achieve optimal patient outcomes. Increasingly, clinical pharmacists around the world are gaining attention as important members of the ambulatory and emergency care team. This article will describe the real and potential scope of practice of clinical pharmacists around the world [5-6].

The aging of the population has increased the burden of chronic disease around the world. There are both ethical and reasonable goals for addressing health inequalities identified in chronic disease management for people of multiple social origins, and existing programs routinely fail to meet the needs of these people. This translates into poor program support, poor management of chronic disease, and more frequent seeking of health care. Unlike acute conditions, chronic conditions require ongoing care and treatment outside of health care settings, in the community or in primary health care settings in terms of medication use, lifestyle management and behavior change in health. Typically, this is a multi-pronged intervention that includes a review of drug

therapy, patient education for treatment, monitoring of medication, immunization, self-care, and support. disease, and /or prescribing authority. Patients who take multiple medications due to chronic disease are at high risk of drug duplication, interactions, or side effects, which can lead to longer hospital stays and higher costs. To improve the safety and effectiveness of the treatment, these patients must have specific needs for the correct use of the drugs encountered. Research has shown that integrating pharmacists into outpatient clinics can improve chronic disease management and optimal medication use. Additionally, involving a pharmacist in patient care can reduce the use of unwanted medications, especially in the past. A study in Canada found that the number of patients taking the wrong drug has decreased, mostly after screening tests and improvement by a group including a pharmacist. Unlike regular nursing, pharmacist-directed medical care was associated with a comparable frequency or pace of office work, major medical care or emergency room visits, and hospitalization and adherence, increased the rate of quantity or quantity of drugs received and improved study choices. indicators, blood circulation and blood circulation. achieve a lipid goal. Another recent study shows that a telemedicine-based chronic disease management program involving clinical pharmacists resulted in statistically significant improvements in diabetes and hypertension outcomes, as well as clinically significant improvements in lipid control. and smoking cessation [7–8].

Clinical pharmacists are specialized medical practitioners who provide direct patient care and holistic treatment. While this practical model has proven itself best in the United States, there are clinical pharmacists around the world who are improving the care of patients of all ages in all areas of emergency and outpatient care. This article discusses training standards, expected skills, and contributions from clinical pharmacists. Clinical pharmacists practice across all healthcare settings and use in-depth knowledge of drugs and medical conditions to manage drug therapy as part of a multidisciplinary team. Clinical pharmacists are responsible for drug treatment and patient outcomes. They are the primary source of scientifically reliable information on the safe, correct and economical use of medicines. Whereas pharmacists may be involved in the management of specific drugs or individual medical conditions the standard of care that ensures that each patient's drugs (prescription, over-the-counter, supplements, or herbal medicines) are individually assessed to determine if they are appropriate whether they are for the patient, effective for the disease, safe for use in concomitant diseases and concomitant therapy, and whether the patient can take them. An individualized care plan defines goals, monitoring and expected outcomes The patient is actively involved in developing the plan with other members of the care team. The impact of conventional medical management provided by clinical pharmacists on an outpatient basis is being studied to identify efficient processes and measure overall patient outcomes. Disease-specific drug management programs have shown a reduction in the incidence of some drug-related problems, including non-adherence, and have reduced some health care costs [9–10].

Clinical pharmacists are pharmacists, physicians who specialize in direct patient care. Although they are expected to follow the steps outlined in the pharmacist's POC, Standards of Practice (SOP) help clinical pharmacists comprehensively assess drug needs and often manage complex and specialized regimens. Documentation requirements are more detailed and, where applicable, should be consistent with billing requirements. The clinical pharmacist can exercise his practice more independently in certain contexts, in particular according to organizational privileges. Clinical pharmacists who have received the appropriate qualifications and certifications should now enjoy hospital privileges such as doctors and providers of excellence. They are required to

maintain a valid license, but have additional certification requirements. SOP for the clinical pharmacist also includes educational, research and quality improvement activities [11-12].

Pharmaceutical education varies across the world. In the United States (USA), a pharmacist is eligible for a license after 6 years of training in pharmacy. While not required, many of these graduates already have a Bachelor of Science degree in another field. Pharmacists interested in direct patient care may receive additional training in postgraduate residency programs in Emergency or Outpatient Care. It is a large-scale accredited expertise in clinical care, drug information, administration, teaching methods projects/research. Those interested in specialization can complete their second year of postgraduate study in areas as diverse as any medical specialty (outpatient care, intensive care, infectious diseases, internal medicine, oncology, and many others). Additional research grants may follow, especially for those interested in an academic or research role. Pharmacists licensed in the United States have received formal training, and many universities are partnering with pharmaceutical schools outside of North America to create clinical pharmacy training opportunities for international students. Additional clinical practice sessions were included in the training programs. Clinical pharmacists may practice under a formal collaborative practice agreement with physicians in their area of practice or under hospital conditions. For example, a pharmacist can change the dose, frequency, or way of taking medications that are covered by a collaborative practice agreement. They may also initiate serum concentration monitoring or other applicable laboratory tests to monitor the effects of therapy. Quality assessments have demonstrated the value of these programs. Hospitals may require people to provide periodic quality assessments or evidence of minimum activity. Pharmacists' laws are governed by the ordinances of state and local hospitals [13-14].

Clinical pharmacists are already part of many medical teams. Most are part of a multidisciplinary emergency or ambulatory care team, but some are in private practice with a wide range of physicians. There are many examples of the influence of clinical pharmacists and this article will highlight some of the recent publications. Since the emphasis is on taking medication, most measures reflect the optimal use of medications and the prevention of adverse events. Widespread use of antihypertensive drugs can cause side effects if the doses are not correctly titrated. The benefits of training, monitoring and intervention by clinical pharmacists have been demonstrated in a prospective randomized trial involving heart failure or hypertensive patients treated in a large public hospital. Patients who received clinical pharmacist intervention had a lower risk of any adverse drug event or medication error, preventable side effects, potential side effects and medication errors compared to control patients treated in the same clinics. Patients with a complicated cardiovascular history took the most drugs and events. The interaction, training and regular communication of pharmacists with the rest of the team improved treatment adherence, patient satisfaction, and reduced the use of medical services and the direct costs of treatment. A systematic review of randomized trials on the impact of a clinical pharmacist on patients with heart failure showed similar benefits with reduced hospitalization rates for all causes and hospitalization rate for heart failure. Other reviews describe additional benefits clinical pharmaceutical monitoring and interventions for various treatment evaluation criteria (blood pressure, lipid profile, weight and glycemic control), a collective care strategy including clinical pharmacists [15–16].

Clinical pharmacists in inpatient emergency teams have been shown to reduce the preventable side effects of drugs. The clinical pharmacist surrounding himself with the intensive care team identified and prevented more drug side effects more effectively than the pharmacists involved in

order entry and verification, and avoided potential costs. A review of studies describing the impact of clinical pharmacists on inpatients suggests that adding a clinical pharmacist to the emergency team resulted in improved treatment without any evidence of harm. Teamwork during rounds, patient interviews, outpatient and inpatient coordination, discharge education and follow-up have all improved outcomes. Patients at greatest risk, such as the very old and very young, have been shown to benefit from the presence and input of clinical pharmacists [17].

A clinical pharmacist is trained to work directly with patients in a healthcare system such as hospitals or clinics. Because the clinical pharmacist has detailed knowledge of drugs and their effects, and because the clinical pharmacist has extensive experience with patients, physicians often give clinical pharmacists significant control over prescribing drugs and monitoring patients. Among other things, clinical pharmacists are responsible for selecting the right drugs, monitoring patients, diagnosing potentially untreated illnesses, consulting with the patient about the effects of drugs, and ensuring patients adhere to prescribed drug regimens. Clinical pharmacists are people who help patients recover from illness or lead healthy lives. The doctor diagnoses and prescribes medications in general terms, but the clinical pharmacist helps make specific decisions. For example, if a patient has an adverse reaction to a particular drug, the clinical pharmacist will recommend alternative treatments. The clinical pharmacist will also help select the best drug combinations for the patient's condition [18].

The clinical pharmacist manages for critical care pharmacist residency program and oversees the resident's progress and interactions with other mentors in our healthcare system. The clinical pharmacist participates in multidisciplinary book club discussions, thematic conferences, and quality assessment meetings. Like other professionals, the clinical pharmacist strives to maintain its role in scientific publishing in the literature, maintain skills, and keep abreast of the growing literature. As a certified critical care pharmacist, a clinical pharmacist must undergo continuing education and maintain certification, and as a licensed pharmacist, a clinical pharmacist must also pursue continuing education. As clinical pharmacy programs around the world are at different stages of development, the need for specialists who specialize in drugs and their optimal use is universal. Clinical pharmacists have supported these training programs and provided training to individuals and groups. Their publications are used by pharmacists around the world to prepare and maintain the certification board. This awareness is expected to continue as more partners are involved and more pharmacists and their multidisciplinary teams recognize the power of clinical pharmacists to improve patient care [19].

The name clinical pharmacy describes the work of pharmacists whose main job is to communicate with other healthcare professionals, to meet, interview, interview and assess patients, to follow up specific pharmacotherapeutic recommendations, to monitor and control a patient's response to pharmacotherapy, and to provide drug information. Clinical pharmacists, mainly working in clinics, hospitals, health insurance funds and emergency services. They provide patient-centered services rather than production-centered services. The clinical pharmacist must know the pharmaceutical sciences, medicine, pharmacology, pharmacotherapy, clinical pharmacology, pharmaceutical care, clinical pharmacy and all pharmacy to be treated with rational pharmacotherapy, which includes the cost of minimum economic conditions for achieve maximum therapeutic effect and ultimately patient health and safety of care. Although the number of pharmaceutical industries is increasing around the world, the approach to life-saving drugs is still inadequate in most parts of the universe. The emerging costs of medical services, limited financial sources, a lack of human potential in the health system, an inept, inefficient and

incompetent health sector, a large number of diseases and changes in the technological, social, d emigration, social, political and economic environment. common or different in many countries, countries and regions. Thus, the evolution of the psychological, mental, social, technological, human, political and economic environment has necessitated the transformation and reorganization of health care in the world. Modern therapies are needed at the personal and community level to ensure modern, effective, safe and reliable drug therapy services for patients in extremely difficult situations [20].

Because in parallel with the development of the pharmaceutical infrastructure and the creation of jobs, we are seeing the growing prominence of the pharmaceutical specialties. Most pharmaceutical specialties are clinical pharmacists. For many years, after a successful, helpful and helpful demonstration of clinical pharmacy services, planning, schema and design in Western countries such as Europe, Canada, UK, USA, Japan, Australia, South Africa and New Zealand, and still part of the universe continued to adapt to changing pharmaceutical practices and services. Along with the adoption of these new projects, these regions and states also require transformation and modification of the existing curriculum for pharmaceutical higher education in order to provide the necessary teaching, education, training and training so that future specialists and practitioners in pharmaceutical departments have the required evidence, knowledge, knowledge and knowledge in clinical skills. The impact of these changes was strong enough that even countries that lacked or lacked the development of appropriate health infrastructure and types of training equipment were eager to prepare future pharmacists trained in these intentions [92–94]. Bachelor's degrees in Pharmacy are multi-certified, such as Bachelor of Pharmacy, Master of Pharmacy (Pharm M), and Doctor of Pharmacy (Pharm D) offered to developing countries. In Western countries such as the European Union, Canada, Australia, USA, Japan, South Africa, New Zealand and many developed countries, the profession of a clinical pharmacist is considered to be successful. Further education programs in pharmaceuticals in developing countries differ significantly from similar degree programs offered in Western countries such as the European Union, United Kingdom, Canada, USA, Japan, Australia, Iceland and New Zealand. The main reasons for the differences in Western countries are differences in need, requirements for specialists, pharmaceutical practice and health care system [21-22].

A hospital pharmacy is a specialized area of a pharmacy that is integrated with a medical center. These include centers such as a hospital, polyclinic, narcological hospital, poison control center, and drug information center in a residential facility. This occupation includes the selection, preparation, storage, preparation and distribution of drugs to patients in a medical environment. Another important area is counseling patients and other healthcare professionals on the safe and effective use of drugs. The main task of a hospital pharmacy is to manage the use of drugs in hospitals and other health centers. The goals include the selection, prescribing, purchasing, delivery, administration and validation of drugs to optimize patient outcomes. When using any medication, it is important to ensure that the correct patient, dose, route of administration, timing, medication, information, and documentation are followed. Hospital pharmacists are responsible for preparing many pharmaceutical products for patient use. Some of these formulations must be sterile, for example when administered with total parenteral nutrition (PN) or for other drugs administered intravenously, such as certain antibiotics and chemotherapeutic agents. This process is complex and requires high qualifications on the part of pharmacists in producing quality products in addition to properly equipped premises [23].

In many cases, the clinical pharmacist works directly with patients to help them understand the drugs they are taking and to encourage them to take the drugs as directed; The Clinical Pharmacist manages patient lines, clinical areas, and therapeutic programs; Promotes pharmacy services, direct patient care programs, drug use systems in designated wards and areas of care to ensure that drug use activities meet patient needs, evidence-based best practices and regulatory standards. Develops and implements control measures and restriction / monitoring programs; The clinical pharmacist monitors and evaluates the prescribed pharmacy programs in terms of operational, quality and financial efficiency and regularly compares himself with the best local and national practices; The clinical pharmacist proactively identifies practice issues that need to be assessed and promotes clinical research projects, quality improvement initiatives, or the training of healthcare professionals as needed to advance the practice; Develops and oversees policies and procedures for drug procurement, drug use, drug distribution and drug control; The clinical pharmacist ensures that the pharmacy is an integral part of the health care delivery system and contributes to the improvement and expansion of pharmacy services / programs; Provides direct patient care and clinical practice, including decentralized and service-oriented programs; The clinical pharmacist is well versed in decentralized pharmacy services and clinical pharmacy programs; Works as an active member of a multidisciplinary team and collaborates with healthcare providers in decentralized patient care areas to provide patient-centered care; Identifies high-risk patients and implements measures to improve quality and safety; Makes appropriate, evidence-based, patient-centered drug recommendations; The clinical pharmacist is involved in the management of emergency medical care; Providing a review of medication intake at discharge, approval and counseling as needed; Provides pharmaceutical services throughout the medical center; Owns hospital IT systems and drug ordering systems; Provides accurate, safe, timely and appropriate drug therapy in accordance with the age and needs of the patient; The clinical pharmacist performs critical patient monitoring and reviews the patient profile / chart to identify, prevent, or mitigate drug-related problems, wrong drug or dose selection, sub-therapeutic dose, overdose, drug adverse reactions, drug interactions, drug missing, no indication to treatment, the use of drugs without indications and treatment failure; The clinical pharmacist communicates effectively and appropriately with healthcare providers and caregivers (doctors, nurses, etc.), and ensures the continuity of pharmaceutical care between shifts and between staff; The clinical pharmacist is actively involved in drug management and restriction programs; Participate in the work of pharmacies and distribution of medicines; Clinical Pharmacist maintains competence and actively participates in operations programs, central pharmacies, subsidiary pharmacies and specialty pharmacy areas, as required by the work assignment; Facilitates the process of purchasing, ordering and dispensing specialized drugs, including but not limited to chemotherapy, parenteral nutrition, controlled substances, etc., as appropriate [24-25].

Pharmaceutical care and clinical pharmacology are a professional discipline that combines fundamental pharmacology and clinical medicine. The Clinical Pharmacist offers invaluable support in developing the final prescription with improved patient care and increased safety. Its development began in the early 1950s, largely thanks to the efforts of Harry Gold. The introduction of pharmacists into hospital services began as early as 1957. Pharmacotherapy became more and more complex. The clinical pharmacist has pioneered a new role for pharmacists in hospital services. The role of clinical pharmacists underwent significant changes from the 1960s to the 1990s as their involvement in direct patient care improved. In the early 1970s, federal funding helped significantly expand the clinical pharmacy teaching staff at

pharmacy colleges. Pharmaceutical Education has discussed the place of clinical pharmacy in pharmaceutical education. With clinical pharmacists overwhelmed with patient numbers and the emergence of new drugs, doctors are increasingly turning to pharmacists for drug information, especially in institutions [36-37]. The clinical pharmacist often takes a slightly different approach to drug use and can provide valuable additional information, such as interactions, in the clinician's decision-making process for potential drug changes and monitoring. The concept of pharmaceutical care emphasizes the responsibility of pharmacists to seek the best possible outcomes for patients from a therapeutic regimen. They possess an in-depth knowledge of medicines that is combined with a fundamental understanding of the biomedical, pharmaceutical, socio-behavioral and clinical sciences. Clinical pharmacists follow evidence-based treatment guidelines, advancing science, the latest technology, and appropriate legal, ethical, social, cultural, economic and professional prescriptions to achieve their desired therapeutic goals. Consistently, clinical pharmacists take responsibility and accountability for the management of drug therapy in a direct patient care setting, whether they practice on their own, in consultation, or in collaboration with other healthcare professionals. Their functions include comprehensive drug management (ie, prescribing, monitoring and adjusting drugs), non-drug counseling, and coordination of care. Interdisciplinary collaboration enables pharmacists to provide direct patient care or telecommuting in a variety of clinical settings, including disease management, primary care, or specialty care. A clinical pharmacist can take responsibility for chronic or acute diseases related to the endocrine, cardiovascular, respiratory, gastrointestinal, or other systems. Clinical pharmacist researchers generate, disseminate and apply new knowledge to drive improvement. In the healthcare system, clinical pharmacists are experts in the therapeutic use of drugs. A clinical pharmacist usually provides patients and healthcare professionals with drug treatment reviews and approvals. Clinical pharmacists are the primary source of scientifically reliable / scientifically logical information and advice on the safe, appropriate and economical use of medicines. They obtain a medical history and medication history, check for medication errors including prescribing, dosing and administering errors, identify drug interactions, track adverse reactions, suggest individual dosing regimen, advise patients, etc. They also provide information on medication use. and medical devices such as an inhaler, insulin pen, eye drops, nasal sprays, etc. [26-27].

There are both ethical and practical imperatives to addressing health inequalities associated with chronic disease management for people with social difficulties, and existing programs often do not adequately meet the needs of these people. This leads to low participation rates, suboptimal chronic disease management and higher utilization of health services. Unlike acute conditions, chronic conditions require ongoing care and treatment outside of health care settings, in the community or in primary health care settings in terms of medication use, lifestyle management and behavior change in health. Typically, this is a multi-pronged intervention that includes a review of drug therapy, patient education for treatment, monitoring of medication, immunization, self-care, and support. disease, and / or prescribing authority. Patients who take a lot of medications due to chronic disease are at high risk for drug duplication, interactions, or ADRS, which can lead to longer hospital stays and higher costs. To improve the safety and efficacy of therapeutic agents, these patients must meet special needs for appropriate drug use. Research has shown that integrating pharmacists into outpatient clinics can improve chronic disease management and optimal medication use. Additionally, involving a pharmacist in patient care can help reduce inappropriate medication use, especially in the elderly. The study shows that the

proportion of patients receiving the wrong drug drops considerably after review and optimization of the drug by a team including a pharmacist. Compared to conventional treatment, pharmacist-directed care was associated with a similar frequency or frequency of office visits, emergency room or emergency department visits, as well as hospitalizations and adherence, increases in the amount or dose of drugs received and improvements in study glycemic choices, blood pressure, and lipid target achievement. Another recent study shows that a telemedicine-based chronic disease management program involving clinical pharmacists resulted in statistically significant improvements in diabetes and hypertension outcomes as well as clinically significant improvements in lipid control and withdrawal smoking [28-29].

The practice of the pharmacy has changed a lot in recent years. Professionals can directly contribute to patient care to reduce drug-related deaths, promote health and prevent disease. Medical organizations around the world are under tremendous pressure from the growing demand for patients. Unfortunately, cure is not always possible, especially in this era of chronic disease, and the role of doctors is limited to controlling and relieving symptoms. The growing number of patients with chronic conditions is associated with high morbidity, health care costs and the burden on physicians. The clinical pharmacy took over the medical care, which the doctors partly refused. Overwhelmed by the number of patients and the emergence of new drugs, doctors are increasingly turning to pharmacists for information about drugs, especially in institutions. After the pharmacists were transferred to the counting and dispensing of drugs, they carried out institutional reviews of drug use and acted as consultants for all types of healthcare facilities. In addition, when clinical pharmacists are active members of the healthcare team, they increase efficiency by: Providing the necessary feedback on drug use and dosage. Work with patients to resolve medication problems and improve adherence [30-31].

Clinical care team in the form of health professionals - physicians, advanced practice registered nurses, other registered nurses, medical assistants, clinical pharmacists and other health professionals - with the training and skills to provide coordinated care high quality, specific to the patient's clinical condition ... needs and circumstances. The clinical pharmacist also provides support for group practice. Although the composition of the teams may vary, the responsibility and authority for specific aspects of the treatment rests best with the person best suited to the task. The effectiveness of a team of clinical pharmacists depends on a culture of trust, shared goals, effective communication and mutual respect. The best interests of the patient should be the driving force behind teamwork. The clinical pharmacist does not need to be in the same place as a member of the medical team and therefore the large group of health professionals certainly includes general practitioners in hospitals, clinics and stores. Although this is only an example, patients benefit from collective management through better BP control, and a large proportion of patients achieved controlled BP when the pharmacist was part of the clinic. the team. The composition of dynamic clinical teams is reflected in the multidisciplinary nature of large professional organizations such as the Society for Resuscitation, the Society for Hospital Medicine, the Nutrition Society, and the Society for Neurocritical Physicians. Most of these organizations include clinical pharmacists in leadership positions, including the chair [32-33]

Pharmacists in the Netherlands have significantly reduced prescribing errors and patient-related harm while on the ward compared to basic central pharmacy services. Children's pharmacists in China have shown significant reductions in adverse drug reactions, length of hospital stay, and drug costs compared to a control group of similar patients without a pharmacist. While these are just a few examples, pharmacists around the world, including in Chile, offer patient-centered

services. Clinical pharmacy is gaining popularity, and some universities offer training programs for pharmacists to become specialists in clinical pharmacy and pharmaceutical services, which is more focused on patients and medical personnel and differs from the academic degree of the Master of Pharmaceutical Sciences or PhD in Pharmacology [34-35].

The statements have been developed to define the core competencies of pharmacists in a number of countries, as well as the International Pharmaceutical Federation. The Pharmacist Training Proposal for Basic Pharmacist Education and Skills includes provisions that are applicable to clinical pharmacists, in particular for documenting patient information and drug therapy management and follow-up. The skills of clinical pharmacists or advanced and specialized practitioners were also described and summarized. Although in many countries the clinical pharmacist has not compiled a uniform list of competencies for medical practitioners, the statement describes a general framework and training criteria for hospital pharmacists who have completed residency training, which form the basis of the knowledge and skills expected from the medical practitioner and also for clinical pharmacists. ... Intensive care pharmacists have developed a peer review process and career program that has resulted in the accreditation of an increasing number of medical practitioners. Referral support, interviews, thematic discussions and peer reviews have been incorporated into this rigorous process that serves as a model for other specialized practices [19-20].

The health systems of many other countries have developed similar claims of competence for pharmacists. As a critical care pharmacy specialist, it is difficult to describe a typical day, but usually busy with the elements of a pharmacist's support process during the day. It is believed that the clinical pharmacist will be responsible for all aspects of the administration of the drug. Every day, the clinical pharmacist assesses and evaluates new patients and updates the progress of previous patients, identifies drug-related issues and potential problems, develops a problem list and treatment plan for optimal dosage based on the renal and hepatic function, potential drug interactions and serum concentration. The clinical pharmacist joins the multidisciplinary rounds with the intensive care team and applies the treatment plan by teaching the medical residents the correct order of entry or by entering the orders themselves according to a collaborative practice agreement and by them. documenting in an electronic health record. A major contribution to medication management is identifying therapies that are no longer needed, reducing the cost and risk of adverse events, and supporting antimicrobial stewardship programs with infectious disease physicians and pharmacists. The clinical pharmacist also supervises the performance of quality measures such as the appropriate prevention of venous thromboembolism, the appropriate use of drugs to prevent stress gastritis, the addition of aspirin to increase the levels of troponin associated with l coronary ischemia, and discussing the need for central tubing and urinary catheters. The clinical pharmacist educates the team on drug-related topics and related literature through tours and didactic discussions. A clinical pharmacist is always available for emergencies and resuscitation, and to answer questions related to mediation [21-22].

For each new patient, a member of the pharmacy team compiles a medication history from electronic records, family, patient, local doctors or pharmacies and documents it in the EMR. The clinical pharmacist will then cross-check this list to determine medication-related reasons for hospitalization, such as non-adherence or overdose, and advise on which medications to choose to avoid withdrawal reactions or other adverse events. While the clinical pharmacist has a more limited role in verifying drug orders in the EMR and has little role in the actual distribution of drugs, the clinical pharmacist serves as a liaison with technicians and pharmacists specializing in

parenteral products and drugs. Distribution systems to ensure medications are present when needed. Nurses have a formidable task of prescribing drugs, and the clinical pharmacist facilitates this process by providing information on intravenous injection compatibility and teaching unknown treatments [23-24].

Other aspects of my role include developing quality assessment tools and data evaluation. EMR is made more efficient by properly designing control systems that are effective and make it easier to make quality measurements and select preferred treatments. Clinical pharmacists make important contributions to these drug therapy control and surveillance systems. They also report the side effects of medications. Many side effects or incidents are related to systemic problems, and the clinical pharmacist regularly provides advice on possible process improvements when programming intravenous pumps, drug safety systems, or other processes [25].

Hospital pharmacists are drug experts who work in multidisciplinary medical teams to manage drug use in hospitals. Hospital clinical pharmacists are integrated into services and departments and provide clinical pharmacy services to patients at the bedside, with each clinical pharmacist (or team) being responsible for patient care in a specific medical ward or department. Hospital pharmacists provide clinical pharmacy services to patients hospitalized at the bedside as well as in other clinical areas such as emergency departments and outpatient clinics, as well as physicians and nurses. Most of them work in hospitals, however, innovations in the practice of hospital pharmacy have led pharmacists to work in community health services, nursing homes, rehabilitation centers and medical clinics. general. Roles may vary depending on the organization and clinical needs of the hospital pharmacy. Most hospital pharmacists provide clinical services in their area of specialization; however, they can apply their skills to other roles including pharmacy managers, purchasing managers, hospital pharmacy consultants. Educational roles are also prevalent, such as giving lectures to pre-registered trainees, making presentations to other medical staff, or providing educational support to pharmacy students [26].

Clinical pharmacists play a key role in drug delivery and patient health monitoring in various healthcare settings. They dispense prescribed medicines to patients and help doctors and other healthcare professionals with medicines. Their responsibilities include helping diagnose, selecting appropriate drugs, monitoring patients' health, checking for side effects of drugs, etc., making appropriate vaccinations, etc. Since these specialists are experts in the clinical effects and composition of drugs, including their chemical, biological and physical properties, they protect the health of the population, ensuring the purity of drugs and the correct dosage of drugs. They use special protective equipment such as masks, gloves, etc. when handling sterile or potentially hazardous pharmaceuticals. Clinical pharmacists work in a variety of environments such as hospitals, clinics, nursing homes, community health centers, pharmacies, pharmacies, etc. They work full time. They may need to work evenings, nights, weekends and holidays [27].

The European Association of Clinical Pharmacy defines that as the health specialty that characterizes the activities of clinical pharmacists and the provision of health services, clinical pharmacists promote and develop rational and appropriate pharmacotherapy, the rational use of pharmaceutical manufacturing and medical devices. Although the American College of Clinical Pharmacy abbreviated it describes and reports that clinical pharmacy is a problem area of modern pharmacy with the knowledge, evidence and practical skills of rational drug therapy using drugs. The practice of clinical pharmacy includes knowledge of pharmacotherapy, pharmaceutical care and first aid; it combines leadership in health care with specific therapeutic knowledge, understanding, cognition, learned habits and assessment to ensure rational and optimal treatment

outcomes for patients. Pharmaceutical care and clinical pharmacy are closely related concepts, although there are differences between professional development structures that determine specificity. For example, the British Clinical Pharmacy Association states that clinical pharmacy includes the theoretical knowledge and understanding, practical skills, values and attitudes needed by pharmacists to promote healthcare and pharmaceutical services to individual patients and populations [28].

Conclusions

Clinical pharmacists are people who help patients recover from illness or lead healthy lives. The doctor diagnoses and prescribes medications in general terms, but the clinical pharmacist helps make specific decisions. For example, if a patient has an adverse reaction to a particular drug, the clinical pharmacist will recommend alternative treatments. The clinical pharmacist will also help select the best drug combinations for the patient's condition. A clinical pharmacist is trained to work directly with patients in a healthcare system such as hospitals or clinics. Because the clinical pharmacist has detailed knowledge of drugs and their effects, and because the clinical pharmacist has extensive experience with patients, physicians often give clinical pharmacists significant control over prescribing drugs and monitoring patients. Among other things, clinical pharmacists are responsible for selecting the right drugs, monitoring patients, diagnosing potentially untreated illnesses, consulting with the patient about the effects of drugs, and ensuring patients adhere to prescribed drug regimens.

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THE SCIENTIFIC STUDY OF THE PECULIARITIES OF UROTENSIN-2 RECEPTOR ANTAGONIST: PHARMACOLOGICAL EFFECTS OF PALOSURAN ON PLASMA RENIN CONCENTRATION AND BLOOD PRESSURE IN LABORATORY RATS WITH RENO-VASCULAR HYPERTENSION

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ABSTRACT

Our aim is to investigate the effect of palosuran, an antagonist of urotensin-2 receptors, on blood pressure and plasma rennin concentration in laboratory rats with renovascular hypertension (2 kidneys + 1 clamp). Blood pressure was measured using the non-invasive tail-cuff method. Studies have shown that palosuran (10 mg/kg/day for 4 weeks) has an antihypertensive effect in test rats. The blood pressure also decreased after administration of the NO synthase inhibitor L-NAME (10 mg/kg, single dose), presumably due to its antagonistic properties against urotensin-2 receptors. In hypertensive rats, the renin concentration in the blood plasma increased progressively compared to the data from healthy rats. Renin concentrations were significantly lower in hypertensive rats treated with palosuran than in hypertensive rats that received no treatment. The decrease in renin concentration persisted after administration of L-NAME, with the exception of late initiation of treatment. From this it can be concluded that in experimental rats with renovascular hypertension the vasodilation effect of palosuran outweighs the inhibitory effect of L-NAME on NO production and the endothelium-independent vasoconstrictive effect induced by urotensin, especially in the early stages and at the beginning of hypertension treatment. Palosuran could represent a new therapeutic option for people with essential hypertension.

Keywords: Urotensin-II receptors, antagonist**,** renin, palosuran, L-NAME, renovascular hypertension.

Introduction

It has been known that the urotensin system plays an important role in the pathophysiology of high blood pressure. Urotensin II, as the strongest known vasoconstrictor in mammals [1,2], is activated in high blood pressure. Plasma urotensin II was increased in hypertensive patients compared to normal blood pressure controls and was directly related to systolic blood pressure. These data increase the likelihood that Urotensin II (U-II) could play an etiological role in hypertension and its complications [3,4]. High blood pressure is a serious condition that significantly increases your risk of heart, brain, kidney, and other diseases. Today, high blood pressure is considered to be the most common cause of cardiovascular diseases worldwide. An estimated 1.13 billion people worldwide have high blood pressure, most (two-thirds) of whom live in low- and middle-income countries [5,6]. Despite the effectiveness of currently available antihypertensive drugs, there is always a need for new treatment strategies that are more effective in certain groups of hypertensive patients [7,8].

U - II is a cyclic oligopeptide with vasoactive potential. By activating the urotensin II receptor (UTR), U-II could influence different signaling pathways depending on the cell and vascular compartment in which the receptor is located [9,10]. The interaction between U-II and UT leads to the activation of phospholipase C and the release of inositol (1,4,5) triphosphate [Ins (1,4,5) P3]. Interact with Ins (1,4,5) P3a receptor located in the endoplasmic / sarcoplasmic reticulum for the release of Ca^{2+} from intracellular deposits, leading totissue-dependent reaction [11,12,13]. In the cardiovascular system, yesthe receptor is located in the cardiomyocytes, increasedContractility is expected. In the vascular system,Constrictor and expander responses were re-recorded.the receptor is located on a vascular or smooth muscle cellEndothelium or endothelial activationNitric oxide synthase Ca2-dependent increaseNitric oxide, which penetrates the blood vessels gently [14,15]. Vasodilation muscle. In contrast to most transport moleculesthe binding of U-II to its receptor is essentially irreversible;this has been reported for recombinants and native UT [16,17]. This restrictive irreversibility is probably related toin the presence of a highly conserved cyclic hexapeptideBasic[18]. The irreversibility of the link has important consequencesfor regulating receiver-controlled signals. Under "normal"Under certain conditions it is likely that the receptor peptide systemfunctionally noiseless[19,20,21].

U-II has been shown to act as a vasodilator: this effect was endothelial-dependent, suggesting that vasodilation is mediated via UTR on the endothelium, while vasoconstriction is mediated via UTR on smooth muscle cells. Activation of the endothelial UTR leads to relaxation via NO formation, while activation of UTR on vascular smooth muscle cells leads to contraction via RhoA/Rho kinase activation [22,23,24].

U-II also plays a role in the regulation of body fluids in lower vertebrates, and this is now being found to extend to mammals as well. The kidneys appear to be the main source of U-II synthesis in mammals. U-II is found in both the proximal tubules and the collecting ducts. UTR is mainly localized in the renal medulla with the greatest expression in the collecting ducts of the internal medulla [25,26].

The goals of antihypertensive therapy are to prevent the occurrence / progression / recurrence of cardiovascular disease associated with persistent hypertension, reduce mortality, and help hypertensive patients lead healthy normal lives [27]. Prescribing antihypertensive drugs to achieve the recommended blood pressure goal remains the most important step in the management of high blood pressure patients [28]. Drugs that target blood pressure must be well tolerated, affordable, and easy to take to promote long-term persistence [29,30].

Administration of palosuran to rats that received streptozotocin improved survival, increased insulin levels and decreased the progression of kidney damage [31,32]. In a rat model of diabetes, treatment with palosuran increased kidney blood flow and delayed the development of proteinuria and kidney damage. Similar effects were not seen in preliminary studies in patients with diabetic nephropathy, but more studies are being conducted to refine the dosage regimen to improve the outcome [33,34]. Recent studies on the therapeutic potential of UTR antagonists have shown that UTR in the kidneys influences sodium and water excretion as well as the glomerular filtration rate [35,36]; U-II can act as a chronic regulator of basal vascular tone rather than in the short term. The term "vascular resistance regulator" has yet to be fully understood, but it is likely that they will find clinical use in the treatment of high blood pressure, heart failure and kidney disease [37,38].

Our experiments showed the antihypertensive potential of palosuran in laboratory rats with renovascularhypertension, which can be explained by its direct effect on UTR, and we thought it would be interesting to investigate the effect of palosuran on serum electrolytes, which play an important role in blood pressure regulation [39]. When treatment was started relatively late, the antihypertensive effect of palosuran was less pronounced. The damaging effect of high blood pressure on blood vessels is said to increase the production of U-II and enhance the endothelial-independent vasoconstrictor effect of U-II [40].

Arterial hypertension is a serious condition that can increase your risk of heart, brain, kidney, and other diseases. About 26% of the population die from arterial hypertension each year. It is the leading cause of premature death worldwide. An overview of current trends shows that the number of adults with high blood pressure rose from 594 million in 1975 to 1.13 billion in 2015. According to WHO estimates, 54% of strokes and 47% of coronary heart disease are a direct consequence of high blood pressure, which is one of the main risk factors for cardiovascular morbidity and mortality [41,42,43].

The goals of antihypertensive treatment are to prevent the onset/progression/recurrence of cardiovascular disease associated with persistent high blood pressure, reduce mortality, and help high blood pressure patients lead a normal life like healthy people [44]. Prescribing antihypertensive drugs to achieve the recommended target blood pressure remains the most important step in the management of patients with high blood pressure. Medicines targeting blood pressure must be well-tolerated, economically available, and easy to take in order to maintain long-term resistance [45,46].

A number of reports indicate the involvement of U-II in the conservation of water, sodium and chloride [47,48] in fish species. Studies have shown that inhibition of UTR activity by the antagonist urantide leads to increased GFR, dieresis and natriuresis, suggesting that endogenous U-II has a tonic effect on basal renal function. Altered expression of U-II in disease states has prompted the development of a number of UTR antagonists [49].

The strongest UTR antagonist is palosuran (a 4-ureido-quinoline derivative, ACT-058362) [15] [16]. Palosuran is selective for human UTR. The use of these and other compounds in various models of disease has shown that UT antagonism has potential therapeutic benefits. Palosuran improves kidney function in rodents and diabetics [50]. However, the potential therapeutic potential of palosuran in the treatment of high blood pressure and its complications has not been investigated [51].

High blood pressure is a serious medical condition that greatly increases the risk of heart, brain, kidney and other diseases. Today, hypertension is considered the leading cause of cardiovascular

disease worldwide. An estimated 1.13 billion people worldwide have high blood pressure, most of whom (two-thirds) live in low- and middle-income countries.

Despite the effectiveness of currently available antihypertensive drugs, there is still a need for new, more effective treatment strategies, especially in hypertensive patient populations [52,53]. The urotensin system is believed to play an important role in the pathophysiology of hypertension. Urotensin II, as the most powerful known vasoconstrictor in mammals [54], is activated in hypertension. Plasma urotensin II was elevated in hypertensive patients compared with normal blood pressure controls and was directly related to systolic blood pressure. These results suggest the possibility that urotensin II (U - II) may play an etiological role in hypertension and its complications [55,56].

Palosuran is a promising non-peptide UTR antagonist designed to inhibit U-II calcium accumulation and mitogen-activated protein kinase phosphorylation. There are few published data on the use of palosuran in patients with hypertension and they are mutually exclusive [57,58]. In rat models of acute kidney failure and diabetes, pallosuran significantly improved renal function, reduced tubular and tubulointerstitial lesions, and improved survival [59,60].

Based on the above, it is interesting to study the effect of the urotensin receptor antagonist - pallosurane - on blood pressure in laboratory rats with experimental hypertension.

In recent years, the interest of researchers and scientists in the cyclic vasoactive neuropeptide urotensin-2 has increased significantly. The role of the UII system in human pathophysiology is not yet fully understood. Urotensin-II (U-II) occurs as a regulator of vascular tone in the cardiovascular and central nervous system, in the kidneys, in the lungs, in the liver, in the ovaries, in the endocrine glands and is involved in many physiological and pathological processes [61,62]. Circulating blood levels of human UR-II, the strongest vasoconstrictor peptide identified to date, are elevated in hypertensive patients. U-II binds to the U receptor, activates the Gq protein, and induces the activation of the inositol triphosphate cycle by activating phospholipase C. U-II is a more powerful vasoconstrictor than endothelin-1, vasopressin, and prostaglandins, which constrict blood vessels. U-II acts as an endothelium-independent vasoconstrictor and endothelium-dependent vasodilator [63,64].

Vasoconstriction is mediated by smooth muscle cell receptors (SMC) and appears to be variable and strongly dependent on the vascular bed, while vasodilation is mediated by endothelium [65]. However, in a painful state of chronic heart failure or hypertension, U-II loses its ability to expand [66]. It goes without saying that such a loss and such dysfunction of endothelial cells will promote a contractile response rather than a relaxing one [67,68].

Elevated U-II levels and overexpression of urotensin receptors (UTRs), which have been demonstrated in high blood pressure, heart failure, diabetes, portal hypertension, and renal failure, suggest that the U-II / UTR system may play a critical role in the development of these diseases. [20], [21]. In this regard, the study of UTR antagonists appears to be interesting and promising for the treatment of high blood pressure and other comorbidities of high blood pressure [69,70].

This study was designed to assess the effect of the urotensin-2 receptor antagonist - Palosuran on blood pressure and serum electrolytes in laboratory rats with renovascular hypertension (2 kidneys + 1 clip) and determine possible changes in sodium, potassium, calcium levels [71,72].

Studies have shown that Palosuran decreases mean arterial pressure in rats with renovascular hypertension. The vasodilating effect of palosuran exceeds the inhibitory effect of L-NAME on NO and the urotensin-induced endothelium-independent vasoconstrictive effect, especially in the early stages of hypertension. The antihypertensive effect of Palosuran was less manifested in the

case of relatively late onset of treatment. Supposedly, the damaging effects of hypertension on blood vessels increase the production of U-II and enhance the endothelium-independent vasoconstrictive effect of urotensin [73,74,75].

There are currently four main classes of antihypertensive drugs available: diuretics, calcium channel blockers, renin-angiotensin system (RAS) blockers, and beta-blockers. Despite their ability to lower blood pressure, significantly improve patient long-term prognosis, and reduce cardiovascular outcomes, it is important to consider the tolerability profile of antihypertensive drugs, as tolerability is a key factor in long-term adherence and side effects. For example, diuretics/thiazides can cause hyponatremia, hypokalemia, hyperuricemia, high cholesterol and LDL cholesterol, serum creatinine/urea and risk of diabetes. Patients may experience weakness, muscle cramps, impotence, and gout attacks. Anti-aldosterone diuretics can cause dizziness, drowsiness, allergic reactions, sexual dysfunction, nausea, vomiting, and hyperkalemia. ACE inhibitors cause persistent dry cough, angioedema, dry mouth, nausea, rash, hyperkalemia, increased serum creatinine levels. Hyperkalemia, elevated serum creatinine, nausea, dry mouth, abdominal pain are common manifestations of angiotensin receptor blockers. Calcium antagonists/dihydropyridines cause peripheral edema, headache, redness, palpitations, constipation, nausea and gingival hyperplasia. Beta-blockers increase the risk of diabetes, increase triglycerides, lower HDL cholesterol, worsen asthma, cause fatigue, insomnia, nightmares, decreased exercise, rash, and weight gain [76,77,78]. Thus we can say that the problem of the effective treatment of arterial hypertension has not lost its relevance and its solution in a given clinical situation often remains very difficult [79,80,81].

The results obtained showed a significant difference between hypertensive and nonhypertensive healthy rats for blood electrolytes. At the early stage of disease modeling, Palosuran significantly decreased serum Na + and increased K+ concentrations in hypertensive rats. Na+ and K+ concentrations were maintained within the normal range even after administration of L-NAME, except during the late-onset of treatment. Palosuran might represent a new therapeutic option in individuals with hypertension disease at early Palosuran is a non-peptide UTR antagonist with promise in drug development has been developed to inhibit the accumulation of calcium by U-II and the phosphorylation of mitogen-activated protein kinase. Data in the literature on the use of palosuran in hypertensive individuals are scarce and mutually exclusive [22,23,24,25]. In rat models of acute renal failure and diabetes, palosuran significantly improved renal function, decreased the number of tubular and tubulointerstitial lesions and improved survival [26]. Based on all of the above, it is interesting to study the effect of the urotensin receptor antagonist - Palosuran on blood pressure in laboratory rats with experimental arterial hypertension.

Materials and methods

The study was carried out on male Wistar rats weighing 200-250 g after an adaptation period of at least 1 week. All rats were housed in a laboratory with eight people per cage under controlled climatic conditions with a 12-hour light-dark cycle and free access to regularly pelleted rat food and drinking water. The protocol used in this study for the use of rats as an animal model for the study was monitored and approved by the Ethics Committee on Animal Welfare and Use of the Tbilisi State Medical University (N39 - 08/17/2019).

For experimental modeling of hypertension, we used the Reno-vascular (the two-kidney, one-clip - 2K1C) H. Goldblatt model [27,28,29]. Under general anesthesia (Nembutal - 50 mg/kg), after

separation of the renal artery from the vein and nerve, the silver clip (0.2 mm internal diameter) was placed on the left renal artery close to the aorta.

The experimental animals were divided into 3 groups: Group I - healthy, intact rats; Group II - hypertensive rats; Group III - hypertensive rats, subjected to treatment with palosuran, started after 4 weeks of disease modeling; Group IV - hypertensive rats, subjected to treatment with palosuran, started after 8 weeks of disease modeling. Palosuran was injected intraperitoneally with the dose of 10 mg/kg, daily, for 4 weeks.

In the group's II and III rats, NO-synthase inhibitor - L-NAME (10 mg/kg, single dose) was administered intraperitoneally also after the completion of the treatment with palosuran.

Systemic arterial pressure (systolic pressure, diastolic pressure) was measured once a week for 12 weeks using arterial pressure measurement system "Систола" (non-invasive tail-cuff method for BP measurement). The mean arterial pressure was calculated. Plasma renin concentration was determined using ELISA (HumaStar HS).

All statistical tests were conducted using IBM SPSS Statistics. Differences between control and treated animals were determined by using the Independent-Samples T-test. The criterion for significance was set to $P < 0.05$.

Results and discussion

Changes in mean arterial pressure (MAP) compared with MAP in animals of the 1st group (healthy rats) were found in experimental rats at various stages of renovascular hypertension.

The results of the experiment (Table N1, N2) showed that after 1 week of modeling of the disease, SBP did not increase significantly, after 2 weeks SBP increased by 24% ($p < 0.05$), after 4 weeks SBP increased by 42%. ($p < 0.02$), after 8 weeks there was a significant increase in MAP by 44% ($p < 0.02$), and after 12 weeks of modeling the MAP disease was 53% ($p < 0.001$) compared to the MAP of the group of 1 animal;

In healthy rats, after the administration of palosuran, SBP decreased by 33% ($p < 0.02$). Against the background of palosuran, after L-NAME injection, there was an increase in MAP by 23% compared to rats receiving palosuran, and a statistically insignificant decrease in MAP by 17% compared to the data for healthy rats.

In hypertensive rats after starting treatment with palosuran at week 4 of illness, MAP was modeled at week 8 of hypertension, decreasing by 32% ($p < 0.001$) compared to untreated hypertensive control rats.

Against the background of palosuran, L-NAME showed a trend towards MAP 18% higher compared with rats receiving palosuran, and a statistically significant decrease in MAP by 20% ($p < 0.02$) compared with MAP of animals of group I.

In rats with high blood pressure, after starting treatment with palosuran at 8 weeks of illness, following the example of 12 weeks of high blood pressure, palosuran showed relatively less effect on SBP than with earlier treatment. However, SBP was still significantly reduced by 23% ($p < 0.02$) compared to the control group (untreated hypertensive rats).

After the administration of L-NAME against the background of palosuran, an increase in MAP of 16% was observed compared with rats receiving palosuran, and, compared with untreated rats, a decrease in MAP of 10% was also not statistically significant.

As the results of the study have shown, there is a progressive rise in serum Na^+ and a decrease in K^+ concentrations compared to the data of healthy rats due to a significant relationship between electrolyte levels and blood pressure [22,23]. Notably, serum total sodium was consistently and

significantly higher in hypertensive groups than in the non-hypertensive, healthy animal group, while, serum potassium was lower.

The increase in serum Na+ at renovascular hypertension develops as a result of renal artery ischemia and activation of RAAS leading to increased sodium reabsorption. By the 8th week of hypertension, the slight decrease in serum Na+ level could be explained as a compensatory reaction of kidneys. In the first, one-clip two-kidney Goldblatt hypertension, the ischemic kidney secretes renin, which leads to increased angiotensin II formation and hence elevation of blood pressure. As blood pressure rises, sodium excretion by the intact contralateral kidney increases (pressure natriuresis), therefore, there is no sodium retention.

Decreased level of serum potassium level revealed in our experimental studies at the late stage of the hypertensive disease could be explained by the sodium and potassium reciprocal relationship in the kidneys. Potassium levels often change with sodium levels. When sodium levels go up, potassium levels go down, and when sodium levels go down, potassium levels go up. Potassium levels are also affected by a hormone called aldosterone. In the case of kidney hypoxia and activated RAAS system the hormone aldosterone acting on the distal tubules triggers potassium excretion and resorption of sodium.

In carried out investigations we could not establish any significant differences in the serum mean levels of calcium between the healthy, control and treated group animals. It is possible that intracellular calcium levels may be more important in systemic hypertension than serum calcium levels, which was not measured in our study. Anumber of experimental studies suggest that intracellular Ca^{2+} concentration is abnormally increased in vascular myocytes from hypertensive animals [24] and calcium intakemay affect blood pressure by increasing intracellular calcium in vascular smooth muscle cells leading to vasoconstriction, and by increasing vascular volume through the renin-angiotensin-aldosterone system (RAAS).

Treatment with Palosuran decreased serum Na+ and increased K+ levels in rats with renovascular hypertension at an early stage of hypertension. Na+ concentration in hypertensive rats' correlates with the results of mean arterial pressure at different stages of hypertension. Although Palosuran reveals a hypotensive effect and maintains serum Na+ concentration within the normal range, at late stages of hypertension and relatively letter onset of the treatment effect of Palosuran on electrolytes was not statistically significant.

As the results of the study have shown, 1 week after hypertension modeling, only a tendency for an increase in MAP was observed, while a statistically significant increase in blood pressure was created after 2 weeks of disease modeling. After 4 weeks, a progressive increase in blood pressure was reliable and statistically significant.

The increase in blood pressure at renovascular hypertension, first of all, develops due to the renal artery ischemia in the clipped kidney leading to hypoxia, activation of the renin-angiotensin-aldosterone system (RAAS), total peripheral vasoconstriction and water retention.

3 weeks after modeling of hypertension, reduction in MAP could be explained by the compensatory reaction of the second, intact kidney, decreasing renin production and inhibiting the RAAS system to restore homeostasis. However, on the 4 weeks of renovascular hypertension, the compensatory reaction of the intact kidney fades away, the pressure regulatory system is unable to maintain the blood pressure within the normal range and it increases significantly. At this stage of hypertension, increased blood pressure and MAP manifested in experimental animals supposedly are caused due to the complex action of RAAS and activated sympathetic nervous system. The latter results in a further increase in renin production and peripheral vasoconstriction.

After treatment with palosuran, the blood pressure significantly was decreased in all study groups. The antihypertensive effect of palosuran was demonstrated in both cases, at early treatment (started after 4 weeks of renovascular hypertension modeling) and at relatively late treatment (started after 8 weeks of hypertension modeling) of hypertensive rats.

Palosuran is known to have an antagonistic effect on U-II receptors, thereby reducing the vasoconstrictive effect of U-II. According to the literature, U-II in small doses induces the active production of NO (by activating NO-synthase) and consequently, the dilation of blood vessels as an endothelium-dependent vasodilator. This phenomenon can explain the decline in MAP in all study groups of experimental animals [30].

After administration of L-NAME, there was not a statistically significant increase in MAP compared to animals treated with palosuran, while MAP was decreased compared to control, untreated hypertensive rats, but this decrease was statistically significant only in the group of rats, where treatment was started earlier.

Table N1. Mean arterial pressure (MAP) in healthy and hypertensive rats after treatment with Palosuran and L-NAME injections at different stages of renovascular hypertension.

N	Groups	Mean Arterial Pressure – MAP (mm/Hg)		
		Before treatment	Palosuran	Palosuran + L-NAME
1	Healthy rats	95 ±3,1	64±3,0**	79± 2,5
2	1 week after modeling hypertension	97±3,5	-	-
3	2 weeks after modeling hypertension	118±4,1*	-	-
4	3 weeks after modeling hypertension	101 ±9,2	-	-
5	4 weeks after modeling of hypertension	135 ± 10,0**	-	-
6	8 weeks after modeling of hypertension	137± 8,3**	93 ± 5,5***	110± 8,2**
7	12weeks after modeling of hypertension	145 ± 10,0***	112± 7,2**	130±9,5

*- p<0.05; **- p<0.01; ***- p<0.001

Table N2. Effects of Palosuran and L-NAME on serum electrolytes (mmol/L) in healthy and hypertensive rats at different stages of hypertension.

	Groups	Without treatment			+ Palosuran			Palosuran + L-NAME		
		Na^+	K^+	Ca^{++}	Na^+	K^+	Ca^{++}	Na^+	K^+	Ca^{++}
1	Healthy rats	145,2	4,5	9,2	137,0	4,9	9,24	139,1	5,0	9,25
2	4th week of hypertension	169,1**	4,1	9,0	-	-	-	-	-	-

3	8th week of hypertension	165,0**	4,3	9,1	144,1**	4,88*	9,25	149,0*	4,6	9,22
4	12th week of hypertension	188,1***	3,0**	9,22	175,3	3,2	9,22	179,1	3,1	9,24

*-p<0.05; **- p<0.01; ***-p<0.001

Table 3. Systolic and diastolic blood pressure in healthy and hypertensive rats after treatment with Palosuran and L-NAME injections at different stages of renovascular hypertension.

N	Groups		Systemic Blood Pressure (mm/Hg)		
			Without treatment	Palosuran	Palosuran + L-NAME
1	Healthy rats	Systole	110 ± 3,4	81 ± 4,1**	98± 3,2
		Diastole	87± 4,8	55 ± 3,1**	69± 4,2*
2	1 week after hypertension modeling	Systole	114± 4,1	-	-
		Diastole	91± 4,5	-	-
3	2 weeks after hypertension modeling	Systole	159 ± 2,7**	-	-
		Diastole	98 ± 4,2*	-	-
4	3 weeks after hypertension modeling	Systole	117± 5,7	-	-
		Diastole	93 ± 4,5	-	-
5	4 weeks after hypertension modeling	Systole	185 ± 9,3**	-	-
		Diastole	110 ± 5,4**	-	-
6	Treatment started after 4 weeks of hypertension modeling - 8th week	Systole	192 ± 9,3**	134 ± 5,7***	143 ±11,3**
		Diastole	110 ± 5,4**	72 ± 3,1**	94± 4,3**
7	Treatment started after 8 weeks of hypertension modeling - 12th week	Systole	205 ±10,1***	149± 8,1**	181± 10,7
		Diastole	115 ±7,1***	94± 5,2**	104± 6,1

*- p<0.02; **- p<0.01; ***- p<0.001

Table N4 Plasma Renin concentration (PR) in healthy and hypertensive rats at different stages of hypertension after treatment with palosuran and injections of L-NAME.

N	Groups	Renin – PR (ng / ml)		
		Before treatment	+ Palosuran	Palosuran + L-NAME
1	Healthy rats	1,72 ± 0,5	1,52 ±0,3	1,65 ±0,4
2	1 week after hypertension modeling	1,79 ± 0,3	-	-
3	2 weeks after hypertension modeling	2,49± 0,4**	-	-
4	3 weeks after hypertension modeling	2,45 ± 1,3**	-	-
5	4 weeks after hypertension modeling	1,94 ± 0,1	-	-
6	8 weeks after hypertension modeling	4,5 ± 1,4***	3,02 ± 0,9**	3,32 ± 0,5*
7	12 weeks after hypertension modeling	5,75 ± 1,5***	4,39 ±1,5**	5,71 ±1,2

* – $p < 0,05$, ** – $p < 0,01$, *** – $p < 0,001$

In healthy rats after administration of Palosurandecrease in serum Na^+ by 6,5% was not statistically significant. The same, unreliable alterations in Na^+ concentrations were detected in rats treated with Palosuran after administration of L-NAME. Serum Na^+ was increased by 1,5% and compared with the results of untreated rats' serum Na^+ was decreased by 4,1% ($p>0,05$).
After 4^{th}, 8^{th} and 12^{th} weeks of disease modeling in hypertensive rats there was progressive and reliable rise in serum Na^+ by 17%, 14% ($p<0.01$) and 30% ($p<0,001$) compared to the data of healthy rats. Although, after 8 weeks of disease modelling serum Na^+ was increased by 14% ($p <0.001$), it was lesser by 3% compared to the data obtained by 4^{th} weeks of disease modelling.
After administration of L-NAME, as a NO-synthase inhibitor, a significant increase in blood pressure was expected compared to the data of the control group animals. But, experiments revealed just the opposite reaction in palosuran-treated rats, especially in the case of the early-onset of treatment. This may be explained by the fact that palosuran inhibiting the effect of urotensin is likely increased NO production thereby inhibiting the vasoconstrictive effect of L-NAME.
In the case of treatment started relatively later, the antihypertensive effect of palosuran was less manifested. We suppose that the damaging effects of hypertension on blood vessels increase the production of U-II and enhance the endothelium-independent vasoconstrictive effect of urotensin [31].
In experimental rats, the plasma rennin concentration (PR) at different stages of modeling of renovascular hypertension was changed compared to the norm (tab N3). In particular, after 1 week of disease modeling, there was a tendency of increase in PR by 4%; On 2nd week, PR was

increased significantly by 45% ($p < 0.01$); In the 3rd week of hypertension increase in PR was relatively less - 42% ($p < 0.01$). By the 4th week, PR decreased and it was not statistically different compared to the norm; After 8 weeks, the PR increased by 162% ($p < 0.001$) and after 12 weeks the PR was increased extremely by 234% ($p < 0,001$).

In healthy rats after administration of palosuran decrease in PR by 12% was not statistically significant. Administration of L-NAME in rats treated with palosuran showed only a tendency of increase in PR by 9% also and compared to untreated hypertensive rats, decrease in PR by 4% PR was not statistically significant as well.

In hypertensive rats treated with palosuran started 4 weeks after disease modeling, by the 8th week of hypertension, palosuran induced a statistically significant decrease in PR by 33% ($p < 0.01$) compared to data from hypertensive, untreated rats. Administration of L-NAME in rats treated with palosuran showed a tendency of increase in PR by 9%. PR was reduced by 26% ($p < 0,05$) compared to data of untreated hypertensive rats.

In hypertensive rats subjected to treatment with palosuran, started after 8 weeks of disease modeling, on the 12th week of hypertension PR was decreased by 24% ($p < 0.01$) compared to control, untreated rats. In treated rats' injection of L-NAME increased PR by 30%. Compared to the control, untreated rats, the effect of L-NAME on PR was not statistically significant.

Thus, the experiment revealed that changes in PR were observed at different stages of modeling of renovascular arterial hypertension, compared to PR in hypertensive rats. In particular, by the 2nd and 3rd weeks after disease modeling, PR was increased almost uniformly compared to the norm, 1.45-fold and 1.42-fold, most likely due to renal ischemia.

4 weeks after modeling of hypertension PR decreased and it was not different from the PR of healthy rats. Although PR was within the normal range that could be explained by a second, intact kidney-compensatory mechanism decreasing renin production [32,33], the BP has remained at high levels.

High arterial pressure which was revealed by experiment in the presence of relatively low PR could be explained by an increase in blood osmotic pressure, increase in circulating blood volume and increase in vascular basal tone due to hyperproduction of aldosterone, leading to the increased sodium reabsorption with further increase in blood osmolality and increased production of antidiuretic hormone, stimulating the secretion of adrenocorticotropic hormone and potentiating peripheral vasoconstriction [34,35].

The increase in basal tone supposedly is caused by an increase in the amount of sodium in the blood vessel walls, leading to water retention causing their swelling and thickening. In addition, sodium increases the sensitivity of α-adrenoceptors in blood vessel walls in response to catecholamine. Aldosterone also facilitates the release of norepinephrine from the sympathetic nerve endings and as a result, increases vascular neurogenic tone also [36,37].

By the 8th week of disease modeling, PR was increased 2,6-fold compared to the norm, and 3.34-fold by the 12th week of hypertension correlating with the data of systemic blood pressure and MAP.

Palosuran produced a significant decrease in PR in all study group animals compared to control (especially in case of early onset of treatment), except in healthy rats, where only a tendency of decrease in PR was observed.

In healthy rats after administration of palosuran arterial pressure and PR were not changed significantly that could be explained by the fact that urotensin production is relatively low in healthy rats, hence the effects of the palosuran is less respectively. It should also be noted that in

healthy rats, both palosuran and L-NAME were administered at a single dose and samples were taken 2 hours after injection of preparations. The hypotensive effect of palosuran supposedly develops due to its vasodilatatory effect, which later is reflected in renin production. Probably, this short period of time (2 hours) at single administration of the drugs is not sufficient for the reliable changes in PR. The same could be said for the tendency of increase in PR after injection of L-NAME in treated rats.

Decreasing effects of palosuran on PR were seen both early and late in treatment at weeks 8 and 12 of hypertension, but PR was significantly lower at the start of treatment than at the late start of treatment.

From the results of the experiments, it can be concluded that palosuran shows an antihypertensive effect in the early stages of hypertension under laboratory conditions. Rats with renovascular hypertension lead to significant changes in serum Na^+ and K^+ levels, with the exception of serum Ca^{++} concentration.

Palosuran reduced the serum Na^+ concentration and increased the K + concentration in hypertensive rats. The Na^+ and K^+ concentrations were also kept within normal limits after administration of L-NAME, with the exception of a late start on treatment. The effect of palosuran on serum electrolyte levels in the late stages of arterial hypertension has not been observed.

Conclusion

Based on the study results Palosuran significantly reduced PR compared to untreated hypertensive rats that persisted with L-NAME except for late initiation of treatment. Palosuran may represent a new treatment option for people with essential hypertension. Palosuran reduced serum Na^+ concentration and increased K^+ concentration in hypertensive rats. Concentrations of Na^+ and K^+ were maintained within normal limits even after administration of L-NAME, except for late initiation of treatment. From the results of the experiments, it can be concluded that Palosuran exhibits an antihypertensive effect in healthy and hypertensive rats. The vasodilatory effect of palosuran is superior to the inhibitory effect of L-NAME on NO and the endothelial-independent vasoconstrictor effect induced by urotensin, particularly in the early stages of hypertension. With stable arterial hypertension, PR gradually increases from the norm.

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THE SCIENTIFIC TALKS OF INVOCATIONS OF SPECIFICITIES OF PHARMACIST PROFESSIONAL AND HIGHER MEDICAL-PHARMACEUTICAL EDUCATIONAL CHALLENGES OUTLOOKS AND ACHIEVEMENTS IN GEORGIA

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ABSTRACT

The main objective of the study was to analyze the challenges of specificities of pharmacist occupation and higher medical-pharmaceutical educational outlook in Georgia. The study was a quantitative investigation and analysis of the challenges of specificities of pharmacist occupation and higher medical-pharmaceutical educational outlook in Georgia, by using questionnaires. Were conducted a survey study. The in-depth interview method of the respondents was used in the study. The 7 types of approved questionnaires were used (Respondents were randomly selected): Questionnaire for chief pharmacists: 410 chief pharmacists participated in the study. Questionnaire for patients: 1506 patients (customers of drug-stores) participated in the study. Questionnaire for the employed pharmacy faculty-student: 222 employed pharmacy faculty students participated in the study. Questionnaire for health-care specialists: 307 public health specialists participated in the study. Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. Were used methods of systematic, sociological (surveying, questioning), comparative, mathematical-statistical, graphical analysis. The data were processed and analyzed with the SPSS program. We conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p< 0.05$ as significant for all analyses. According to the study results, the level of basic training of pharmacists should be in compliance with the contemporary requirements. The pharmacist should have deep knowledge in pharmacology, in pharmacotherapy, in toxicology, in pharmaceutical care, in clinical pharmacy, in pharmacokinetics, in pharmacodynamics, in basic of medicine and in other pre-clinical and clinical directions. Such knowledge can be obtained only in the higher pharmaceutical education institutions. Therefore, pharmacist working in pharmacy must have only higher pharmaceutical education. It is necessary to provide a deep cooperation between pharmacists and physicians on the issues of pharmacotherapy and healthcare to ensure the patients' health state effective improvement, and also to provide the best feedback regulation and revision in the healthcare specialists'

team work. Pharmacists also should be responsible for registration of the drugs' side effect, as well as be attentive in case of improperness and professional defects of drugs they provide.
Keywords: Pharmacist, occupation, higher medical, pharmaceutical, educational, outlook, Georgia.

Introduction

Clinical pharmacists work directly with physicians, other healthcare professionals, and patients to ensure that medications prescribed to patients contribute to the best possible health outcomes. Clinical pharmacists work in healthcare settings, where they communicate frequently and regularly with physicians and other healthcare professionals, which contributes to better coordination of care. Clinical pharmacists are educated and trained in many direct patient care settings, including medical centers, clinics, and many other healthcare facilities. Clinical pharmacists are often granted patient care privileges by collaborating physicians and / or healthcare systems, which allows them to perform the full range of drug decision-making functions within the team. medical condition of a patient. These privileges are based on the clinical pharmacist's demonstrated knowledge in pharmacotherapy and on his clinical experience record. This specialist knowledge and clinical experience is usually acquired through residency training and specialist certification.

Aim of the research

Aim of the research was to study and analyse specificities of pharmacist occupation and higher medical-pharmaceutical educational outlook in Georgia.

Methodology

The study was a quantitative investigation and analysis of the challenges of specificities of pharmacist occupation and higher medical-pharmaceutical educational outlook in Georgia, by using questionnaires. Were conducted a survey study. The in-depth interview method of the respondents was used in the study. The 7 types of approved questionnaires were used (Respondents were randomly selected): Questionnaire for chief pharmacists: 410 chief pharmacists participated in the study. Questionnaire for patients: 1506 patients (customers of drug-stores) participated in the study. Questionnaire for the employed pharmacy faculty-student: 222 employed pharmacy faculty students participated in the study. Questionnaire for health-care specialists: 307 public health specialists participated in the study.

Results and Discussion

During research the factors, influencing on the pharmacy faculty students' professional development were found and evaluated. These factors included interesting and valuable work, the favorable psychological climate within the colleagues' team, possibility of career development, professional training, social importance of profession and independence in the work.

The employed pharmacy faculty students' vast majority considered that the Government should make the certification of pharmacists to raise professional standards licensing and certification of pharmacists. The certification of higher pharmaceutical education pharmacists is very essential for the pharmacist's professional perfection, for pharmacists' career enhancement, for vocational advancement and it is main determine detector factor for pharmacist professionalism level. Pharmacist position should become regulated health profession as the member of other health profession team (but now unfortunately pharmacists are not member of regulated health teams). Pharmacists' periodic licensing, certification and accreditation should increase pharmacists' professionalism level and is guarantee upper quality pharmaceutical care. All above mentioned is indicator factor of the health care system service quality.

First time were complex studied professional peculiarities of the pharmacists per vision by pharmacists specialists, professional peculiarities of the employed pharmacist-student, professional peculiarities of the pharmacists by vision of the chief -pharmacist, peculiarities of professional for pharmacists via per vision of the health-care specialist, pharmacists' professional features as per view of the patients, professional peculiarities of the young pharmacist-specialists, professional peculiarities of the pharmacist-student. To reveals influencing factors for the specificities of the role, achievements, innovations, professional and enhancement prospects of pharmacists in health care sector. In result of the study and evaluation of the pharmacist's professional peculiarities news, objectively reasoned comprehension of the problems in this field has been adopted, which became a base for developing recommendations. In particular, for the first time the following have been studied and established: the peculiarities of professional and career improvement strategy for pharmacists, pharmacist specialist's professional features, specificities of the role, achievements, innovations, professional and enhancement prospects of pharmacists in health care sector globally. First time the process of professional formation of pharmacists in the scope and context of pharmaceutical care, including the stages of professional development was studied and scientifically established. First time the most influenced factors for the pharmacist's professional formation were identified. Deepen defined the role of pharmacist and the specific features for the pharmaceutical specialists' formation at various stages were studied and identified. On the bases of comprehensive studied was revealed, that pharmacist specialists in contradistinction to other medical specialists like physicians, dentists etc do not have continuous education, periodic certification and licensing. Pharmacists' profession removed from the regulated and certified health professional members' team.

The results of our study have been shown and substantiated, that the pharmacists, as well as doctors and stomatologists, who are obliged to take part in the mandatory certification by the Government, in order to improve the responsibility on their own professional specialization for motivate and improve their vocational knowledge and skills with the help of continuous education.

It would be promoted, that pharmacist to become more responsible, accountable and liable on for enhance their professional knowledge, skills and competencies. All the above mentioned first time we conducted a comprehensive and deep study of the scientific research for specificites of the role, achievements, innovations, professional and enhancement prospects of pharmacists in health care sector globally.

A little less than a fifth of higher pharmaceutical education pharmacists have realized professional capabilities, skills and habits to the full extent, A little bit less than half of higher pharmaceutical education pharmacists have realized professional capabilities, skills and habits partially, more than 50% of own potential, about a quarter of higher pharmaceutical education pharmacists have realized professional capabilities, skills and habits - partially, less than 50% of own potential . At the same time the vast majority of the pharmacists and health care specialists noted that pharmacists' knowledge in disciplines, such as the pharmacology, pharmacotherapy, pharmaceutical care and clinical pharmacy were a lack or insufficient for the successful work. Health care specialists' vast majority think that pharmacists are in need of additional- further regular study in the above-mentioned directions. Approximately half of the respondents considered that just 50% of their own potential was realized at the work position. Anyway, the overwhelming majority of the young pharmacists would not like to leave their profession. The vast majority of young pharmacist specialists consider that in pharmacology, in

pharmacotherapy, in pharmaceutical care, in clinical pharmacy their knowledge is a lack or is not enough for successful work.

The vast majority of the pharmacists (84.4%) considered that for full pharmaceutical activity it is necessary to provide continuous professional education; therefore, higher pharmaceutical education pharmacists consider that professional education should not be ceased. The vast majority of pharmacy faculty students consider that education should not be ceased. Pharmacy faculty students' more than a third was working by specialty. The huge part of the pharmacists (55.6%) considers the continuous professional education is essential for the career growth and professional development, which enables getting information of new drugs and updated knowledge of some diseases' pharmacotherapy, pharmacology and the pharmaceutical care. At the same time, the minority of respondent pharmacists (8%) had not used knowledge obtained from the professional publications and literature in their practice, while less than half of them (41%) had partially used. Competent pharmacist specialist who is capable of providing qualified pharmaceutical care (assistance) is formed in the professional training process.

A large majority of chief pharmacists (76.6%), vast majority of patients (82.6%), of the vast majority of the employed pharmacy students (95.9%), the large majority of the healthcare specialists (94.8%) and a big majority of pharmacists (71.9%) considered that the Government should imply the pharmacists' certification in the way acting for other medical specialists. That is very essential for pharmacists' professional perfection, for self-realization, for career advancement, for continuous professional education, for professional growth.

Mostly essential pharmaceutical activity issues for the respondents' pharmacists' majority were: new drugs, generic drugs, chemical and brand names of them; psychology of communication (relationships) with customers; issues of pharmacotherapy of certain diseases, pharmacology, pharmacodynamics, ppharmacokinetics and pharmaceutical care. It is apparent, that in the higher pharmaceutical education universities programs should be emphasized on the following subjects: pharmacotherapy, pharmacology, pharmaceutical care, clinical pharmacy and drugs toxicity.

The most impacting factors influencing on the young pharmacists' work satisfaction were found and evaluated during the research. These factors included the correspondence of qualification to work, correspondence of the work nature to capabilities of personality, existence of perspective for professional promotion, possibility to qualifications enhancement, existence of high degree of responsibility for the result of work, information about affairs of the company and of the staff activity, working conditions, existence of the labor contract of working regimen and salary, existence of benefits' scheme for employees, support and assistance of the chief, direct relations with manager(s),relations with colleagues, possibility for the career enhancement.

The study of the professional adaptation of pharmacists indicated that inadequate professional knowledge, improper performance of the acquired professional skills were the main reasons for imperfect pharmaceutical care supply. The majority of the pharmaceutical organizations' heads and also the young specialists considered the coexistence of a mentor (experienced professional pharmacist) as the main factor of professional improvement for pharmacists' professional adaptation. The pharmacists' personnel must show stirring involvement in sharing their cognition, understanding, science, skill and contributing partnership and cooperation within the colleagues and other health care professionals in pharmacy direction.

It is quite significant, that pharmaceutical companies regularly perform study of pharmacists' work satisfaction. The pharmaceutical companies should determine combination of factors that effect on the pharmacists' work satisfaction. Pharmaceutical companies should create favorable working conditions for pharmacists to enable the maximal realization of the pharmacists' professional capabilities, skills and habits. A balance between the workload and pharmacists' personal life should be more harmonized,

convenient, resourceful and more poised. This will increase the quality of pharmaceutical care in pharmacies.

It should be noted, that pharmacist's satisfaction with income is a very sensitive factor that has a significant impact on the quality of pharmaceutical services performed in pharmacy, so the pharmacists' salary should be revised and increased.

It should be noted that in developed countries and in many developing countries pharmaceutical specialty is regulated profession alike the family medicine. In western countries pharmacist as a family doctor need higher pharmaceutical education, diploma and continuous pharmaceutical education, pharmaceutical license and periodic accreditation. Only pharmacists with higher pharmaceutical education have the right to work as pharmacists' position in the pharmacies. On the pharmacists' certification programs should be only involved pharmacists who have graduated pharmaceutical faculties from state recognized and accredited universities.

The majority of higher pharmaceutical education pharmacists' specialists were female; among them the largest majorities were working on the pharmacist position at pharmacies. The Government and pharmaceutical companies should create promotional conditions for males to make pharmacist profession attractive for men. It is very important for career advancement and satisfaction to provide a balance between the workload and man personal life for the satisfaction by income, for pharmacists' professional satisfaction, for pharmacist job satisfaction, and also for the career promotion perspectives.

The Government should take care of the profession of pharmacist authority. The pharmacist's profession in the health care system should increase the authority and social importance by the state support. Pharmacist's profession should become of more power and authority; a pharmacist should have a much higher status in the healthcare system. Therefore, the role of a pharmacist is significantly increased in the healthcare system and is directly related to his professional education level. Therefore, pharmacist should have appropriate higher pharmaceutical education. All the mentioned is achieved then, when the pharmacist profession will move into the health-regulated professions list.

The level of basic training of pharmacists should be in compliance with the contemporary requirements. The pharmacist should have deep knowledge in pharmacology, in pharmacotherapy, in toxicology, in pharmaceutical care, in clinical pharmacy, in pharmacokinetics, in pharmacodynamics, in basic of medicine and in other pre-clinical and clinical directions. Such knowledge can be obtained only in the higher pharmaceutical education institutions. Therefore, pharmacist working in pharmacy must have only higher pharmaceutical education.

To increase the pharmacist's professional qualification, professionalism, professional knowledge and competency the higher pharmaceutical education universities programs should more emphasize the mentioned subjects. It is too important, that a pharmacist should realize and understand that qualification upgrading study courses, professional trainings and professional workshops are of great necessity for further professional advancement. Thus, the Government should develop continuous pharmaceutical education programs accessible to all pharmacists. The qualification upgrading study courses, professional education or training courses should be available for all pharmacists. Pharmacist's education process should not be stopped. Developing a continuous pharmaceutical education system will enhance the professionalism of the pharmaceutical personnel. Experiential education should encourage perfection of critical opinion and the problem resolving processes along with the medicine discovery.

Pharmacy faculty students should take part in the patient care practice in hospitals, society proceeding settings and in other practical experiences. Students should have the possibility to apply the clinical and pharmaceutical information taught in classes when studying in medical facilities by working under the supervision of volunteer mentors (the healthcare specialists or professionals). The research activity of the pharmaceutical faculty students in all fields of pharmaceutical practice should be encouraged.

Quality reliance refers to the necessity to improve higher pharmaceutical education to guarantee a useful, sustainable and steady activity and appropriate skills and competencies of the tomorrow's labor resources.

The pharmacy degree programs should be proposed at the higher pharmaceutical institution level and entire experimental constituent element in the clinical facilities.

It is necessary to provide a deep cooperation between pharmacists and physicians on the issues of pharmacotherapy and healthcare to ensure the patients' health state effective improvement, and also to provide the best feedback regulation and revision in the healthcare specialists' team work. Pharmacists also should be responsible for registration of the drugs' side effect, as well as be attentive in case of improperness and professional defects of drugs they provide. To achieve that it is necessary to raise awareness of specialists on the essence of pharmacists' profession and functions among the medical personnel and general public.

On the basis of the theoretical and logical analysis the structure and composition of the factors have been developed, considering the objective (external), subjective (internal) and universal factors, which influence on the professional formation of the pharmacist. These factors comprised the content of work, position, correspondence of qualification and nature of work to capabilities, aspirations and inclinations of the pharmacist, the existence of perspective for professional promotion. The existence of perspectives for career promotion, the possibility to enhance qualifications, a high degree of responsibility for the work results, regimen, labor salary and the system of benefits scheme for employees, support and assistance of a manager, direct relations with manager and colleagues serve the essential base for the pharmacists' successful work. The unity of criteria for pharmacist professional formation, for the common professional formation (characteristic to all stages) and the specific professional formation (characteristic to the separate stage) had been developed.

The main underlying motives, while making professional (occupational) choice of respondent pharmacist were the following: desire to obtain high-quality professional education (training) – 44.8%, guarantee to be employed – 42.6%, interest in a profession-39.4%, the desire to care for the health of people – 43% (tabl.).

Table 1. Factors, mostly influenced on the respondents' (pharmacists) profession choice.

The most influencive on the profession choice (one answer is accepted)	Frequency	Percent (%)
1. Parents' advices (will)	186	23.0
2. Teachers' advices	32	4.0
3. Advice of an expert-specialist of professional orientation (of career guidance)	28	3.5
4. The desire to obtain a profession in compliance with own trends, aspirations and inclinations	108	13.3
5. There was nowhere to go	15	1.9
6. Dissatisfaction with the previous education	18	2.2
7. Personal desire	306	37.8
8. Specialty love from childhood	117	14.4
Total	810	100.0

About a quarter of respondent pharmacists have realized professional capabilities, skills and habits partially – less than 50% of their own potential; about half of them have realized professional capabilities, skills and habits partially – more than 50% of their own potential (fig. 1). Pharmaceutical companies should create constructive working conditions for pharmacists to maximally realize their professional capabilities, skills and habits for improving the quality of pharmaceutical care in pharmacies.

Figure 1. Extent of the respondents' (pharmacists) realization of the professional capabilities, skills and habits

The chief pharmacists' majority considered that the most effective forms of professional assistance while adaptating of the specialist to work were an independent practical activity and personal conversation. Less than half part of the respondents considered that to be a discussion on work of young employees within the colleagues' team and on special training programs. About one third each of them considered necessary to work with a mentor, internship and qualification upgrading courses (tabl. 2).

Table 2. The respondents' opinion about the most effective forms of professional assistance while adaptation of the specialist

The most effective forms of professional assistance while adaptation of the specialist (several answers were possible)	**Count**	**Percent (%)**
1. Independent practical activity	262	63.9
2. Working with a mentor	142	34.6
3. Internship	137	33.4
4. Discussion of work of young employees within the colleagues team	196	47.8
5. Personal conversation	293	71.5
6. Qualification improvement upgrading courses	120	29.3
7. Special training programs	169	41.2

The respondents' vast majority considered that for successful work their knowledge was not enough in the subjects of pharmacology, pharmacotherapy, clinical pharmacy and pharmaceutical care (fig. 3). Therefore, in our opinion, at university pharmaceutical programs and syllabuses need upgrade, adaptation and fit on new demands reality. In pharmacy faculty programs there should increase credits in the following subjects: pharmacology, pharmacotherapy, clinical pharmacy and pharmaceutical care. Above mentioned complex would help formation of the highly qualified pharmacist specialist with deep and systematic knowledge. It is obvious that the academic hours in the pharmacology, pharmacotherapy, clinical pharmacy and the pharmaceutical care subjects within the pharmaceutical education programs should be increased to ensure deep and systemic knowledge for the successful work.

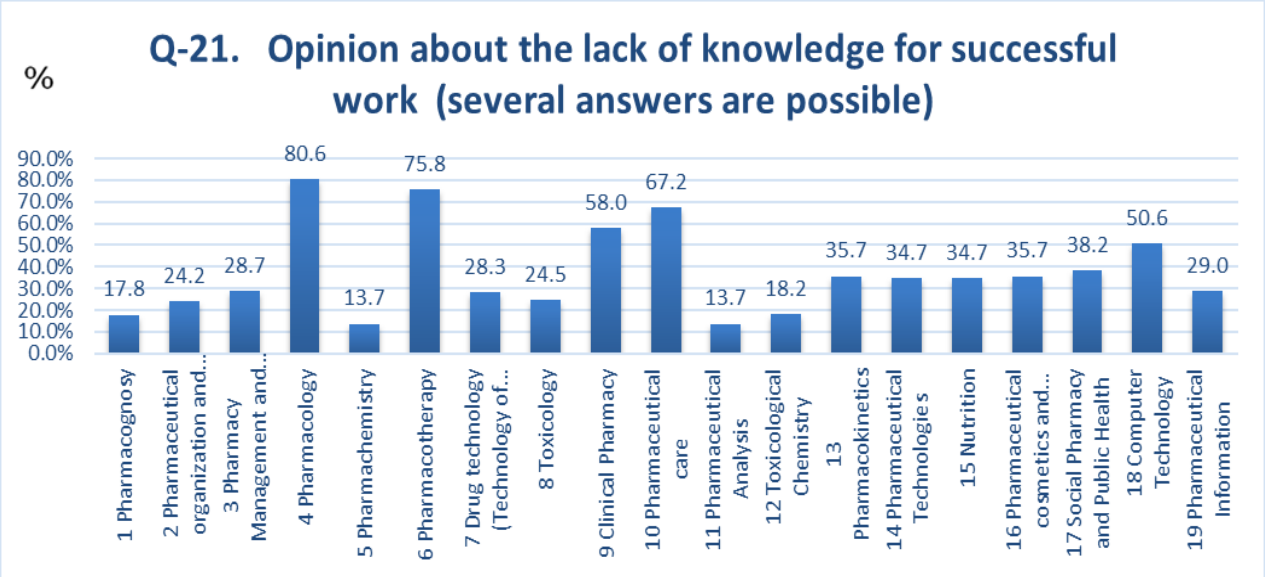

Figure 3. The respondents' opinion about the lack of knowledge for their successful work

We have conducted surveys with the questionnaires and analyzed the respondents' answers, which are presented in the third chapter of the dissertation thesis. Afterwards, a coupling of the results by the cross analysis was conducted, and the following was established:

Chi-square test of independence have revealed that pharmacists who have completed postgraduate education were more likely to hold higher position (Chi-square=4.9, $p < 0.03$).

Statistically, a significant association was revealed between pharmacists' position and their satisfaction with a professional career and job. Holding high positions were associated with increased career and job satisfaction (Chi-square=9.4, $p=0.002$ and Chi-square=5.5, $p<0.02$, respectively), but not with professional choice satisfaction.

The analysis indicated also that lasting years in the current position was associated with lower career and job satisfaction (Chi-square=6.4 and 13.2, $p=0.001$).

A consideration that the professional capabilities and skills of respondents have been realized to the full extent in the current job was associated with higher career and job satisfaction (Chi-square=15.9, $p=0.001$ and Chi-square=5.7, $p<0.02$, respectively). Having a positive opinion about the importance of continuing professional development was also associated with the increased job and career satisfaction (Chi-square= 5.0 $p<0.001$ and Chi-square= 24.8, $p<0.03$, respectively).

Use of the knowledge obtained from professional literature by a pharmacist in practice was significantly related to higher job satisfaction (Chi-square=13.6, $p<0.001$), but not to career satisfaction. Pharmacists' engagement in planning of professional career wasn't associated with increased job and career satisfaction. One of the main predictors of pharmacists' career and job satisfaction was also their income (Chi-square=23.9, $p<0.001$and Chi-square=50.4, $p<0.001$). Pharmacists who were satisfied with their income were more often also satisfied with their job and career. There wasn't statistically significant association between the main motive of professional choice and job satisfaction in all three observed groups (pharmacists, young specialist and students).

Conclusion

Pharmacists also should be responsible for registration of the drugs' side effect, as well as be attentive in case of improperness and professional defects of drugs they provide. To achieve that it is necessary to raise awareness of specialists on the essence of pharmacists' profession and functions among the medical personnel and general public. It is necessary to provide a deep cooperation between pharmacists and physicians on the issues of pharmacotherapy and healthcare to ensure the patients' health state effective improvement, and also to provide the best feedback regulation and revision in the healthcare specialists' team work.

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STUDY OF THE METHODS OF DETERMİNİNG AND MANAGİNG THE ENTERPRİSE'S EXPORT CAPACİTY BASED ON İNTERNATİONAL BUSİNESS PRACTİCES

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ABSTRACT

Export potential, being a part of the country's economic potential, is the ability to produce and export various types of material goods and services in the quantity and quality corresponding to the demands of foreign market consumers as a result of the full use of the means of production of the economy and its sectors.

It should be noted that there must be a demand for them to be exported. Considering that the amount of products that the country can produce is quite small compared to the number of products in the world market, the country's demand potential for oil products may always be there. When analyzing the export potential, other factors to consider are quality, compliance with global base standards, and prices. In our opinion, if the price of the product in the domestic market is lower than the price of this product in the international market, then there is export potential. In other words, when evaluating the export potential of products, prices should be compared and it should be determined whether the product in question can be sold profitably at international prices.

One of the main factors determining the formation and development of export potential is the availability of natural resources in the country and the level of their use. The availability of natural resources and the level of their exploitation determine the development of the productive forces of the country, especially the means of material production and, based on this, the export potential. Therefore, the export opportunities of this or that country directly depend on the number of natural resources discovered and exploited by the country and the natural conditions. Thus, it can be said that the export potential existing during a certain period is based on both used and unexploited cumulative natural resources.

One of the constituent elements of export potential is labor resources determined by a system of quantitative and qualitative indicators. This includes scientific personnel, workers working in different fields of industry, and persons engaged in organizational and management work related to the export of products and their realization in the foreign market.

The quantitative increase and qualitative change of labor resources are the basis for the acceleration of ETT, the improvement of the efficiency of the use of productive forces, and the development of the country's export potential based on this. In this regard, it is necessary to pay more and special attention to more efficient use of labor resources, increase, and improvement of their qualifications, and other factors.

Currently, in connection with the development of science and technology, technological development plays an important role in expanding export potential by increasing the country's

competitiveness in foreign markets. Technological innovation leads to differences between production processes in individual countries, and due to this innovation, that country has a comparative advantage. At this time, until the new technology spreads to other countries, the innovative country becomes a monopoly in the export of this product, even if temporarily, and thereby gets the opportunity to ensure the maximum level of development of its export potential.

As it is known, historically underdeveloped countries have dominated the export of raw materials. However, the low level of demand for raw materials in developed countries, the policy of protectionism introduced by them, the application of technologies that save raw materials and the use of synthetic substitutes, etc. depending on the reasons, the country's opportunities to expand its export potential due to raw materials are limited. In particular, taking into account that comparative advantages have gradually changed towards technology-intensive production in recent times, increasing the share of the processing sector, mainly science and capital-intensive products, in the commodity composition of exports is considered more appropriate and promising.

Recently, the trade and economic relations of the Republic of Azerbaijan with a number of countries in the world have expanded. This has led to an increase in import-export relations.

A systematic approach, programming, and other methods, reflected in the experience of developed countries of the world, operate in such a way that the export potential structure of the systematic approach is predicted as a component of economic growth.

It should be noted that in addition to the problem of expanding the country's export opportunities, it is also necessary to consider the country's import policy. Because the import substitution strategy plays no small role in the development of the country's export potential. Although the export-oriented model is the main strategy aimed at the development of the export potential by making maximum use of the existing and potential opportunities of the leading industrial and agricultural sectors of the developing and, especially, transition economies, during the formation period, the protection of the national industrial and agricultural sectors from the negative effects of imports, their increasing import substitution policy should also be used to increase its competitiveness and gain access to the foreign market in the future.

Keywords: export potential, import, foreign trade, risk, international trade, competition.

Introduction

The experiences of the countries of the world confirm that in modern times, no country can stay outside the international trade system and ensure the development of the national economy without export-import operations. The development of national economies directly depends on the effective participation of countries in the international division of labor, the effective organization of international integrations, and the effective use of the export potential of real sectors of the economy.

At present, the acceleration of globalization processes in the economy has necessitated the active participation of countries in the international economic specialization. The modern development of the world economic system embodies the further expansion and development of international trade, its liberalization, and the dynamic change of trade and economic relations between countries from year to year in terms of both geographical and commodity structure.

Under the leadership of the President of the Republic of Azerbaijan, Ilham Aliyev, the volume and value of exports in the non-oil sector have increased in recent years. As a result of the diversification of the economy, the assortment and variety of products belonging to the non-oil sector, including geographical diversification, have a positive effect on the balance of payments of

our country, and at the expense of the balance of current accounts, macroeconomic and provided financial stability. When we talk about the diversification of exports, it is not only the variety and comprehensiveness of goods and products that is meant. In most countries of the world, especially in the brotherly Republic of Turkey, when export statistics are given, the export of services is emphasized. Unlike the export of goods and products, the added value generated by services is often more productive than that of commodities. According to the indicators of the balance of payments covering the months of January-March of this year, the export of services of Azerbaijan amounted to 1.01 billion US dollars, of which 73.7% is included in the share of non-oil exports. During that period, non-oil exports amounted to 727.2 million US dollars. According to the data, the export of Azerbaijan in the non-oil sector for the first quarter is worth 1.74 billion US dollars. Undoubtedly, the development of the services sector, such as the production of goods and products, took place at the expense of huge infrastructure projects. The main share in the services sector in non-oil fields is formed at the expense of transport services. Thus, during the first quarter of 2022, 346.4 million US dollars were earned on non-oil transportation services, which is 47% of non-oil services. The strategy carried out by President Ilham Aliyev in the field of cargo transportation for many years has made Azerbaijan attractive not only for subjects carrying out internal transportation but also for non-residents. Improving the quality of road infrastructure along with solid political stability, and rehabilitation of shorter and more convenient roads is the main principle of success achieved in the road infrastructure services sector for foreign trade participants engaged in trade activities.

Ensuring sustainable economic growth, which is the main direction of the "National Priorities - 2030" document approved by President Ilham Aliyev, will be implemented based on the investment, production, export, and employment (IIIM) model. It is an inevitable factor that the mentioned IIIM model is possible based on Azerbaijan's diversification policy. It must be admitted that the economy depends on oil and gas resources. Nevertheless, it is possible to observe the diversification of production in industry and agriculture in recent years. In particular, it is possible to see the transformation of the commodity structure in non-oil production and export through statistical indicators. Compared to previous years, fruit and vegetable products were dominant in the top 10 exports, but currently, industrial products occupy a place in the commodity structure. Undoubtedly, compared to fruit and vegetable products, industrial products have a higher added value capacity. However, the mentioned industrial products, being raw material-intensive, have significant competitive conditions in the international market. This makes the production and export of branded products with a comparative and competitive advantage even more urgent and sets new goals for our country as the main challenge. According to the calculations, the productivity of products with an export basket is lower. The main reason for this is that 70% of the corresponding basket is made up of intermediate products. It is not difficult to understand the concept of productivity, considering that the export basket of the IEE includes high-tech equipment, electronic products, as well as branded food products.

The purpose of the study is to analyze the effectiveness of the state policy on the international activity of small and medium enterprises (SMEs). Specifically, we examine the impact of public export promotion programs (EPP) on two types of organizational capabilities, namely export capabilities already used in the previous modeling, and international risk management practices as an original variable. Policies on the international activity of SMEs. It uses a quantitative methodology based on a structural equation modeling approach applied to a sample of 147 international French SMEs using EPPs. The results add value to the theoretical and empirical

knowledge on the effectiveness of public support programs for the international activity of SMEs, as it demonstrates an indirect effect between EPPs and international performance through export opportunities and risk management practices. It is also shown that by strengthening risk management practices, EPPs stimulate SMEs in pursuing foreign direct investment strategies. Our model is based on the RBV of the firm, which emphasizes that the firm's resources and capabilities are crucial to understanding business performance. According to this theory, the conception and implementation of a particular strategy require a variety of resources and capabilities that are vital to achieving sustainable competitive advantage.

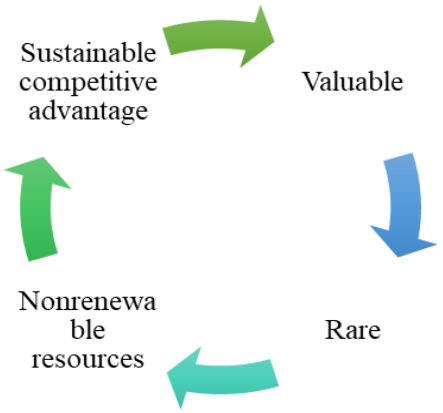

Figure 1. VRIO framework.

VRIO framework (valuable, rare, inimitable resources, appropriate organizational support to create sustainable competitive advantage). It requires that these resources are valuable for exploiting opportunities or neutralizing threats from the environment, and there must be appropriate organizational support that is difficult to replace with equivalent substitutes that can be imperfectly imitated by potential competitors, competitors, and ultimately allow achieving the same positional advantages. These characteristics are the basis for developing and implementing strategies that subsequently help the firm achieve sustainable competitive advantages and increase effectiveness and efficiency.

EPPs should be reflected in the positive impact on the international activity of the SME's organizational capabilities, that is, the strengthening of export capabilities. Indeed, to develop and implement an effective international strategy, SMEs must have both an adequate collection of basic resources and the right combination of these resources to effectively use them in various strategic activities in foreign markets. In the context of internationalization, certain key capabilities provided by EPPs are particularly important in developing effective export marketing strategies. These include having specialized marketing knowledge and exclusive information about international markets and previously developed export capabilities related to identifying, evaluating, and exploiting emerging opportunities in foreign markets. healthy relationships with distributors, customers, and other parties to better understand and meet their requirements. Then, instead of studying the direct effect between EPPs and a firm's international performance, which provides conflicting or ambiguous results, we assess its indirect effect in this study. EPPs will play a role by improving the resources and capabilities that benefit the firm and the latter will have a positive impact on their performance. This indirect effect has been widely demonstrated in

international business, and in particular in research aimed at explaining public support programs and the implementation of the internationalization strategy of SMEs.

The ability to better identify corruption risk or customer failure in a foreign country is an advantage. However, if a firm can regularly review internal controls to manage this particular risk, share information and knowledge about it widely across the firm, and regularly address and report on changes like that risk, then that firm is well positioned for international success. has a special advantage. Risk management practices are a valuable opportunity to support business strategy development by mitigating potential risks and effectively exploiting opportunities. Other firms that do not have this capability will either stay out of the foreign market if the expected risks are too high, or withdraw if the risks that eventually occur are too impressive. The literature on the impact of risk management ability on firm performance is relatively large. Empirical results are mixed, such as the size of the variables (the nature of risk management practices, the degree of maturity of these practices, the performance of the firm), the effect of contingencies, or the potential non-linear effect.

In terms of development strategy, some authors have shown that companies adopting "active" risk management practices are more likely to have aggressive strategic orientations that invest in gaining competitive advantages, especially in product development and expansion into new markets. More advanced risk management practices can clarify the types of risks identified as critical and illuminate ways to mitigate them. By allowing risk monitoring and management, these practices increase managers' awareness of the level of risk they may be exposed to, which facilitates better operational and strategic decision-making by the organization. As a result, these practices are likely to limit the negative impact of various risks on the achievement of the firm's objectives and prevent the deterioration of production capacity and market share, as well as the occurrence of financial losses or bankruptcy problems. This positive economic impact can be explained by other organizational outcomes. For example, risk management practices can enhance cost optimization and efficiency, or lead to positive attitudes among employees by increasing clarity and understanding of work roles within an organization, reducing work conflicts, and improving task coordination.

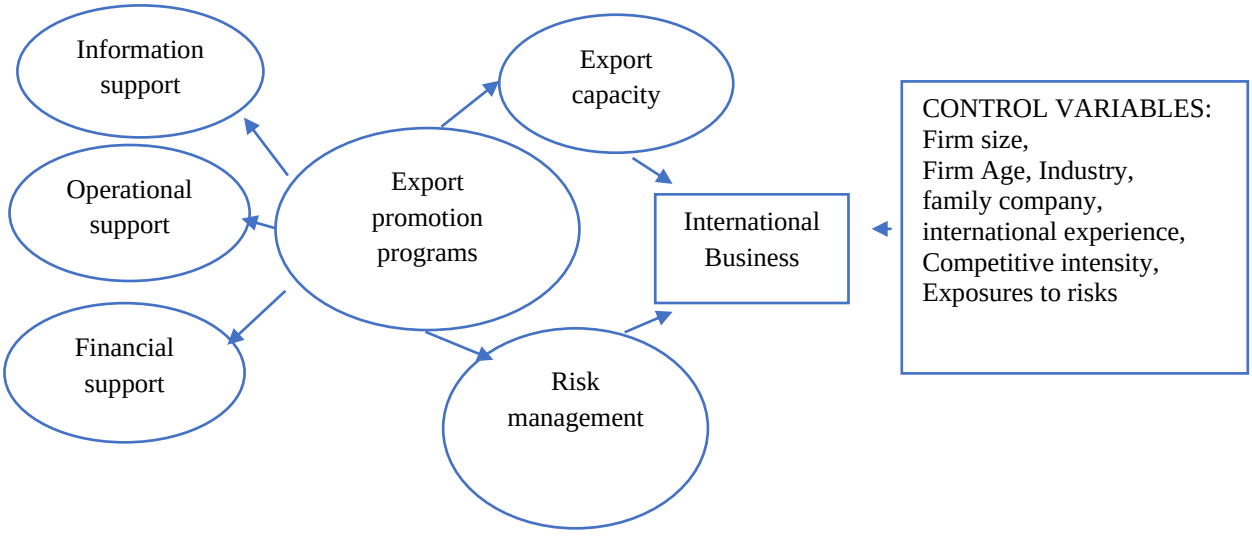

Figure 2. Hypothesized research model.

With export opportunities, risk management practices become an important and relevant organizational support for creating a sustainable competitive advantage, as they can ensure the implementation of an international growth strategy. This competitive advantage corresponds both to the company's ability to export more and to have a more direct presence abroad. The following hypotheses derived from previous developments allow us to conclude our research model in a resource-based framework to empirically test the indirect effect of public support on firm performance.

Conclusıon

The development of foreign trade relations is one of the main factors for increasing the efficiency of the country's economy and for its inclusion in international economic cooperation. To increase the efficiency of export, first of all, the weight of the finished product in its structure should be increased. One of the main directions for the development of the country's export potential and the strengthening of the economy is to enter regional economic integration.

There are several methods of export stimulation for Azerbaijan:

- Application of tax and customs benefits;
- Regulation of mutual relations between monopolies and priority areas of industry;
- Development of targeted investment programs in priority areas related to foreign trade;
- Development of leasing can also be an important condition for export stimulation;
- Formation of strong credit institutions that can ensure crediting of import-export operations;
- Creation of special export-oriented and scientific-technical zones as a type of free economic zones.

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TRAMETES QUEL. EVALUATION OF PHYSICAL FACTORS AFFECTING THE GROWTH OF FUNGI BY THEIR SPECIES

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ABSTRACT

Main aim of the article is to explore evaluation of physical factors affecting the growth of fungi by their species. There is a certain group of basidiomycetes that are adapted to live only in wood. From an eco-trophic point of view, these fungi belonging to saprotrophs, biotrophs, and polytrophs are called xylotrophs. The main function of these fungi is the destruction or biological decomposition of lignocellulosic substrates.

The genus Trametes belongs to the division Basidiomycota, class Basidiomycetes, subclass Homobasidiomycetidae, order Aphyllophorales, family Poriaceae (Poliporaceae). 627 species include to this genus (Trametes Fr.), including cosmopolitan representatives (*Trametes versicolor* (L.: Fr.) Lloyd). Representatives of this genus are well known as producers of many biologically active substances: polysaccharides, polysaccharides, glucans, glycoproteins, triterpenes, flavonoids, chitin, extracellular hydrolytic and oxidative enzymes, unsaturated fatty acids, high-quality proteins including all amino acids, vitamins, easy trace elements in the form of absorbable organic compounds.

Keywords: Trametes, fungi, polysaccharides, glucans, glycoproteins

Introduction and objective

It was determined that biologically active substances are present in the fruit bodies and vegetative mycelia of the species belonging to this genus, formed under natural conditions in the conducted studies. Nevertheless, in a number of studies, when studying the chemical composition of mycelium and fruit body, it was clear that the amount of extractive substances in the mycelium is greater than that of the fruit body, and the amount of metabolites extracted from both structures is consistent with temperature, that is, the difference between the yields during cold and hot extraction is 3.9 can be up to times.

A similar situation can be found in relation to the protein contained in the mentioned substances. Thus, the amount of protein in the fruit body is almost 2 times less than that in the mycelium.

During the comparative assessment of the amino acid content of the proteins in the fruit body and mycelium of the mushrooms belonging to this genus, it became clear that the amount of non-replaceable amino acids is greater in the fruit body than in the mycelium, and at the same time, leucine and tyrosine are predominant in the fruit body, and isoleucine, leucine and tyrosine in the mycelium. contane.

As mentioned, fungi belonging to the genus Trametes, especially Trametes versicolor, can produce large amounts of multifunctional polysaccharides, which can be broadly divided into

easily hydrolyzed and difficult to hydrolyze. These fractions differ from each other both in terms of quantity and function. For example, easily hydrolyzable polysaccharides make up 41.6% and 12.9% of the biomass produced by the mushroom during 15 days of cultivation.

The composition of the biomass of fungi belonging to the genus Trametes also includes lipids, the amount of which can be up to 1.5%. The lipid fraction contained in biomass includes neutral lipids, glycolipids and phospholipids. In most studies, the specific gravity of neutral lipids has been determined to be high.

One of the conditions that make it difficult to obtain the required amount of biomass is the relatively poor growth rate of selected producers, which they use various factors to overcome. Physical, chemical and biological factors are used to accelerate the growth of stunted producers. Thus, in this type of research, optimization is mainly carried out according to the carbon and nitrogen sources of the environment, initial acidity, cultivation temperature, the method and duration of planting material preparation.

Light and the visible part of the spectrum are used as promising environmentally friendly regulatory factors in the deep cultivation of mycelial fungi [1]. For example, infrared waves are used to enhance the growth of cultures of the medicinal mushrooms Coriolus vaporarius and Serpula lacrimans. At the same time, the practical use of monochromatic light in biotechnological processes is limited due to the lack of information - precise light regulation mechanism, wavelength efficiency and illumination mode [2].

It has been shown that low intensity light increases the growth rate of the studied genera Lentinus edodes, Pleurotus ostereatus and Hericium erinaceus due to more densely formed mitles, and also stimulates the formation of the beginnings of the fruiting body. Sequential illumination with light sources increases the biomass yield of the fungus G. lucidum in solid nutrient medium up to 11% in stationary cultivation and up to 19% in deep cultivation. In order to evaluate the prospective application of laser beams in production, a study was conducted on the effect of HeNe-argan laser beams on the colonization and fruiting of basidiomycetes P. ostreatus, L. edodes and H. erinaceus on the substrate. It is shown that lighting causes the end of cycle, early bearing, time of fruiting, and also a sufficient increase in the productivity of the fruit body is observed [3].

In addition to light waves, acoustic waves in the audible frequency range can also be used as stimuli. Numerous studies have been conducted on the evaluation of the effectiveness of the acoustic effect on biological objects in a wide frequency range. The effect of low-intensity ultrasound (US) has been studied quite widely, when the power effect does not exceed 2 W / cm2 in the frequency range of 20-66 kHz and 0.5-10 MHz. [4,5]. It has been shown that low-intensity US improves the production functions of seed cells, thereby increasing plant productivity, improving the permeability of the biomembrane structure, while high-intensity US causes negative effects, such as nutrient breakdown, growth retardation, and morphology change [6]. In production, US is used for stimulation of various technological processes - sterilization, emulsification [5].

Influence of acoustic waves in the audible frequency range has not been studied in depth, but, according to the results of recent studies, it has begun to gain scientific interest. It has been found that the wave in the specified range improves the germination and phytoplankton of sugarcane seeds. The use of this method can be considered prospective in terms of increasing the productivity of plants [7]. In addition, acoustic processing can be applied to enzyme preparations, for example, "Animal pepsin", which is used in the technology of cheese yeast and shows sensitivity in the wave frequency of 250-2000 Hz. Studies have shown that the application of low-

power acoustics is effective for proleotic enzyme preparations and is of scientific importance in the production of cottage cheese, cheese, and soft cheese.
As it can be seen, the results of these studies have a positive effect on the process, and for this reason, it was considered appropriate to carry out studies on the optimization of biomass yield due to these factors in the studies, as mentioned.

Material and methodology
Representatives of the genus Trametes found in the nature of the Republic of Azerbaijan were used as research objects: Trametes cervina, T. heteromorpha, T.hirsuta, T. hohneli, T.ochraceus, T.pubecsens, T.suaveolens, T.*trogii*, T.versicolor, T.zonata.
Biomass extraction from the pure culture of fungi was carried out under deep culture conditions (DCC), in which dry glucose-peptone medium (DGPM) was used. The content of this medium (g/l) was as follows: glucose – 10; peptone – 3; NH4NO3 – 1.5; NaCl - 0.5; MgSO4x7H2O; K2HPO3- 0.4; FeSO4- a small amount, ordinary water 1 l. Sterilization conditions – 0.5 atm, 0.5 hours, the acidity of the medium after sterilization is 5.5-5.7.Irradiation was performed by means of a laser with a power of 34 mW and a wavelength of 1.2 nm, exposure for 15 and 70 seconds. Re-irradiation was carried out 3 times in 3 days of cultivation. In addition to the laser, light-emitting diodes have also been used (Table1).

Schedule 1. The power of the light and length of the wave which used in irradiate strains.

№	Power (mVt)	Lengh of wave
1	0,5	578
2	2	400
3	2	578
4	2	518
5	7,5	460
6	7,5	578

The indicators and composition of the nutrient media are given in the following schedule (Table 2).
Table 2. Used nutrient environment and their composition.

№	Nutritious environment/medium	Composition
1	Mushroom agar	50 qr fresh mushroom for eat, aqar 5 gr agar , 20 gr agar which soluble in water, 1000 ml water
2	Cabbage agar	200 ml cooked cabbage extract, Maltax 10 – 5 gr, 2,5 gr corn starch, 20 gr agar, 1000 ml water
3	Potato agar	Cooked potato extract 200 ml, agar 20 g, water 800 ml
4	Wheat agar	Wheat flour 20 g, agar 20 g, water 1000 ml
5	Čapek environment	glucose - 20 g, magnesium sulfate - 0.5 g, potassium chloride - 0.5 g, calcium carbonate - 3 g, potassium hydroorthophosphate - 1 g, iron sulfate - 0.1 g,agar 20 gr, water 1000 ml

6	Maltax environment 10 №1	1 % oduncaq yonqarı (opilka)– Maltax 10 – 50 q, aqar – 20 q, oduncaq yonqarı – 10 q, su - 1000 ml
7	Maltax environment 10 №2	3% sawdust (sawdust) - Maltax 10 - 50 g, agar - 20 g, sawdust - 30 g, water - 1000 ml
8	Maltax environment 10 №2	5% sawdust (sawdust) - Maltax 10 - 50 g, agar - 20 g, sawdust - 50 g, water - 1000 ml

Cultures were incubated in a thermostat at 27±1ºC, and growth diameter was measured daily. The measured areas are the shape of the colony, the pigmentation of the mycelium, etc. Daily weight loss (BA) was calculated using the following formula:

$$BA=D-d/2*t$$

Here D-colony diameter, d-inoculation block diameter, t- time of the cultivation Growth factor (GW) was calculated using the following formula:

$$GW= (D-d)*h*g/t$$

Here D-colony diameter, d-inoculation block diameter, h-colony height, g-colony completeness, t-cultivation time.
Sound generators were used to study the effect of low-frequency sound acoustic waves. The initial inoculum was affected by waves of 200, 1000 and 2000 Hs power. The exposure time was 60 seconds. The growth indicators caused by the effect of acoustic waves were measured in the above manner.

Results and discussion
Trametes hirsuta and Trametes versicolor representatives were characterized by a higher index during the screening of the selected species in previous studies according to many parameters, mainly growth rate and biomass yield during cultivation. For this reason, it was considered more appropriate to use these species in the studies we have mentioned.It should be noted that the growth rate of these strains is almost not behind any of the known strains considered promising in this direction, and in some cases it is even higher. For example, the amount of biomass produced by fungi such as G. lucidum, L. sulphureus, and P. ostretus, which are considered promising as producers of biologically active substances with various effects, does not exceed 4.6-8.0 g/l during the same period of time.
From the results obtained from the studies conducted in this regard, it was clear that the irradiation of the material used for planting with light exposure doses of 1.8 c and 0.36 c for 1, 2 and 3 hours leads to an increase in the biomass formed in both fungal strains, at which time the maximum effect is observed in both mushrooms at a light dose of 1.8 c, and in both cases it is considered more favorable to have an exposure time of 2 hours (Schedule 3-4). It is interesting that the increasing effect in both fungi is characterized by almost the same quantitative index, that is, in the optimal variant, the biomass yield increases by approximately 10.3% in both fungi. In our opinion, this can be considered as a fact that gives reason to note that the effect of light occurs with the same mechanism at the genus level in fungi.

Table 3. Influence of coherent light at different exposure doses.

Exposure dose	Exposure time (hours)	Biomass yield (5 days, DB, q/l)			
		Trametes hirsuta F-2		Trametes versicolor F-35	
		2 days	10 days	2 days	10 days
1,8	1	38	84	42	90
1,8	2	38	84	41	90
1,8	3	37	85	40	90
0,36	1	29	82	38	90
0,36	2	29	82	38	90
0,36	3	29	81	38	90
Control		29	80	37	88

Table 4. Influence of incoherent light at different exposure doses.

The power of the wave	The length of the wave	Biomass yield (5 days, DB, q/l)			
		Trametes hirsuta F-2		Trametes versicolor F-35	
		7 days	30 days	7 days	30 days
0,5	578	19	87	20	90
2	400	20	87	21	90
2	578	20	87	21	90
2	518	21	84	22	86
7,5	460	21	85	22	87
7,5	578	22	87	23	90
Control		18	79	19	82

It should be noted that since fungi are chlorophyll-deprived organisms, their relationship to light differs from that of higher plants, that is, light plays a different role in their life. According to some researchers, in some cases, for example, the formation of the fruit body is formed in the dark phase, that is, the absence of light is considered more effective for the process. From the obtained results, it is clear that light, especially its part located in the visible range, has a positive effect on fungi. Therefore, taking into account not only traditional parameters during the optimization process, but also those of this type promises new perspectives for obtaining higher results.

Another physical factor used in the studies was the effect of low-frequency sound on biomass yield. It became clear from the results obtained during the research conducted in this regard that this factor can be considered as one of the factors affecting the biomass yield in a certain sense,

but in this case, the increase in the biomass yield at the optimal dose does not exceed 6.3% (Table5).

Table 5. Influence of low-frequency sound on biomass yield in active producers.

Low frequency sound dose	Biomass yield (5 days, DB, q/l)	
	T.hirzuta F-2	T.versicolor F-35
200 Hs	8,1	7,8
1000 Hs	8,3	8,0
2000 Hs	8,5	8,3
Kontrol	8,0	7,8

Thus, in the course of the research and the obtained results, it became clear that the factors (low-frequency sound, different doses of visible light) that have not been paid enough attention during the optimization of the environment for the strains that produce a high amount of biomass can have a certain effect on increasing the effectiveness of such a process.

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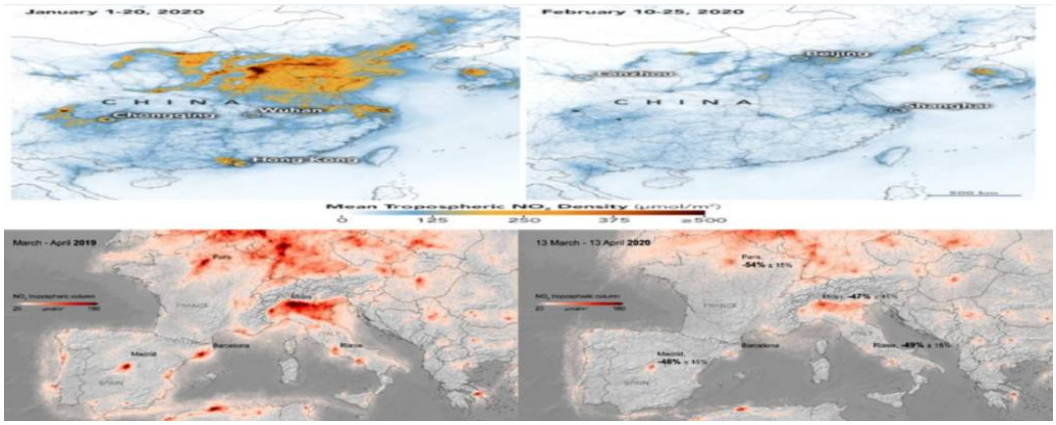

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