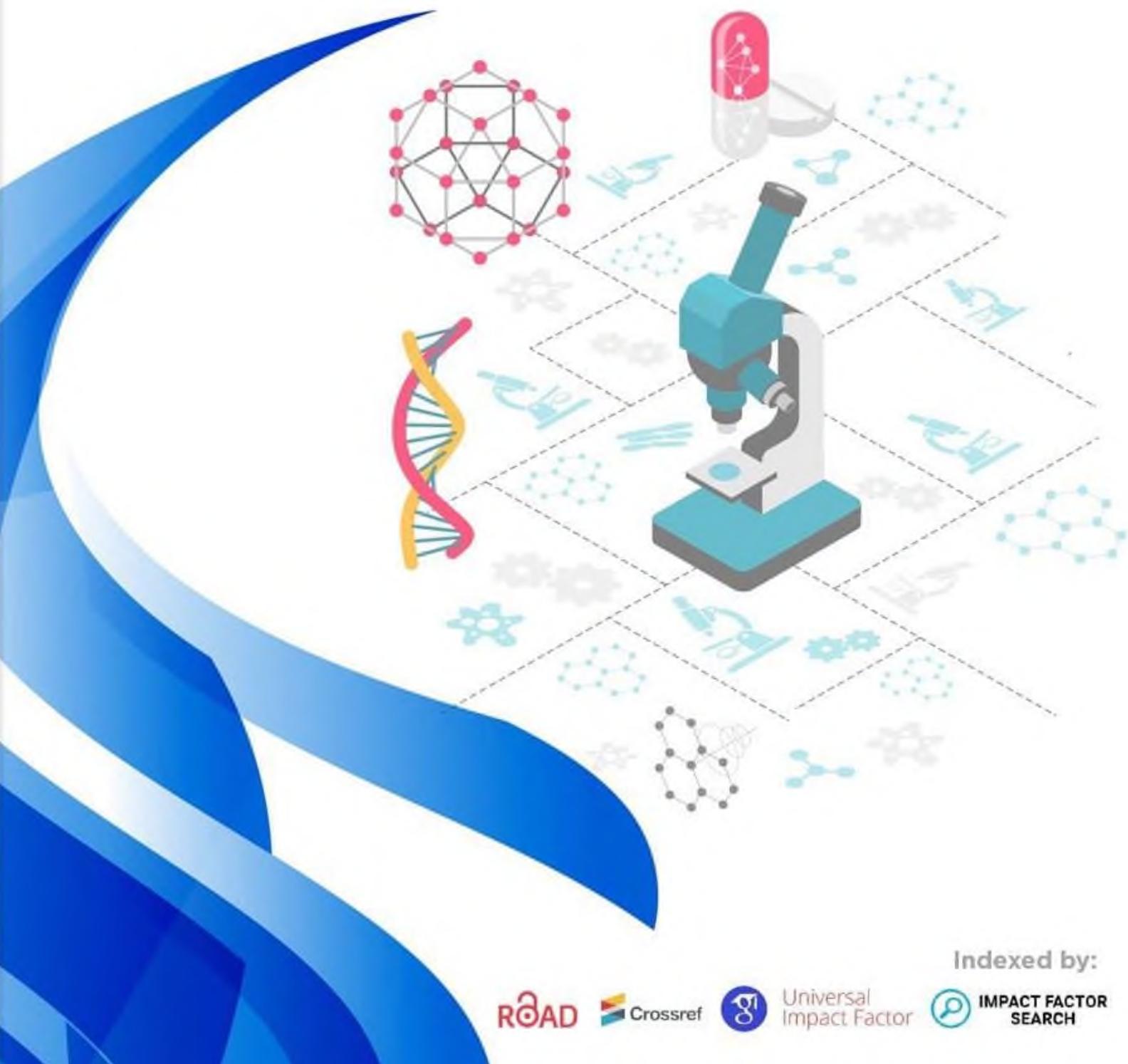


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Study of import-substituting drugs of hypertensive action based on medicinal plants

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Abstract. This report presents the results of a study of theoretical and experimental substantiations of the local pharmaceutical market for antihypertensive drugs. The literature data are generalized and systematized and the expediency of increasing the volume of import-substituting funds is shown. In addition, the results of studies to assess the prospects for the creation and use of antihypertensive drugs based on medicinal plants with the subsequent organization of production by domestic manufacturers of antihypertensive drugs based on natural raw materials, including medicinal balm, are presented.

Keywords: antihypertensive dosage forms, pharmaceutical market, technology.

Currently, comprehensive scientific research is being carried out all over the world to develop easy-to-use medicines and dietary supplements based on the complex use of medicinal plants with high therapeutic activity due to the synergy of biologically active substances contained in them.

Certain scientific results have been achieved in the republic in providing the population with guaranteed and high-quality medical care, in the development of medicines and biologically active additives from herbal compositions based on local medicinal plants with high therapeutic activity. In this bundle, special attention is paid to the identification of hypotensive, blood pressure-regulating properties. According to the World Health Organization, 65-70% of the adult population (aged 60-67 and over) has arterial hypertension.

The main goal of the pharmaceutical industry is to provide the population with safe, effective and especially affordable medicines for every patient. Currently,

domestic pharmaceutical companies are producing new effective drugs and are successfully competing with foreign drug manufacturers. For the development of modern pharmaceutical science, one of the important directions is the expansion of the range and the search for effective natural medicines, as well as on the basis of well-known, studied raw materials of plant origin [1].

Hypertension or arterial hypertension is a chronic non-infectious disease characterized by an increase in arterial blood pressure. And this, in turn, leads to an increase in the tone of important organs and pathology of the functions of blood vessels, heart, kidneys and central nervous system. Hypertension occurs mainly in people over the age of 40, but today hypertension as a disease is "younger" and occurs even among adolescents. Over 20% of the world's population suffers from this disease. An increase in blood pressure leads to vascular atherosclerosis, which is life-threatening for the patient.

Arterial hypertension is considered a factor causing heart ischemia, acute myocardial infarction, and cerebral stroke. 30% of mortality is associated with hypertension.

An increase in arterial blood pressure is often depends on the following factors:

- increased nervous tension and emotional stress;
- obesity, kidney disease, diabetes mellitus and other chronic diseases;
- use of salt in large quantities;
- working hours and noise;
- hypodynamic;
- bad habits (overeating, drinking alcohol, smoking).

It is known that in the treatment of a number of symptoms of cardiovascular diseases and the causes of their occurrence, medicinal plants are used on the basis of many years of traditional medicine practice. In most cases, medicinal plants are used separately or in the form of collections, from which other dosage forms are further prepared (extracts, tinctures, ointments, gels and phyto films, etc.) [1,5,6].

It has long been known the use of medicinal plants in folk medicine as antihypertensive (sedative) agents, indicated in the writings of Abu Ali ibn Sino and others. It should be noted the studies of domestic scientists H.Kh. Kholmatova, Kh.M. Komilov, F.F. Urmanova, U.M. Azizov, Kh.D. Kambarov on the creation of new antihypertensive drugs based on local medicinal raw materials. Scientific research on the development of antihypertensive drugs to study their action was carried out by foreign scientists N. Kreiger, L.H. Ople and others.

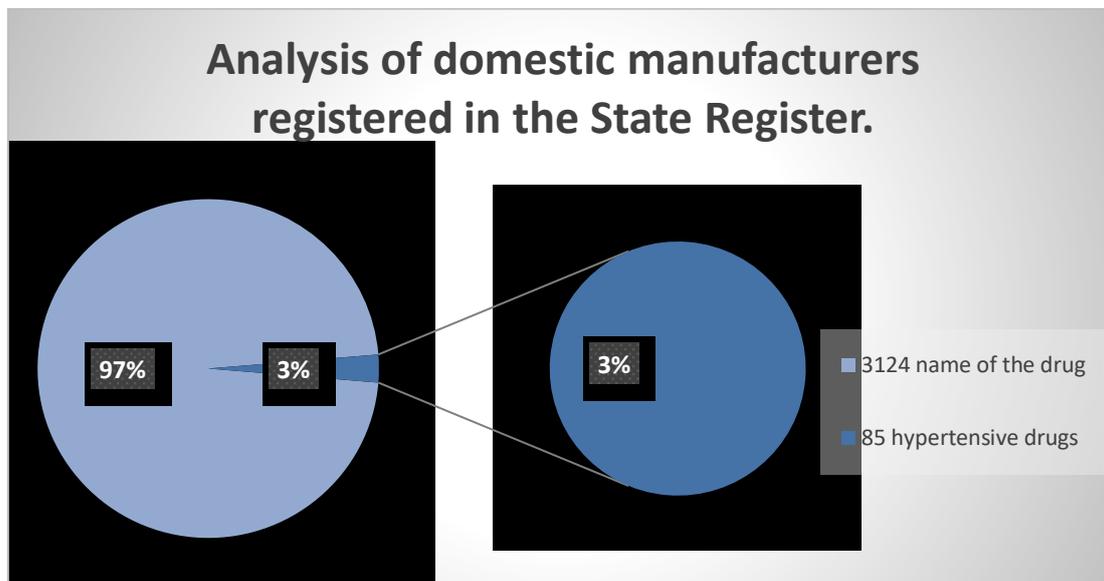
For example, Razzokova N.U., Safarova D.T. when creating a medicinal balm for the treatment of hypertension, a sufficient amount of dry extract from the leaves of lemon balm was obtained using a continuous spray dryer [5]. A biopharmaceutical evaluation of oleogel and ointments based on a liquid extract of the three-part marigold, dioecious nettle, field horsetail, as well as phytofilms containing liquid extracts of nettle and calendula, which have been used for many years by folk medicine as sedatives (marigold, calendula, field horsetail) [6].

Despite the significant progress in science in the development of new effective drugs for the treatment of arterial hypertension, there is an increase in this disease [2].

The aim of the work is to conduct scientific research on the study of the current state of the pharmaceutical market of antihypertensive drugs of the Republic of Uzbekistan, the analysis of herbal medicines registered in our country, the analysis of domestic and foreign literature, reflecting the importance of the production of herbal medicines, as well as the development of the composition and technology of a new antihypertensive drug on based on a combination of extracts of seven medicinal plants to create its dosage form of balm. As a result, it will make it possible to expand the range of domestic antihypertensive drugs.

A comparative analysis of medicinal hypertensive drugs registered in the State Register of the Ministry of Healthcare of the Republic of Uzbekistan (2021) was carried out. Data from domestic, CIS and foreign manufacturers were taken. The diagram below provides an analysis of domestic manufacturers (diagram 1).

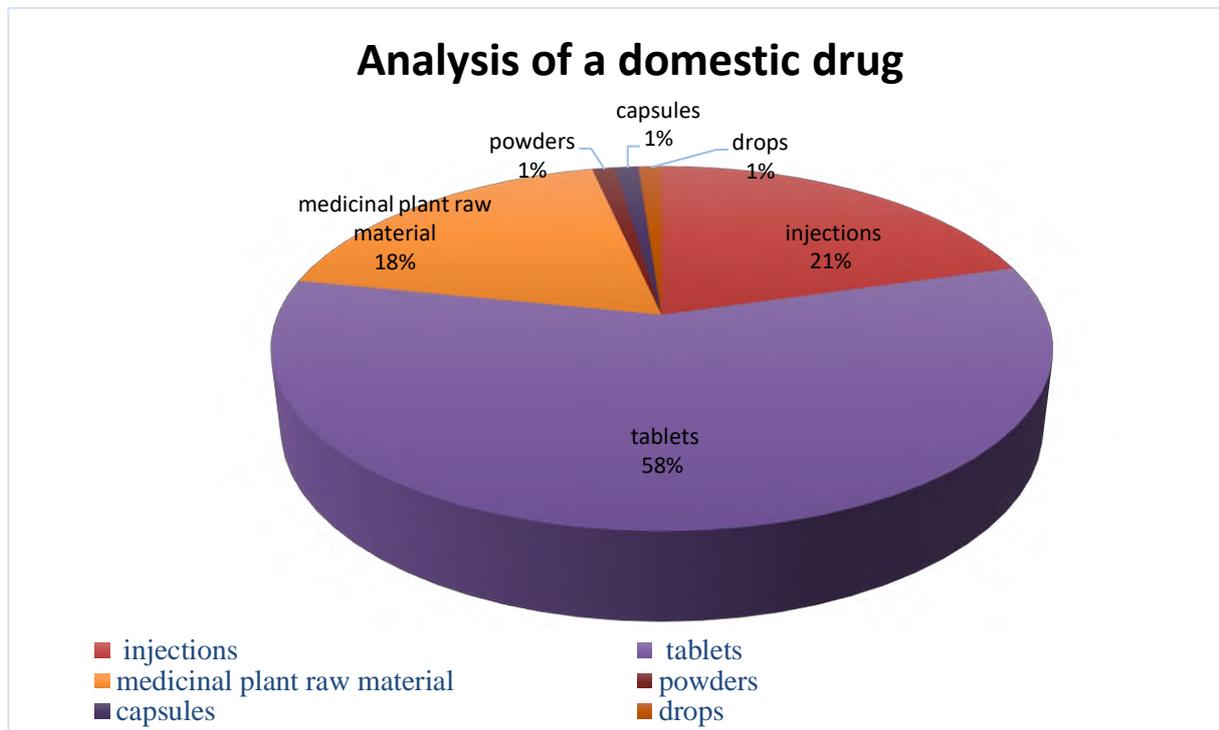
(Diagram 1)



The diagram shows that there are 3124 registered names of drugs, of which 85 are hypertensive drugs, which is 3% of the total registered number. In turn, 85 types of hypertensive drugs are produced by 48 domestic enterprises.

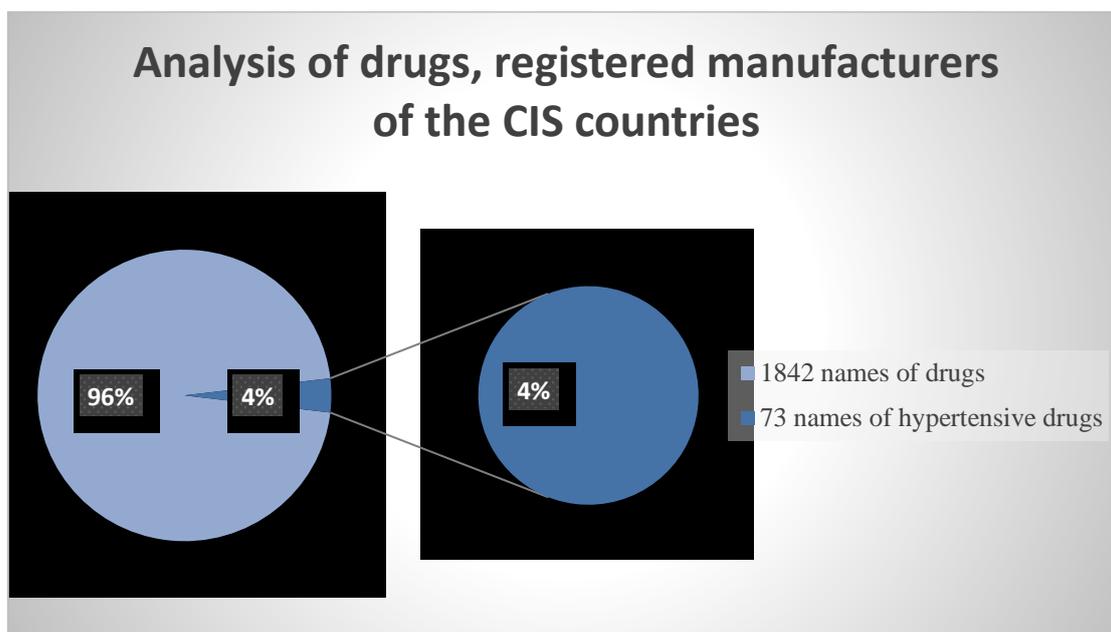
In the State Register of the Ministry of Health of the Republic of Uzbekistan № 25 in 2021, 85 names of hypertensive drugs of domestic manufacturers are registered, which is only 3% of the total amount (3124 units). If 85 names of hypertensive drugs are taken as 100%, of which the dosage form - tablets - 58%, injections - 21%, medicinal plant raw materials - 18%, powders, capsules and drops - 1%, and they are presented in diagram 2.

diagram 2



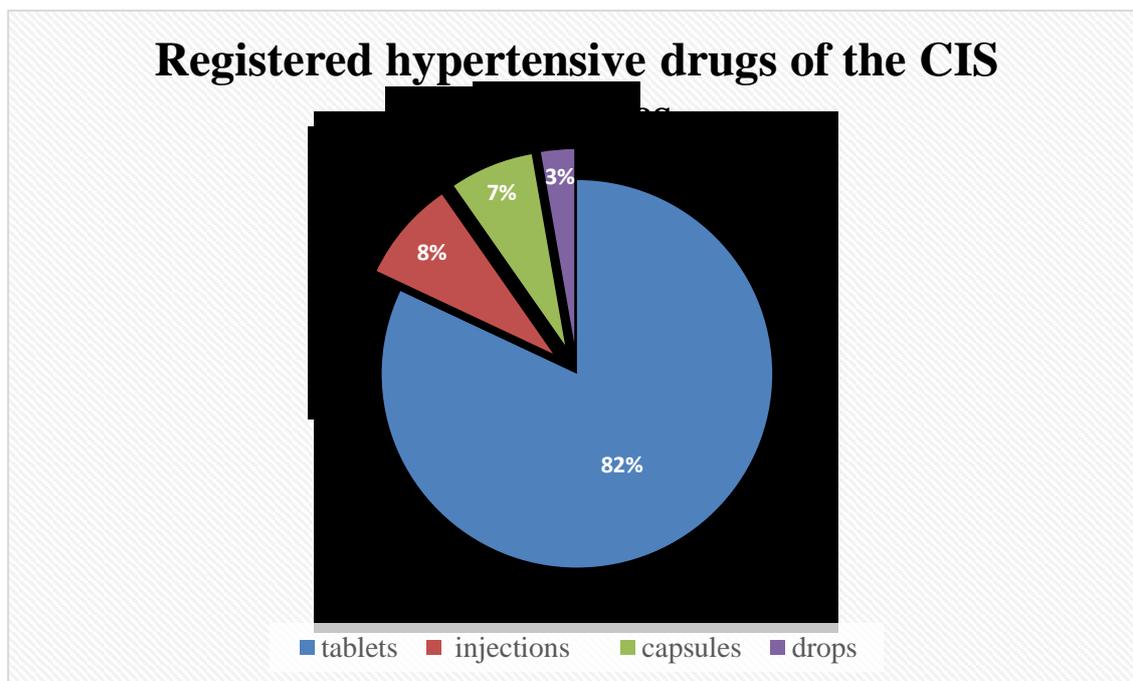
In the State Register of Medicines and Medical Devices (2021), 1,842 names of drugs from CIS manufacturers are registered, of which 73 are drugs of hypertensive action, which make up only 4% (Diagram 3).

diagram 3



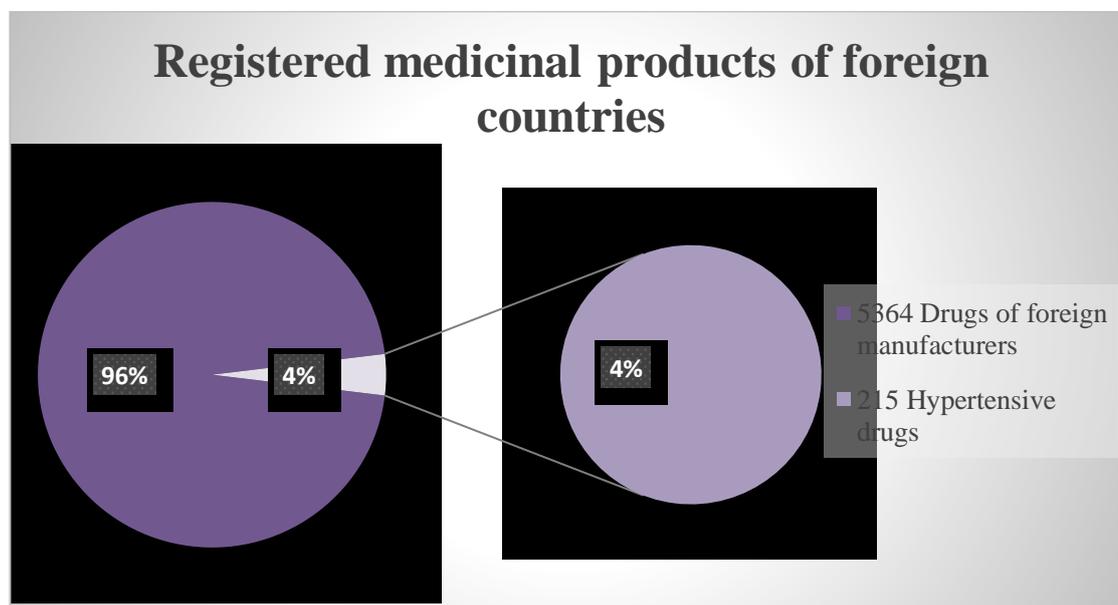
Moreover, hypertensive drugs in the dosage form tablets - 82% (59 items), injections - 8.2% (6 items), capsules - 6.8% (5 items), drops - 2.7% (items). (Diagram 4)

diagram 4



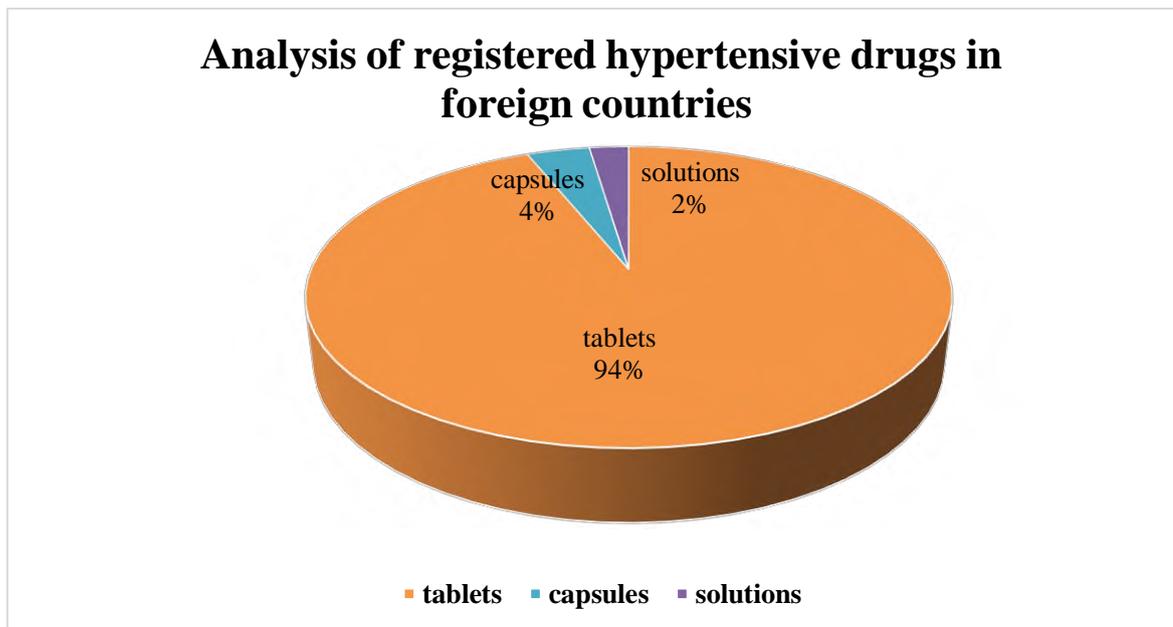
The state register of medicines and medical devices (2021) includes 5364 medicines of foreign manufacturers, of which: 215 are of hypertensive action and this is 4% of the total number of drugs (Diagram 5).

diagram 5



Of 4% (215 items) of hypertensive drugs, 94% (200 items) are tablets, 4% (8 items) are capsules: 2% (5 items) are solutions (diagram 6).

diagram 6



From the results of the study of the types of dosage forms produced for the treatment of arterial hypertension, which are presented in the diagrams, it can be seen that a significant part of 85-94% is taken by tablets. This is the most convenient dosage form, especially for elderly patients with arterial hypertension. In the next place are drugs injections - 8.2%. This is due to the need to quickly administer the drug for hypertensive crises, when a sudden increase in pressure occurs. Drops, solutions, syrups for oral administration occupy the 3rd place, about 2% of the total number of drugs used to treat arterial hypertension.

Thus, the analysis of the assortment of drugs used for the treatment of arterial hypertension is the basis for the formation of a rational and optimal assortment composition of new drugs being created. The systematization of the assortment of drugs for the treatment of arterial hypertension by production showed that most of the

commercial drugs for the treatment of arterial hypertension are registered by foreign companies - 94-96%. Domestic medicines account for only 4%.

In the conditions of ecological trouble, a promising direction is the correction of the states of maladjustment with the use of drugs of mild prolonged action, especially immunomodulatory agents that neutralize toxic substances. The use of balms has historical background and is an adequate preventive and complementary method in difficult environmental conditions.

The tasks of the research include the development of an original composition and methodology of a new generation of balm. Based on the achievements of predecessors, using the raw material base of the republic, an original recipe was created from 7 components for the preparation of phytoadaptogenic balsam, which contains safe plant species listed in table 1.

Table 1

The name of the medicinal plants that make up the balm for hypertension

№	Name of raw materials in Russian	Name of raw materials in Latin
1	Motherwort herb	Herba Leonuri cardiaca L.
2	Blood red hawthorn fruit	Fructus Crataegusganguinea L.
3	Rosehip Fedchenko	Fructus Rosae fedtschenko ana Regel
4	Leaves of lemon balm	Folium Melissaе officinalis L.

5	Columns of corn stigmas	Stigma Maydis
6	Rhizomes with Valerian officinalis roots	Rhizoma et radices Valerianae officinalis L.
7	Peppermint leaves	Folium Menthaepiperitae L.

When creating an antihypertensive drug (extracts and further balsam), as can be seen from Table 1, we used medicinal plants that are often used in such formulations and have sufficient reserves in the republic [3].

The selected herbal remedies for lowering blood pressure are usually plants with a wide range of effects, including on the digestive and excretory organs.

Lowering blood pressure by pharmacological drugs that block the mechanism of increasing blood pressure is a very important means for improving the patient's condition, for reducing the risk of cardiovascular complications. However, herbal medicine is a good adjunct to pharmacotherapy, because improves the condition of the digestive (stomach, pancreas, liver, gallbladder) and excretory (kidneys, intestines) organs.

Materials and methods: the research materials were medicinal plant raw materials that meet the requirements of regulatory documents. Based on the literature data on the chemical composition [3] and pharmacological properties [4], a recipe of 7 types of medicinal plant was chosen as the objects of study: motherwort herb, hawthorn fruit, rose hips, lemon balm leaves, columns with stigmas of corn, peppermint leaves, rhizome with the roots of Valerian officinalis [5].

In the proposed complex extract, the use of motherwort herb is recommended, containing bioactive substances (alkaloids-stachydrin, saponins, tannins, essential oil, bitter and sugary substances, flavonoids), which help lower blood pressure and slow the heart rate, has sedative properties [3,4].

The fruits of blood-red hawthorn contain anthocyanins, flavonoids, pectin substances, coumarins, triterpenic acids (ursolic and oleanolic), which have a

cardiotonic effect, are agents regulating blood circulation in atherosclerosis and cardiac neuroses [4].

Fruits of brown rosehip are used as a source of vitamins (C, B₂, E and K), flavonol glucosides, sugars, pectins, organic acids (citric, malic). They participate in redox processes, reduce blood cholesterol, slow down the deposition of atheromatous masses in blood vessels [3,4].

Lemon balm leaves contain essential oil, ascorbic acid, tannins and triterpenic acids. Together, they lower blood pressure, make heartbeats infrequent, and slow breathing [3,4].

Corn stigmas are a rich source of organic acids and carbohydrates; micro and macro elements, vitamins and essential oils, which are involved in metabolic processes, improve liver function [3,4].

Rhizomes with Valerian officinalis roots contain essential oil, sexviterpenes, nitrogen-containing and cessilic alcohols, tannins, sugars and organic acids. They enhance the process of inhibition in the cerebral cortex, reduce reflex excitability, and have a normalizing effect on the central nervous and cardiovascular systems [3,4].

Peppermint leaves contain an essential oil, the main constituent of which is menthol. The leaves contain carotene, hesperidin, betaine, as well as ursolic and oleanolic acids. They help relieve angina pain. The irritating and antiseptic effect of essential oil leads to limitation of the processes of decay and fermentation and increased secretion of the digestive glands [3,4].

Conclusions: based on the foregoing, an urgent solution would be the possibility of obtaining antihypertensive drugs by a rational combination of the given medicinal plant raw materials in the ascertained ratios of components, followed by a study of their pharmaco-toxicological properties.

References:

1. Ivaschenko A.A., Kravchenko D.V. The concept of innovative development of the domestic pharmaceutical industry //Remedium.-2008. - №.5. - pp.14-18
2. Fomina I.G. Arterial hypertension: clinical picture, diagnosis, treatment. Handbook / I. G. Fomin, Bragina A. E. -M.: MCFER, 2004.-p.336.
3. Kholmatov Kh.Kh., Akhmedov U.A. Pharmacognosy. Textbook "Medicine", Tashkent.-2007. - p.399.
4. Weiss R.F. Phytotherapy. Manual: per. from German / R.F. Weiss, F. Fintelmann. - M.: Medicine, 2004. - p.534.
5. Razzokova N.U., Safarova D.T. Dorivor limon o't (Melissa officinalis) o'simligidan purkab quritgich ukunasi yordamida quruq ekstrakt olish // IV International Scientific and practical conference "Abu Ali ibn Sino (Avicenna) and Innovations in modern pharmaceutics" May 20th 2021.-pp.91-92. –Tashkent city, Uzbekistan
6. Nazarova Z.A., Tureeva G.M., Faizullaeva N.S., Khusenova Sh.Sh. Makhalliy khomashyolar asosida olingan phytoapplikatsion dori vositalarini samaradorligini aniqlash // Pharmaceutical journ., 2019.- №3. - pp.52-57