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MAIN ASPECTS OF QUALITY CONTROL OF HOMEOPATHIC MEDICINES IN UKRAINE

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Today, according to the World Health Organization, adverse drug reactions are the fifth leading cause of death worldwide. Natural methods of treatment (for example, phytotherapy) have significantly fewer contraindications, but even they have their limitations. Priority is given to natural products, among which herbal and homeopathic medicines play an important role.

Homeopathic medicines have been used effectively for decades all over the world. Despite the significant achievements of modern organic chemistry and the production of high-quality synthetic biologically active substances, the popularity of homeopathic medicines is constantly growing, both in Ukraine and abroad. With the worldwide increase in the use of homeopathic medicines by the population and the rapid expansion of the world market, the safety and quality of homeopathic medicines have become an urgent issue for health authorities, the pharmaceutical industry and consumers. The production of homeopathic medicines is carried out in accordance with the rules of good manufacturing practice. The safety of homeopathic medicines mainly depends on their quality. Since the quality requirements of homeopathic medicines correspond to the general pharmacopoeial requirements for dosage forms, their production and quality control must be carried out in compliance with all the rules of good manufacturing practice, and quality control methods must be developed for each product, validated and included in the company's regulatory documentation.

Requirements for quality control of homeopathic medicines also depend on the content of active pharmaceutical ingredients in them, and quality control of the finished homeopathic medicine must be carried out both for the final product and for the initial, intermediate materials. Therefore, in order to organize the production of high-quality and safe homeopathic medicines, it is important to carry out in-depth research of raw materials and basic homeopathic medicines.

Key words: *quality control, identification, homeopathic pharmacy, medicines, good manufacturing practice.*

Лілія Вишнеvsька, Світлана Олійник, Ілона Коноваленко, Марина Буряк, Тетяна Ковальова, Катерина Ромась. Основні аспекти контролю якості гомеопатичних лікарських засобів в Україні

Сьогодні, за даними Всесвітньої організації охорони здоров'я, побічні реакції на ліки є п'ятою основною причиною смертності в усьому світі. Природні методи лікування (наприклад, фітотерапія, апітерапія) мають значно менше протипоказань, але навіть вони мають свої обмеження. Пріоритетними є натуральні продукти, серед яких важливу роль відіграють рослинні та гомеопатичні лікарські засоби.

Гомеопатичні лікарські засоби ефективно використовуються протягом останніх десятиліть у всьому світі. Незважаючи на значні досягнення сучасної органічної хімії та виробництво високоякісних синтетичних біологічно активних речовин, популярність гомеопатичних лікарських засобів постійно зростає як в Україні, так і за кордоном. Усесвітнє збільшення використання гомеопатичних лікарських засобів населенням та швидке розширення світового ринку, безпека та якість гомеопатичних препаратів стали актуальними питаннями сьогодення для органів охорони здоров'я, фармацевтичної промисловості та споживачів. Виробництво гомеопатичних лікарських засобів проводиться відповідно до правил належної виробничої практики. Безпека гомеопатичних препаратів переважно залежить від їхньої якості. Оскільки вимоги до якості гомеопатичних лікарських засобів відповідають загальним фармакопейним вимогам до лікарських форм, їх виробництво і контроль якості повинні здійснюватися з дотриманням усіх правил належної виробничої практики, а методи контролю якості повинні бути розроблені для кожного продукту, валідовані та включені в нормативну документацію підприємства-виробника.

Вимоги до контролю якості гомеопатичних лікарських засобів також залежать від умісту в них активних фармацевтичних інгредієнтів, а контроль якості готового гомеопатичного препарату має проводитись як для кінцевого продукту, так і для початкових, проміжних матеріалів. Тому для організації виробництва якісних та безпечних гомеопатичних лікарських засобів актуальним є проведення поглиблених досліджень сировини та базисних гомеопатичних препаратів.

Ключові слова: *контроль якості, ідентифікація, гомеопатична фармація, лікарські засоби, належна виробнича практика.*

Introduction. Today, according to the World Health Organization, side effects from pharmacological agents rank fifth among the causes of death in the world. In addition, they play a big role in the allergy of the population. Contraindications or limitations to the use of pharmacotherapy are often observed, and drugs can also cause toxic effects, as a result of which patients receive medication complications instead of a therapeutic effect. Antibiotics cause 40.6 % of cases of drug-induced illness. In second place are sulfonamide drugs – 17.9 % of cases. A high number of reactions to analgin (11.5 %) and painkillers (10.5 %). Medicinal diseases are caused by vitamins of group B – 8.6 %. Tranquilizers and hormonal medications are quite often the cause of drug-induced illness. Complications may also appear upon discontinuation of the drug (especially potent substances). (Fig. 1) [1; 2].

Natural remedies and methods of treatment (phytotherapy, apitherapy, etc.) have significantly fewer contraindications for use, but even they have their limitations. In Europe, 60 to 80 % of the population, in Ukraine, about 50 % of consumers give preference to natural preparations, among which the most important place belongs to herbal and homeopathic medicines.

At the same time, every year 100 billion dollars are spent on eliminating the effects of pharmacological agents in the USA alone, while homeopathic treatment remains available to everyone [2].

American and Canadian scientists are seriously investigating the phenomenon called "assignment cascade". Its principle is roughly as follows: receiving a prescription for medication from a doctor, the patient complains about side effects during the next visit, after which he receives several more prescriptions from the doctor. By the time of the third visit to the doctor, the number of his diseases increases again. After all, the more drugs are used, the greater the probability of a drug-induced disease [3].

The main priority direction of the state policy of Ukraine in the field of providing the population with medicinal products is the availability of affordable and high-quality medicinal products on the pharmaceutical market.

According to the Law of Ukraine "On Medicinal Products", a homeopathic medicinal product is any medicinal product manufactured from homeopathic raw materials in accordance with the procedure for the manufacture of a homeopathic medicinal product, defined by the State Pharmacopoeia of Ukraine or the

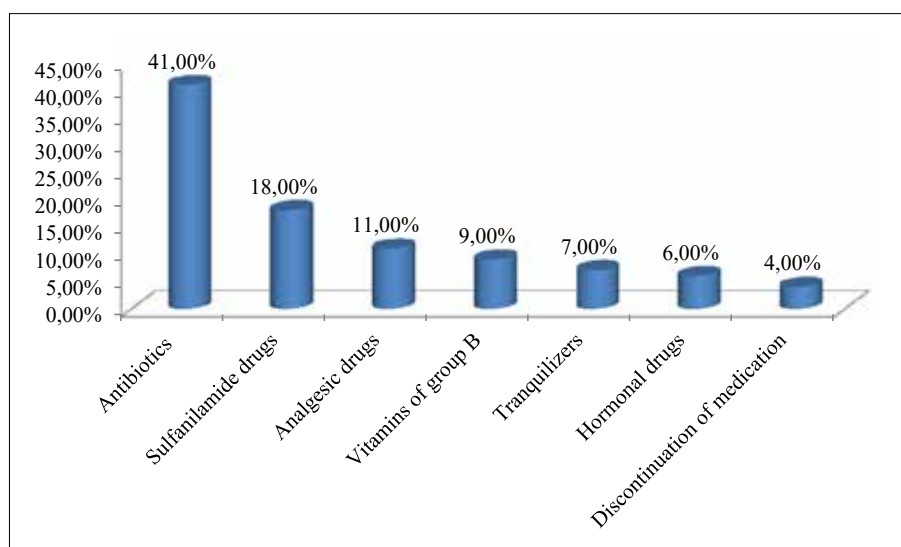


Fig. 1. The frequency of complications after taking drugs

European Pharmacopoeia, or in the absence of such a description – by the current official pharmacopoeias of the states – members of the European Union, Great Britain, the Homeopathic Pharmacopoeia of the United States of America. In Ukraine, homeopathic preparations have the status of medicinal products and are entered into the State Register of Medicinal Products as a separate pharmacotherapeutic group [4; 5]. Traditionally, most of them are manufactured in specialized pharmacies in the form of extemporaneous dosage forms. In addition, a wide range of homeopathic drugs is produced by a number of domestic manufacturers [4]. It should be noted that homeopathic medicines are made from basic preparations – substances, products or preparations, which usually represent for raw materials of plant, animal or human origin – matrix tincture or glycerin macerate; for raw materials of chemical or mineral origin – the substance itself [6]. Thus, basic drugs are used as starting materials for the production of homeopathic medicines, so a lot of attention of specialists and researchers of different countries of the world is paid to their quality control.

The purpose of the article. Conduct a problem-target analysis and summarize data on quality control of homeopathic medicines in Ukraine.

Methods of the research. Structural and logical, comparative analysis of literary sources.

Research results. Today, quality control of medicines, including homeopathic medicines, is among the most urgent health care problems around the world [7].

Quality control of homeopathic medicines is a set of legislative norms and rules that ensure at the state level the effectiveness and safety of medicines obtained by homeopathic technology from substances used in homeopathy [8].

The production of homeopathic medicines should be carried out only in accordance with the rules of good manufacturing practice – GMP.

Good manufacturing practice (GMP) guidelines regarding the manufacturing process, premises, personnel, packaging and labeling apply to both conventional pharmacotherapeutic medicinal products and homeopathic medicinal products. Failure to apply GMP requirements can lead to serious quality and safety issues such as misidentification, impurity of source material, cross or accidental contamination [9; 10].

The unique features of the manufacture of homeopathic preparations have a number of requirements for the mastery of specific skills and abilities of specially qualified and experienced personnel. They must handle toxic materials, especially fresh ones, and those prone to degradation processes and microbial contamination; as well as homeopathic preparations obtained from substances of animal and human origin. The pharmacotherapeutic properties of homeopathic medicines can be impaired during accidental or intentional contamination of starting materials, fillers or diluents, or containers in which dilution is carried out [11].

– In order for the manufacturer of homeopathic medicines to be able to guarantee the quality of the products, he must organize a control system consisting of a set of measures, namely:

- control of compliance of the original products with their specifications;
- control over the conditions of conservation and storage of raw products;
- control over the quality of the production procedure, in particular: production and storage of granules; production and storage of purified water;

storage of alcohol and alcohol-water solutions; production of matrix tinctures, glycerol macerates; production of breeding; saturation of granules;

– control over the condition of working areas and equipment;
– sanitary and hygienic control [8].

All these operations must take place under systematic supervision, which must be reflected in written protocols. We can hope that the implementation of all the listed organizational points in practice will make it possible to obtain a safe homeopathic medicine. However, the quality of the homeopathic medicine and its clinical effectiveness mainly depend on such points:

1) the original substance corresponds to the inscription on the label;

2) potentiation and dynamization are carried out correctly both quantitatively (number of shakings) and qualitatively (observance of shaking technology).

In order to identify the active substances in homeopathic preparations, attempts were made to identify the active ingredients of matrix tinctures and low potencies of homeopathic remedies in the world's largest production laboratories by the method of spectroscopy, high-performance liquid and thin-layer chromatography. The search for suitable analytical tests is ongoing [12].

In recent decades, there have been reports of changes in the nuclear magnetic resonance spectrum of high dilutions. NMR spectrophotometers and photocolimeters were used to study high potencies at the National School of Medicine and Homeopathy in Mexico City. An accurate fluorescent pattern of many polycrosses was obtained at high potencies that do not contain molecules of the starting substance. Studies based on pH measurements of such potencies were conducted [13]. Brazilian scientists described a method of checking the purity of the potencies of some substances

based on spectroscopy in ultraviolet light. Others tried to measure freezing point, redox potential, conductivity, boiling point, and density. But the development of these areas of research in homeopathy is slow. They require the use of complex and very expensive equipment [14].

Homeopathic medicines can contain substances in high potencies, so the requirements for their quality control will depend on the content of active ingredients in them, and the pharmaceutical analysis of the finished homeopathic medicinal form should be carried out not only for the final product, but also for the starting and intermediate materials, in order to compliance with product quality at all stages of production (Table 1) [7; 11].

In connection with the above (Table 1), special attention is paid to the quality control of the input raw materials, as it is not always possible to carry out qualitative and quantitative determination of active substances in the finished drug. Products that meet high quality standards are necessary to allow the patient to use homeopathic medicines safely. Currently, it is becoming more and more important, because due to globalization, a significant amount of raw materials and basic drugs used in the homeopathic production system are supplied from different countries of the world [9; 15].

The diverse origin of raw materials used in the production of homeopathic medicines requires a number of approaches to ensure the quality of the final product. During quality control, identification and, if necessary, quantification of raw materials (prior to processing) should be carried out using approved methods and appropriate analytical tests for the identity of raw materials. These tests should be pharmacopoeial [16].

The raw materials used for the manufacture of homeopathic preparations should be characterized by a number of indicators depending on the ori-

Table 1

Requirements for quality control of homeopathic medicines depending on the content of active ingredients

№	Content of active ingredients	Quality control requirements
1	Medicines containing active ingredients lower than C2 dilution	the same requirements apply as for medicinal products described in the Pharmacopoeia
2	Medicines containing active ingredients in dilution from C2 to C3	quality control after carrying out special methods of concentration by one of the suitable methods, based on its suitability
3	Medicines containing active ingredients in dilution from C4 to C6	quality control in the sample corresponding to the prescribed daily dose, in some cases – in the sample corresponding to the dose prescribed for the course of treatment
4	Medicines containing active ingredients higher than C6 dilution	quality is ensured by compliance with the technological process

Table 2

Quality indicators of raw materials of various origins for the manufacture of homeopathic preparations

№	Origin of raw materials	Quality indicators of raw materials
1	plant origin	scientific name, genus, species, subspecies/variety, family name
		ecotype, chemotype and phenotype
		applicable part
		material condition
		possible biologically active or toxic substances
		macroscopic and microscopic description
2	biological (animal) origin	description of the physical state of raw materials
		description of the anatomical state of the raw material
		description of the histological state of the raw material
3	mineral or chemical origin	characteristic of physical form
		characteristic of the structural formula
		relative molecular weight

gin of the raw materials (plant, animal or mineral) (Table 2).

Conclusions. The requirements for the quality of drugs based on ultra-small doses correspond to the general pharmacopoeial requirements for dosage forms, so their production and quality control must be carried out in compliance with all the rules of good manufacturing practice, quality control methods must be developed for each drug, which must be validated and included in the regulatory documentation of the enterprise.

If the composition of the homeopathic medicine includes active substances in low potencies, they can be analyzed according to the "identification" indicator, if in high potencies, it is recommended to evaluate homeopathic medicines according to the organoleptic and general quality indicators characteristic of this type of dosage form.

In order to organize the production of high-quality and safe homeopathic medicinal products, it is timely to conduct an in-depth study of the raw materials and basic homeopathic medicines.

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