

Treatment of allergic rhinitis: A review of homeopathic therapy

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ABSTRACT

Allergic rhinitis (AR) is a global health problem affecting more than 400 million people in our world. The constant increase in the incidence of AR is associated with an unfavorable environmental situation, social and family stress, unfavorable living conditions, improper nutrition, increased bad habits, intensive development of industry, chemicalization of production, agriculture, uncontrolled use of drugs. It should be noted that the risk of hay fever (pollinosis) occurs precisely at the age of 5–15 years in England, Denmark, and the USA. At the same time, 10-15% have symptoms of convenient rhinitis. The significant expansion of this disease increases the demand for anti-functional agents, which use one of the important segments of the pharmaceutical market. Understanding the pathophysiology and treatment methods is critical in the development of new homeopathic medicines. Homeopathic medicines have almost no side effects and remain a safe influence on the body. The range of modern homeopathic remedies for the prevention and treatment of AR on the pharmaceutical market of Ukraine is mainly represented by drugs of foreign production and the assortment does not meet the needs of consumers. Solving this problem is possible due to the expansion of domestic production of effective, safe and affordable homeopathic medicines.

Keywords: Allergic rhinitis, Pharmacotherapy, Pharmaceutical market, Homeopathy, Homeopathic drugs, Safe and effective methods of treatment

Introduction

Allergic diseases (AD) have been known to mankind since ancient times and occupy one of the leading places in the structure of human pathology. Over the past 30-40 years, the constant increase in the incidence of allergies has become a worldwide epidemic [1].

According to the epidemiological data of the World Health Organization (WHO), today, AD occupies one of the first places in the morbidity structure after cardiovascular and oncological diseases [2]. 20% of the European population has various allergic reactions, and in some environmentally unfavorable regions, it reaches 40-50%. According to forecasts of the European

Commission on Allergology, as early as 2025, every second inhabitant of the planet may suffer from allergies [3, 4].

Allergy (Greek “allos” - other, “ergon” - action) is a qualitatively changed reaction of the body to the action of any substances of an antigenic nature, associated with the restructuring of the immune system, which leads to various disorders in the body - inflammation, spasm of the bronchi, necrosis, shock, and other changes [5, 6].

In modern medicine, the following forms of AD are distinguished: angioedema, urticaria, anaphylactic shock, hay fever, allergic rhinitis (AR), allergic conjunctivitis, allergic dermatitis, etc. Over the past 20 years, the prevalence of such diseases as AR, atopic dermatitis, and bronchial asthma has increased significantly [7, 8].

According to the document developed by the specialists of ARIA (Allergic rhinitis and its impact on the asthma initiative) in cooperation with the WHO, AR is a global health problem and tends to constantly grow [9, 10].

AR is an allergic disease characterized by allergic (IgE-mediated) inflammation of the mucous membranes of the nose, which develops as a result of exposure to allergens in the mucous membrane of the nasal cavity [7].

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The analysis of literature data shows that during the last decade, the incidence of AR worldwide has increased by approximately 50%, and therefore AR is one of the most urgent problems of allergology [7, 9]. This is evidenced by:

- a significant decrease in the quality of life of patients, including work capacity, the ability to study, the ability to rest;
- economic damage caused by this disease;
- connection with sinusitis, damage to the eyes and, often, other organs;
- transformation of AR in a significant part of patients with bronchial asthma [3, 5].

According to statistics, AR affects 10-25 % of the world's population. In the USA, the number of allergy sufferers exceeds 40 million people, of which 25-30 million suffer from AR. In England, the prevalence of AR is 16 %, in Denmark – 19 %, in Germany – from 13 to 17 %. The results of epidemiological data conducted in different regions of Ukraine show that AR affects 4 to 30 % of the total population [7, 9].

Materials and Methods

In this work, information and search databases and scientific articles were used, as well as methods of system analysis, direct observation, and generalization of information. To evaluate the market of domestic and foreign homeopathic medicinal products, information resources were used: the State Register of Medicinal Products of Ukraine, electronic databases, and price lists of “Pharmacy 911” as of 03/02/2023. Graphical, comparative, statistical, and logical methods were used.

Results and Discussion

Clinical manifestations of allergic rhinitis

Symptoms of AR are similar to the common cold. But they are caused by an inadequate reaction to substances that are harmless to most people [11]. The immune system perceives them as invaders, reacting with inflammation [12, 13].

AR is characterized by hyperplasia of the mucous membrane of the nasal cavity. Patients complain of nasal congestion, sneezing attacks, abundant clear discharge of a seasonal nature, itching in the nose, irritation, redness, swelling of the eyes, and sometimes wide dark circles under them [12, 14]. Differences in manifestations of seasonal and year-round forms of AR are summarized in the **Table 1**.

Table 1. Characteristics of Allergic rhinitis

Characteristics	Seasonal Allergic rhinitis	Allergic rhinitis all year round
<i>Nasal congestion</i>	not permanent	always prevails
<i>Discharge from the nose</i>	watery, often	serous-mucous drainage in the nasopharynx, non-constant
<i>Sneeze</i>	always	not permanent
<i>Disorders of smell</i>	non-permanent	often
<i>Conjunctival symptoms</i>	often	not often
<i>Asthma</i>	inconstant	often
<i>Chronic sinusitis</i>	sometimes	often

Allergic inflammation spreads to the mucous membrane of the pharynx (irritated throat) and paranasal sinuses, sometimes weakness is manifested. With seasonal AR, the attack lasts for several hours, with year-round AR – usually several days or more. The cyclic nature of the disease is noted, and during the period of remission, the patient can completely normalize [10, 12, 15].

There are several stages in the course of AR:

- *vasotonic*, characterized by periodic nasal congestion associated with vascular tone disorders;

- *vasodilatation*, characterized by frequent nasal congestion, which is accompanied by dilation of the vessels of the nasal mucosa;
- *the stage of chronic edema*, characterized by constant nasal congestion; the mucous membrane of the nose acquires a bluish color;
- *hyperplasia*, characterized by constant nasal congestion, growth of the nasal mucosa, and formation of polyps.

Clinical manifestations and functional disorders caused by various biochemical mediators are presented in **Table 2** [16, 17].

Table 2. Biochemical mediators, functional disorders and clinical manifestations in Allergic rhinitis

Clinical symptoms	Biochemical mediators	Functional impairment
Itchy nose	Histamine, prostaglandins	Increased dryness of the mucous membrane, hyperemia of the nasal mucosa
Sneeze	Histamine, leukotrienes	Irritation of nerve endings
Nasal congestion, wheezing	Histamine, leukotrienes, bradykinin	Swelling of the nasal mucosa, increased vascular permeability
Constant, abundant secretions from the nose	Histamine, leukotrienes	Increased secretion of mucous and serous glands

Also, the distribution by severity of the course of the disease is based on the influence of AR on the quality of life of patients and the severity of the symptoms of the disease (**Table 3**).

The course of AR is defined as mild in those cases when the symptoms of the disease do not affect the patient's sleep and daytime activity, as well as professional activities and studies [18].

Table 3. Types of course of Allergic rhinitis

Indexes	Easy run	Moderate/severe course
<i>Sleep</i>	Normal sleep	Sleep disturbance
<i>Daily activity</i>	Normal daytime activity, sports, rest	Violation of daytime activity, limitation of opportunities for sports and recreation
<i>Efficiency</i>	Normal working capacity and ability to learn	Violation of working capacity and ability to study
<i>The severity of rhinitis symptoms</i>	Absence of very disturbing symptoms	Very disturbing symptoms

With a moderately severe form, the patient's sleep and daily activity are disturbed, and the quality of life deteriorates [19]. The severe form is characterized by painful symptoms that prevent normal sleep, work, sports, and rest [20].

Given the similarity of the structure and functioning of the mucous membrane of the upper and lower respiratory tracts, untimely therapy of AR can lead to the formation of symptoms of bronchial asthma. It is well known that from 20 to 38% of AR patients have asthma, while 60-78% of asthma patients have symptoms of rhinitis [16, 21].

Pharmacotherapy of allergic rhinitis

The main goal of AR therapy is to achieve complete control over the symptoms of the disease. Taking this into account, treatment is built taking into account the severity and frequency of rhinitis symptoms [22].

Treatment of AR patients includes:

- reduction of contact or elimination of the causative allergen;
- pharmacotherapy;
- allergen-specific immunotherapy;
- patient education.

Reducing contact with the allergen is the first and necessary step in the treatment of AR patients. The complex measures to

eliminate contact with allergens include reducing the concentration of aeroallergens in residential premises, eliminating pets, birds, cockroaches, and mold, and reducing contact with pollen allergens during the flowering period [23-25].

AR pharmacotherapy is aimed at eliminating the symptoms of the disease, inflammation in the nasal mucosa, and preventing the occurrence of irreversible changes in the form of thickening of the mucous membrane of the nasal concha and includes the use of the following main groups of drugs:

- antihistamine medications;
- glucocorticosteroids;
- mast cell membrane stabilizers (cromons);
- vasoconstrictors [26].

In combination, these agents affect such AR manifestations as itching/sneezing, nasal discharge, nasal congestion, and impaired sense of smell. The place of each drug is determined by its effect on various links of pathogenesis, the symptoms of the disease and their severity, as well as the age of the patient and the presence of diseases that limit the appointment of certain drugs. Taking into account these features, **Table 4** presents the AR treatment scheme [23, 26].

Table 4. Effectiveness of various drugs in the treatment of Allergic rhinitis

Group of drugs	Oral antihistamines	Local antihistamines	Local glucocorticosteroids	Local vasoconstrictors	Nasal cromons
<i>Rhinorrhoea</i>	++	++	+++	0	+
<i>Sneeze</i>	++	++	+++	0	+
<i>Itchy nose</i>	++	++	+++	0	+
<i>Nasal congestion</i>	+	+	+++	++++	+
<i>Eye symptoms</i>	++	0	++	0	0
<i>Start of action</i>	1 hour	15 min	12 hours	5-15 min	Variable
<i>Duration of action, hours</i>	12-24	6-12	12-48	3-6	2-6

Notes: «0» - no effect on the symptom;

«+» - little effect on the symptom;

«++» - moderate effect on the symptom;

«+++» - effective effect on the symptom;

«++++» - complete elimination of the symptom.

Antihistamine drugs remain the main pharmacological group in the treatment of AR, as they bind histamine receptors in blood

vessels and reduce the manifestations of the disease. Due to several serious side effects, antihistamines of the 1st generation

are not recommended for use in the treatment of AR. Drugs of the 2nd generation, which do not have a sedative effect, are in the widest demand. Local antihistamines in the form of an endonasal aerosol avoid most of the side effects inherent to oral antihistamines [27, 28].

Preparations of sodium cromoglicate belong to the means with low anti-inflammatory activity, in the form of a nasal spray, they prevent the appearance of new attacks.

Modern intranasal glucocorticosteroids are highly effective means in the treatment of AR. They have a pronounced anti-inflammatory effect, affect both the early and late phases of allergic inflammation, and are prescribed when treatment with antihistamines and cromolyns is ineffective [14].

Nasal vasoconstrictors – decongestants that “eliminate swelling” of the mucous membrane and nasal congestion, prevent stenosis of the natural openings of the paranasal sinuses and the development of sinusitis - are also considered to be "first aid" means for the treatment of AR. But decongestants do not affect the pathogenetic mechanisms of allergic inflammation and the most frequent side effect is the risk of drying the nasal mucosa [9, 29].

In addition, the use of vasoconstrictor drugs is possible for no more than two weeks in a row, since their effect weakens over time, and the treatment only increases swelling of the nasal mucosa, leading to atrophy of the mucous membrane and the development of a chronic process. It should be noted that all these drugs are chemical compounds, which is what causes side effects [12].

In Ukraine, the modern pharmaceutical market of drugs for the treatment and prevention of AR is mainly represented by foreign manufacturers (Figure 1), and only 33 % of the entire assortment consists of domestic products.

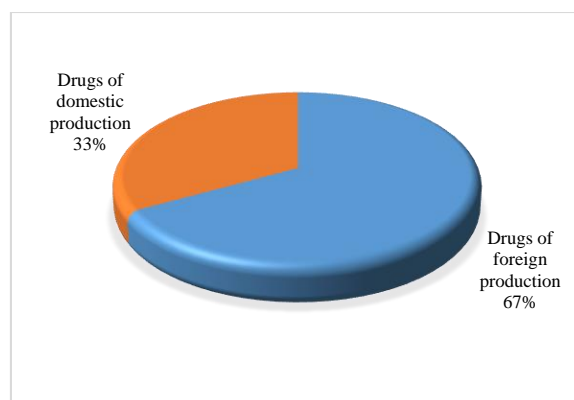


Figure 1. Mass share of drugs for the treatment of Allergic rhinitis by manufacturers

Therefore, the primary task of modern medicine and pharmacy is to increase the assortment of domestic drugs for the treatment of this pathology.

It may also be advisable to use several medical products (devices for washing the nose and nasopharynx) to prevent the occurrence or exacerbation of allergy symptoms.

In addition to the above groups of drugs, specific and sublingual immunotherapy are used to treat AR.

Specific immunotherapy (SIT) is a treatment method aimed at reducing the body's sensitivity to allergens. This type of therapy is indicated for patients suffering from AR with clearly identified allergens, in the absence of contraindications determined by an allergist.

The SIT course usually consists of an accumulation phase, when increasing doses of allergens are administered subcutaneously, and a phase of using maintenance doses of allergens, when extracts are administered at intervals of 1-2 months. An adequate course of SIT (3-4 years) can lead to the prolongation of disease remission [30].

Sublingual immunotherapy (SLIT) is also able to alleviate the symptoms of AR with allergies to house dust mites and plant pollen. The SLIT technique includes an accumulation phase followed by a maintenance phase at maximum doses when allergens are administered twice a week.

In addition, infusions, decoctions, and other forms of drugs (phytopreparations) obtained from medicinal plants are also widely used in AR therapy [31].

Despite a fairly large assortment of allopathic drugs, in the modern pharmaceutical market of Ukraine, drug therapy, unfortunately, is ineffective and sometimes dangerous in the treatment of such a widespread pathology as AR. Symptomatic drugs (adrenomimetics, antihistamines, glucocorticoids) cause only a temporary improvement in the condition, and have many side effects (Figure 2) [32].

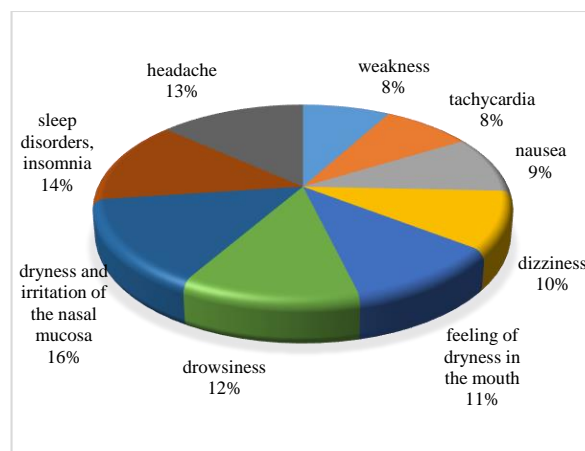


Figure 2. Mass share of side effects caused by modern allopathic drugs for the treatment of Allergic rhinitis

Medicines that dissolve stagnant masses in the nasal passages provoke new stagnation. Antibiotics contribute to the development of resistance of microorganisms, lead to dysbacteriosis, and weaken the immune system.

Nasal drops that reduce swelling dry the nasal mucosa, reducing the barrier functions of the epithelium, which increases the ability of microflora to penetrate still uninfected areas. Also, the side effects of antiallergic drugs are manifested in the form of depression of the central nervous system (CNS), increased blood clotting and blood pressure, ulcerogenic effects, etc. [12, 14].

In this regard, homeopathic therapy is an alternative to classical treatment schemes for this disease.

The main argument in favor of prescribing homeopathic drugs is the need to use anti-allergic drugs in long courses. In addition, these drugs are devoid of allergic effects on the body and have almost no side effects [33].

Thus, to date, the use of homeopathic drugs for the treatment of rhinitis of various etiologies is promising from a clinical and pharmaco-economic point of view, because in the first hours of the disease, it is quite difficult to establish an etiologically significant factor, and the patient's well-being requires the start of symptomatic therapy.

Use of homeopathic therapy in the treatment of allergic rhinitis

The requirements of modern therapy determine the relevance of research in the field of alternative areas of medicine, and the search for highly effective and safe methods of treatment of these diseases [34].

In contrast to the traditional pharmacotherapy of AD, homeopathic medicines are not inferior to official drugs in terms of effectiveness but can treat almost without the occurrence of side effects, toxic effects, and allergic effects on the body, which is especially important in the treatment of AD [33, 35].

In addition, the high efficiency of homeopathic medicines, ease of administration, complex effect on the body, and the possibility of use against the background of concomitant therapy are advantages when choosing the homeopathic method of treatment.

In addition, the natural components that are part of such drugs, due to the breadth of the pharmacological action and low toxicity, show a mild complex effect and less often cause side reactions than synthetic agents, which allows for long-term treatment of chronic diseases.

In recent years, more and more doctors and pharmacists are interested in the homeopathic method of treatment, and many patients prefer homeopathic treatment of diseases. Thus, 45 % of doctors in Great Britain, 32 % in France, and 25 % in Germany constantly use homeopathy in their practice. The number of such doctors is also growing rapidly in Ukraine. According to statistical calculations, 16 % of folk and non-traditional medicine specialists use homeopathy [36].

The basic principle of homeopathy "like cures like" has been known for more than one thousand years. However, the development of homeopathy as a medical system began with the research of the German physician, pharmacist, and chemist Christian Friedrich Samuel Hahnemann (1755-1843).

C. Hahnemann developed a system that consists in treating the whole organism as a whole, rather than individual symptoms. He conducted tests on about 100 medical devices, almost all of which are still widely used today. In addition, many new drugs have been discovered since Hahnemann's time [37].

Homeopathic treatment is carried out by strengthening the protective and adaptive reactions of the body specifically for this pathology, which naturally contributes to the completion of the pathological process and the development of a full-fledged response of the body to this disease. Homeopathic treatment

increases the body's resistance to adverse external and internal environmental factors. This is due to the draining, regulating, and immunomodulating effects that homeopathic medicines have on all body systems [38].

The production volume of the homeopathic industry has increased almost 10 times over the past 20 years in most countries. The number of homeopathic drugs manufactured abroad is 5-10 thousand names. A large number of homeopathic drugs from foreign and Russian companies are available in the pharmaceutical market of Ukraine. Also, over the past decades, homeopathic drugs developed by domestic companies have appeared, however minimal.

The development of the industrial production of domestic homeopathic medicines is carried out at a slow pace since the regulatory and legal framework for pharmaceutical homeopathic activity is extremely insufficient; problems of standardization and quality control of medicinal raw materials have not been resolved; there is no single nomenclature of homeopathic medicines approved for production, as well as a single supply center for basic drugs [39].

Currently, homeopathic medicines are classified as medicinal products (Law of Ukraine "On Medicinal Products" dated 04.04.1996). The regulatory and legal base of homeopathy in our country is represented by the State Medical Center (2nd ed.), as well as in order No. 165 "On the development of the homeopathic method of treatment in medical practice and the improvement of the organization of providing the population with homeopathic remedies" (from August 2, 1989), an appendix to which is the "Temporary list of homeopathic medicines recommended for use in a homeopathic pharmacy", which includes only 536 names (**Figure 3**) [40].

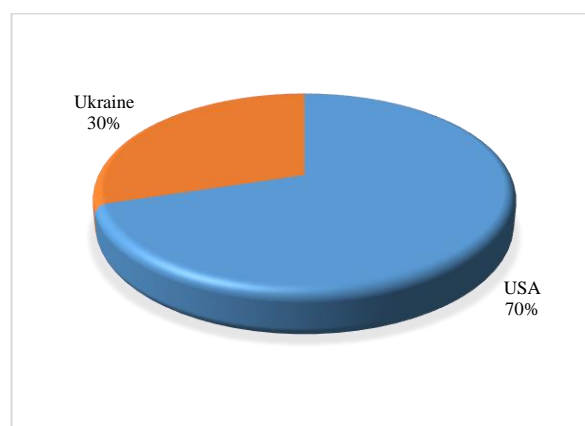


Figure 3. Number of homeopathic mono preparations registered in the USA and Ukraine

The data shown in **Figure 3**, shows that the Ukrainian market lags in the level of presentation of homeopathic medicines by at least 3 times. Thus, there is an obvious need for domestic homeopathic pharmacies to develop a modern legal framework and, first of all, to create a unified state nomenclature of homeopathic medicines.

In the period from 2012 to 2022 inclusive, there were about 100 trade names of homeopathic medicines in Ukraine, the main assortment of which is formed by 9 foreign manufacturers and

only one domestic one (“National Homeopathic Union”). The total share of domestic production is 20%, and foreign is 80% (Figure 4).

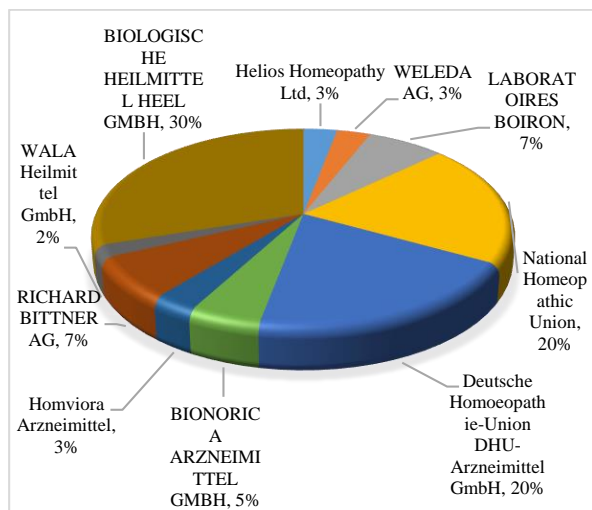


Figure 4. Assortment of homeopathic drugs by manufacturing companies

The study of the market structure of manufacturers of homeopathic drugs made it possible to identify the leading positions of the well-known companies “Heel” and “DHU” (Germany) – 30.7 and 18.8 % of the total assortment, respectively. The share of other foreign subjects in this market is in the range of 1.3 - 9.3 %. A comparative analysis of the assortment of domestic and foreign markets indicates that the nomenclature should be increased at least by 2-2.5 times to reflect the real needs of the pharmaceutical market of Ukraine. At the beginning of the 21st century, thanks to the achievements of modern medicine, molecular biology, microbiology, vaccine therapy, immunology, and allergology, the position of C. Hahnemann, formulated in 1810 in the book “Organon of the Medical Art”, became clear and found an explanation. Hahnemann wrote: “It is likely that certain drugs can treat symptoms similar to those they can cause” (“Similia Similibus curantur”). After repeatedly testing more than 2,000 natural minerals, acids, salts, plants, poisons, and toxins and obtaining an individual clinical picture of medicinal diseases for each case (including repeatedly reproduced pollinosis), he took as the basis of treatment ultra-small doses of the same substances as the essence of the treatment of each from diseases. Hahnemann pathogenetically substantiated the principle of similarity - an obligatory and necessary law of homeopathy, and, as can be seen from the further development of medicine, it became the basis of vaccine prevention and vaccine therapy, as well as one of the most promising directions of modern allergology - specific immunotherapy of AD, as a method of alleviating symptoms for certain time allergies (histamine blockers, mast cell membrane stabilizers). According to Hahnemann, to cure a disease means to make a “Homeopathic diagnosis”, to find the drug, mineral, substance, or plant from the homeopathic pharmacopeia (Materia Medica) that best reproduces the picture of the disease observed in a given patient, down to his mental sensations, vegetative and hormonal changes. This is what modern allergen vaccination

seeks and is based on, in the search for a substance that causes allergic rhinitis, asthma, and dermatitis [36, 40].

The second ingenious prediction of Hahnemann is the use of ultra-small doses, sub-physiological, sub-minimal, sub-pharmacological, i.e. intact healthy organs, and tissues, which are obtained thanks to multiple dilutions of medicines in tens, hundreds, thousands of times in carriers (water, alcohol), i.e. we see the same dilutions, which official medicine took as a basis, producing vaccines and allergens for non-specific immunotherapy. Finally, the classic method of introducing homeopathic medicinal substances into the body is sublingual, and in the last decade subcutaneous, intramuscular, and intravenous. As we can see, modern allergology has completely repeated Hahnemann in this regard, having come to sublingual, intranasal-specific immunotherapy with allergens in the letters of recommendation [35, 37].

Treatment with ultra-small doses of official medicines, proposed in homeopathy, has been confirmed in research in recent years in pharmacology: the high efficiency of diluting histamine (D12), and cortisone (D13, D28) in inhibiting allergic reactions has been proven. Dilution of penicillin 1:100000000 in the experiment delayed the growth of bacteria.

The mechanism of action of complex homeopathic drugs in low dilutions (D1–D14), which are also used for the treatment of AR, has not been sufficiently studied until now [38].

The experimental studies of Professor Hartmuth Hein (1998) were the first to study potentiated (D2-D6) substances of plant and animal-organic origin, and it was proved that these potencies give a high synthesis of TGF- β cytokine of Th3 lymphocytes in whole blood culture, indicating anti-inflammatory and analgesic effect [41].

If we take into account that most of the drugs used in the treatment of AD in homeopathy can reproduce in significant concentrations the symptom complex of AD of the nose, eyes, and mucous membranes of the upper and lower respiratory tract, and cause skin allergies, which was recorded and described in the studies of Professor Hartmuth Hein, then low concentrations of these drugs in dilution D1-D14 will be used (according to the principle of homeopathy) for the treatment of an allergic symptom complex that a particular patient has. Homeopathic medicine in potencies D1–D14 contains a sufficient amount of substance to stimulate macrophages to produce an antigenic response after entering the body. This is a prerequisite for the synthesis of Th3 regulatory lymphocytes. Th3 cells chemotactically detect anti-inflammatory lymphocytes (T4, Th1, Th2) with similar antigenic responses and suppress them through TGF- β synthesis [41, 42].

Professor Hartmut Hein showed that a homeopathic preparation containing proteins of vegetable (animal) origin in medium or low potencies contacts macrophages (as well as macrophage-related M-cells of the intestinal mucosa). Then these proteins lyse macrophage proteosomes, and a part in the form of an oligopeptide of 5-15 amino acids appears as a response on the surface of an antigen-presenting cell (APC), bound by proteins of the histocompatibility complex – class II (the main histocompatibility complex (MHC – Major Histocompatibility

Complex), in humans it is called the HLA system (Human Leukocytes Antigens) [41, 43].

The next stage is unmotivated T-lymphocytes (naive), which are transported, perceive the response of the MHC complex, bind them to their receptors, and become regulatory anti-inflammatory Th3 lymphocytes.

In the nearest lymph node, according to the number of responses, they undergo the cloning stage of Th3 regulatory lymphocytes. This reaction occurs only in the potency range of about 1–10 µg/kg body weight/day (Very low dose antigen). High concentrations of proteins prevent the formation of Th3 cells. At medium (starting from D15) and high potencies, the formation of “responses” does not occur, since macrophages are not activated [33, 42].

“Motivated” Th3 cell clones from the lymph nodes travel throughout the body via the bloodstream and lymphatic system. Th3 cells (chemokines, factors of the complement system) are chemotactically attracted to the source of inflammation and are met with inflammation by T4 lymphocytes and their subpopulations Th1 and Th2 – cells that also carry “responses” (antigens of the focus of inflammation). When Th3 and Th1, Th2 responses are similar (even approximate) (molecular-biological principle of similarity – Similia), there is an immediate release of Th3-lymphocyte cytokine - tissue growth factor - TGF-b (transforming growth factor).

This cytokine affects the downregulation of inflammatory lymphocytes, and the IL-4 and IL-10 released by them support the synthesis of TGF-b again, which is clinically manifested by the anti-inflammatory and analgesic effect of complex homeopathic drugs [41, 44].

TGF-b binds to cell receptors Th1 and Th2, inhibits IL-1 expression, and induces the synthesis of IL-1 receptor antagonists, which suppresses the synthesis of other pro-inflammatory cytokines. TGF-b-producing Th3 lymphocytes have a low-level regulatory effect on anti-inflammatory cells (macrophages, Th1) and the inflammatory cytokines synthesized by them (interferon, interleukins, and TNFα) and nitric oxide (NO₂). TGF-b stimulates Th2 cells to increase the synthesis of anti-inflammatory interleukins (IL-4, IL-10), and IL-4 reactivates Th3 cells. Cell-stimulated interleukins (IL-4, IL-5, IL-6, IL-13) from Th2 cells lead to stimulation of antibody synthesis (IgG, IgM, IgA) [43, 44].

Thus, potentiated complex drugs were selected taking into account the maximum similarity of inflammatory manifestations in the patient, corresponding to the modern directions of development of immunology.

Achievements of modern allergology, studies of the mechanisms of specific allergy vaccination (SAV) (which is a classic homeopathic drug) show that, on the one hand, the number of IgG (blocking) and not IgE antibodies increases during SAV, or T-lymphocyte tolerance is formed. But SAV still acts on all pathogenetically significant links of allergic inflammation, maintaining its effect for a long time. This ability is not found in any of the known pharmacological preparations. As you can see, there is a deep commonality, almost identity, with homeopathy, one of the modern and effective, pathogenetically appropriate

methods of treatment with allergens. This is the best proof of the necessity and validity of the use of the homeopathic method in the modern therapy of AD in children. It is AD (atopic dermatitis, allergic rhinitis, bronchial asthma) that is a homeopathically well-proven pathology [41, 44].

Therapy with complex homeopathic drugs is a multi-stage treatment. First, treatment of an acute crisis according to the principle of similarity, taking into account the so-called modality (time of day of the attack, the influence of temperature on the occurrence, nature of eye damage, damage to the nasal cavity - congestion, discharge, and their nature, presence of pain, itching, its localization; conditions of deterioration or improvement). Elimination of acute crisis with maximally similar drugs is replaced by therapy with a basic constitutional remedy, which can completely cure chronic diseases. As we can see, Hahnemann also predicted in this regard that immunological markers of atopic, autoimmune types of constitutions, which are now well-known to immunologists and allergists, would be proven and determined. The choice of the basic drug is based on a set of personal somatic and mental symptoms, and basic and preventive therapy is carried out with it [36, 45].

Currently, complex homeopathic drugs intended for doctors of traditional medicine are widely used for the treatment of patients. When developing complexes of anti-allergic therapy, it is understood that such diseases affect several organs and systems, therefore, drugs are selected that act as irritants on several systems and organs, and with pathomorphological and pathophysiological changes characteristic of allergies, and so-called drainage agents are also introduced. which enhances the elimination of intermediate metabolic products from the body, eliminating endogenous intoxication [37, 40, 45].

The homeopathic principle of treating AD, in addition to eliminating the symptoms of the disease (which is typical for official remedies), is also aimed at stimulating the metabolic and immunological processes of the body.

Homeopathic medicines allow you to eliminate the allergic disposition of the body, and reduce the threshold of sensitivity to allergens while maintaining a normal reaction of the immune system to a threatening danger [46].

Official medicine, at the first manifestations of AD, recommends the use of antihistamine drugs that block the immune response to the recognized allergen. Homeopathy, while not denying the usefulness of the use of these drugs, proceeds by eliminating increased sensitivity to the allergen.

An important property of homeopathic medicines is the almost complete absence of contraindications and the possibility of their use in almost all population groups. This is especially important for people with concomitant pathologies and people receiving etiotropic therapy in the treatment of these diseases [47].

Homeopathic medicine long ago became the norm and the basis of all allergology in the form of specific allergy therapy using extremely small (decimal) dilutions of the main allergens that cause allergic manifestations in the patient.

The presence of allergies indicates the instability of the immune system. Homeopathic treatment of RA takes into account the entire clinical picture, taking into account etiological factors, and

consists of two stages: treatment of an exacerbation and the appointment of a constitutional homeopathic medicine. Correctly selected basic constitutional treatment allows you to prevent seasonal exacerbations of AR and significantly reduce the burden of pharmacological agents on the body [33].

If we take into account that most of the Homeopathic medicines used in the treatment of AD are capable of reproducing in significant concentrations the AD symptom complex of the nose, eyes, mucous membranes of the upper and lower respiratory tract, skin, which is recorded and described in the homeopathic reference books “Materia Medica”, then low concentrations of these drugs in the dilution of X1-C6 are used (according to the principle of homeopathy) for the therapy of an allergic symptom complex [48].

Therefore, the primary tasks of pharmaceutical homeopathy are:

1. development of the composition and technology of new homeopathic drugs;
2. creation and improvement of the regulatory framework regulating the production and quality control of homeopathic medicines;

3. creation and continuous development of a pharmacy and production base for the manufacture of homeopathic medicines;
4. improvement of modern methods of quality control;
5. active participation in the scientific development of the theoretical base of the homeopathic treatment method [49].

In the pharmaceutical market of Ukraine today, you can buy several foreign complex homeopathic medicines for the treatment of AR, which is in great demand among the population, and only 1 drug of domestic production “Ryno-gran” (Table 5).

All of the above-mentioned drugs have a complex effect on AD, besides, their quantity is insufficient and the assortment is mainly represented by drugs of imported production, which does not meet the needs of consumers.

Table 5. Homeopathic medicines for the treatment of Allergic rhinitis

Name / Manufacturer	Medicinal form	Active substances	Indications for application
Euphorbium composite nazentropfen C / <i>Biologische Heilmittel Heel GmbH, Germany</i>	Aerosol	Euphorbium D4, Pulsatilla pratensis D2, Luffa operculata D2, Mercurius bijodatus D8, Mucosa nasalis suis D8, Hepar sulfuris D10, Argentum nitricum D10, Sinusitis-Nosode D13.	Viral rhinitis, bacterial rhinitis, allergic rhinitis, hyperplastic rhinitis, atrophic rhinitis, ozena, adenoids, sinusitis (sinusitis), otitis
Rhinital / <i>Deutsche Homoeopathie-Union DHU-Arzneimittel GmbH, Germany</i>	Drops Sublingual tablets	Luffa operculata D4, Galphimia glauca D3, Cardiospermum D3.	Hay fever (pollinosis) and year-round allergic rhinitis
Rhino-gran / <i>National Homeopathic Union, Ukraine</i>	Homeopathic granules	Allium cepa C200, Arsenicum album C100, Sabadilla C30.	Allergic runny nose with liquid discharge, sneezing
Delufen / <i>Richard Bittner AG, Austria</i>	Nasal spray	Sinapis nigra D2, Euphorbium D6, Pulsatilla D6, Luffa D12, Mercurius bijodatus D12	Local treatment of runny nose (rhinitis, rhinosinusitis) of any etiology (infectious, viral or bacterial, vasomotor, allergic, including hay fever, hay fever) and form (acute, chronic, hypertrophic, atrophic); inflammation of the auditory tube (eustachitis)
Sinupret / <i>Bionorica SE, Germany</i>	Syrup Oral drops Tablets for internal use	Radix Gentianae, Flores Primulae cum Calycibus, Herba Verbenae, Herba Rumicis, Flores Sambuci	Гострі та хронічні запалення приносових пазух носа
Corysalia / <i>Boiron, France</i>	Tablets for internal use	Allium cepa 3CH, Belladonna 3CH, Gelsemium 3CH, Kalium bichromicum 3CH, Pulsatilla 3CH, Sabadilla 3CH	Symptomatic treatment of acute respiratory viral infections and rhinitis
Famulan / <i>Richard Bittner AG, Austria</i>	Oral drops	Allium cepa D1, Euphrasia D6, Sabadilla D6, Kalium iodatum D12, Arsenicum album D12	Allergic diseases of various etiology and their manifestations: allergic rhinitis, allergic conjunctivitis

Also, in homeopathic practice today, the following homeopathic mono preparations are used for AR therapy: Allium cepa, Arsenum iodatum, Arsenum album, Bromium, Dulcamara, Euphrasia, Sabadilla, Scilla, Wyethia, etc. [50]. Homeopathic

mono preparations used in AR therapy: Allium sulfur – acute rhinitis, burning in the nose, mouth, throat, and skin, hay fever (pollinosis); Arsenum iodatum – rhinitis, painful sneezing, burning in the throat and larynx, swollen tonsils; Arsenum album

– rhinitis with nasal congestion and burning sensation, sneezing, epistaxis; Bromium – rhinitis with soreness of the nose, swelling of the wings of the nose, a tendency to thickening of the lymph nodes; Cyclamen – acute rhinitis with nasal congestion, painful sneezing, hay fever (pollenosis), itchy eyes; Dulcamara – nasal congestion, runny nose, Quincke's edema, and urticaria; Euphrasia – rhinitis with severe cough and conjunctivitis, swelling, itching of the eyes, clouding of the cornea of the eyes; Sabadilla – spastic sneezing with a runny nose, pain in the forehead, redness of the eyes with tearing, allergy to house dust, animal fur; Scilla – constant violent sneezing with rhinorrhea; Wyethia – Hay fever with very severe itching and tickling in the throat.

The range of mono preparations for the treatment of this disease is limited and is represented only by pharmaceutical products. Additionally, among these drugs, only *Allium cepa* and *Cyclamen* have a sufficient raw material base in Ukraine.

Therefore, the number of the above-mentioned drugs is insufficient to meet the modern needs of consumers. Therefore, the solution to this problem is possible due to the expansion of domestic production of effective, safe, and affordable homeopathic medicines.

Thus, the noted prevalence of AD increases the demand for antiallergic drugs, which occupy one of the important segments of the pharmaceutical market, and the creation and research of new homeopathic drugs for the prevention and treatment of AR is an important issue in the development of homeopathic technology and pharmacotherapy at the current stage.

Conclusion

The high prevalence and constant increase in the frequency of AD all over the world put the problem of treatment and prevention of patients with AR among the most urgent healthcare problems. In this regard, it is very important to choose the right drugs for the treatment of AR, which will have a wide spectrum of pharmacological and therapeutic effects, low toxicity, and will not cause drug dependence syndrome. In this aspect, it is advisable to use alternative methods of treatment, namely homeopathic therapy. In addition, homeopathic medicines are made from raw materials of natural origin, which reduces the likelihood of side effects. Analysis of the state of the Ukrainian pharmaceutical market of homeopathic drugs for the treatment of allergic diseases of the nasal cavity showed that the pharmaceutical market of domestic drugs is limited and does not meet the needs of consumers. This article aims to provide an overview of the pathophysiology, and available treatment options, namely homeopathic medicines.

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