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**QUALIFICATION WORK**

on the topic: «**ANALYSIS OF THE RANGE OF ANTI-ALLERGIC DRUGS IN UKRAINE AND THEIR COMPARATIVE CHARACTERISTICS»**

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## АНОТАЦІЯ

Кваліфікаційна робота присвячена аналізу асортименту антиалергічних препаратів на фармацевтичному ринку України та їх порівняльній характеристиці. У роботі проведено порівняльний аналіз ефективності, безпеки та клінічних аспектів застосування різних груп антиалергічних лікарських засобів. Робота складається зі вступу, основної частини (огляд літератури, методи дослідження, результати дослідження та їх обговорення), висновків, списку використаних джерел та містить 50 сторінок, 6 таблиць, 3 рисуни, 44 посилання на джерела літератури.

*Ключові слова:* антиалергічні препарати, фармацевтичний ринок, асортимент препаратів, доказова база.

## ANNOTATION

The qualification work is devoted to the analysis of the assortment of antiallergic drugs on the pharmaceutical market of Ukraine and their comparative characteristics. The work provides a comparative analysis of the effectiveness, safety and clinical aspects of introduction of different groups of antiallergic drugs. The work consists of an introduction, the main part (literature review, research methods, own research and their discussion), conclusions, a list of used sources and contains 50 pages, 6 tables, 3 figures, 44 references.

*Key words:* antiallergic drugs, pharmaceutical market, assortment of drugs, evidence base.

**LIST OF CONTENTS**

## ABBREVIATION LIST

Ig – immunoglobulin

AAD – antiallergic drug

ASIT – allergen-specific immunotherapy

BP – blood pressure

BA – bronchial asthma

WHO – World Health Organization

BBB – blood-brain barrier

GCS – glucocorticosteroids

IL – interleukine

IHD – coronary heart disease

LT – leukotrienes

INN – international nonproprietary name

MOH – Ministry of Health

NA – noradrenaline

PG – prostaglandins

SE – side effect

Tx – T-helper cells

cAMP – cyclic amino monophosphate

cGMP – cyclic guanidine monophosphate

CNS – central nervous system

HR – heart rate

GIT – gastrointestinal tract

# INTRODUCTION

**Relevance of the topic.** Allergic diseases are an important clinical problem of medicine, the significance of which is due to the increase in their prevalence in the world. Modern epidemiological data indicate that today allergic diseases are one of the groups of the most common chronic diseases in the world, affecting more than 150 million people, and this figure continues to grow. At the same time, the prevalence of allergic diseases in European countries reaches 30%, and about 10% of patients have chronic diseases of allergic origin [6, 18]. According to statistics, annually in the world 12.7–28.5% of people seek medical help for allergic rhinitis and urticaria, which are among the most common allergic diseases and one of the most frequent reasons for a patient to visit a general practitioner, allergist or dermatologist. According to WHO, almost 90% of the world's population has experienced an allergic reaction at least once in their lives. According to forecasts of the European Commission on Allergy, in the 21st century about half of the world's population may suffer from allergies [24].

Rational pharmacotherapy of allergic diseases is based on four basic principles: elimination of the allergen from the patient's body; use of drugs that nonspecifically suppress allergic reactions without taking into account the characteristics of a particular allergen; immunosuppressive therapy; specific hyposensitization or specific immunotherapy.

Today, modern methods of treating allergic diseases include elimination measures, if possible, pharmacotherapy, and allergen-specific immunotherapy. Basic pharmacotherapy includes $H_1$-histamine receptor blockers, serotonin receptor blockers, leukotriene receptor antagonists, mast cell membrane stabilizers and glucocorticoids [7].

Each group of AADs has its own advantages and disadvantages. The number of drugs in this group increases every year, the range of antiallergic drugs on the pharmaceutical market is constantly changing, therefore, for a rational choice of drugs for the treatment of a particular patient, the doctor and pharmacist must be

familiar with the range of AADs, as well as have information about the pharmacological characteristics and features of the use of individual drugs.

**The aim of the study.** To analyze the assortment of drugs for the treatment of allergic diseases on the pharmaceutical market of Ukraine, provide their comparative characteristics and, based on the analysis of the evidence base, determine aspects of the clinical use of modern antiallergic drugs.

**The objectives of the study:**

1. To determine the place of AADs in the pharmaceutical market of Ukraine.
2. To analyze the assortment of AAs in Ukraine.
3. To provide a comparative pharmacological characteristic of different groups of AAs.
4. To determine the features and aspects of the clinical application of modern AAs based on the analysis of evidence-based medicine data.

**The study object:** optimization of pharmacotherapy of allergic diseases.

**The study subject**: AADs registered in Ukraine as of early March 2025.

**The research methods.** Methods of systems approach and systems analysis, methods of marketing analysis.

**Practical significance of the obtained results.** It was established that 221 antiallergic drugs are registered in Ukraine. It was established that the first-choice drugs are $H_1$-histamine blockers. They account for 86% of all antiallergic drugs registered in Ukraine. Antihistamines of the third generation are the most popular in Ukraine. Desloratadine preparations prevail in terms of the number of trade names. Medicines containing levocetirizine are in second place.

Based on the results of the analysis of literature data, a comparative pharmacological characteristic of different groups of antiallergic drugs was provided. The conditions for rational use and certain clinical aspects of antiallergic drugs of different groups were determined. The creation and study of $H_3$- and $H_4$-histamine receptor blockers is a promising direction in the therapy and prevention of allergic diseases.

**Elements of scientific research.** The assortment of antiallergic drugs registered in Ukraine as of mid-March 2025 has been analyzed. A comparative pharmacological characteristic of different groups of drugs for the treatment of allergic diseases has been provided.

Based on data from international clinical guidelines, systematic reviews and clinical studies, an analysis of the evidence base of the clinical effectiveness of drugs of this group has been conducted. Aspects of rational choice and clinical aspects of the use of AADs have been identified.

**Approbation of research results and publications**. The results of the work were tested at the V International Scientific and Practical Conference "Problems and Achievements of Modern Biotechnology" (March 28, 2025, Kharkiv, National University of Pharmacy) and covered in 1 abstracts.

**Structure and volume.** The work consists of an introduction, the main part (literature review, research methods, own research and their discussion), conclusions, a list of used sources and contains 50 pages, 6 tables, 4 figures, 44 references to literature sources.

# CHAPTER 1
# MAIN DIRECTIONS OF PHARMACOTHERAPY OF ALLERGIC DISEASES
# (literature review)

## 1.1. Main etiological and pathogenetic aspects of allergy

Allergy is a pathological reaction of the immune system to the action of substances of antigenic nature, which leads to various disorders in the body, such as inflammation of the skin, mucous membranes, bronchospasm, anaphylactic shock, etc. An allergic reaction occurs upon repeated contact with an allergen (antigen) and is accompanied by damage to one's own cells, the development of inflammation and/or a violation of the functional state of individual organs and tissues. Damage to one's own cells during allergic reactions occurs as a result of the activation of effector mechanisms of immunity and antibody-mediated triggering of the release of inflammatory mediators. Allergic diseases are a group of diseases whose development is based on damage caused by an immune reaction to exogenous antigens – allergens. Autoallergic (autoimmune) diseases are a group of diseases whose development is based on damage caused by an immune reaction to antigens of one's own tissues [42].

There are several classifications of allergic reactions. The most common is the classification based on the time of manifestation of the reaction after contact with the allergen:

1. Immediate-type allergic reactions (immediate-type hypersensitivity) develop within 15-30 minutes, corresponding to type I allergic reactions according to P. Gell & R. Coombs.

2. Delayed-type allergic reactions (delayed-type hypersensitivity) develop after 24-48 hours.

However, this classification does not reflect all possible manifestations of allergy that occur in clinical practice. In classical immediate-type reactions, delayed manifestations are observed after 12–24 hours (for example, late

bronchospasm in bronchial asthma (BA)), some reactions develop after 4–6 or 12–18 hours.

Allergic diseases are one of the most common causes of general morbidity in the world and cause a significant burden on health care and the medical system of different countries. At least 30% of the population suffers from diseases such as BA, allergic rhinitis, atopic dermatitis, urticaria and life-threatening cases of food, drug, and insect venom allergies, and these conditions occur in almost 80% of families, and their prevalence continues to grow worldwide. These diseases are a current "disease of civilization". According to statistics, more than 20% of the population in the world suffers from allergies, that is, every fifth person [3].

The cause of allergies can be substances that exhibit antigenic properties and cause an immune response in the body in the form of antibody production or activation of the corresponding clone of lymphocytes (allergens). Allergens are divided into exogenous and endogenous. Exogenous allergens include: non-infectious (airborne, inhaled), food, contact, those that act on the skin and mucous membrane (dyes), injectable, infectious: (bacteria, viruses, rickettsia), medicinal. Endoallergens (according to the classification of A.D. Ado) are divided into natural (primary) and acquired (secondary). Natural endoallergens, or autoallergens, include components of the body's own normal tissues to which the body can produce antibodies – the lens of the eye, myelin. Secondary allergens are divided into infectious and non-infectious (burn, cold, radiation). Infectious allergens are divided into complex (tissue + bacterial cell, tissue + toxin) and intermediate (products of tissue damage by microbes or viruses). Allergens can be complete antigens and incomplete – haptens. Allergens can be drugs, food additives and household items. Drugs are also often incomplete antigens - haptens, which are converted into complete antigens by irreversible binding to proteins, which leads to sensitization of the body. Allergy mediators: histamine, bradykinin, serotonin, PG, cytokines, LT. Histamine is a natural ligand of $H_1$-, $H_2$- and $H_3$-histamine receptors. Allergic reactions are mainly associated with the excitation of $H_1$-receptors, which are located in the smooth muscles of the bronchi, intestines,

biliary and urinary tracts, in blood vessels, and also in the myocardium. Excitation of H1-histamine receptors causes activation of phospholipase in the cell membrane, which increases the influx of calcium ions into the cell, which stimulates the formation of cGMP. This leads to bronchospasm, dilation of blood vessels and restriction of blood return to the heart, reduction of cardiac output and minute blood volume, reduction of blood pressure and deterioration of tissue perfusion, inhibition of atrioventricular conduction, increase in capillary permeability and transudation of the liquid part of the plasma through the expanded intercellular spaces (tissue edema), blood thickening and reduction of circulating blood volume. Histamine stimulates the release of adrenaline and glucocorticoids by the adrenal glands, and irritates sensitive skin receptors, causing a burning sensation, itching and pain. Serotonin, together with histamine, is involved in allergic reactions, which excites serotonin receptors, which causes contraction of smooth muscles of the uterus, intestines, bronchi, vasoconstriction, increased platelet aggregation [42].

An allergic reaction has three main stages of development. The immunological stage begins with the first contact of the body with an antigen or hapten and ends with the interaction of antibodies with antigen, while allergic antibodies are formed in the body as a result of the sensitization process, fixed on cell and tissue structures. At this stage, the allergen is recognized by the cells of the immune system, the interaction of immunocompetent cells, their proliferation and differentiation into effector cells – antibody-forming, T-killers, activated T-helpers). During this period, sensitization occurs – an immunologically mediated increase in the body's sensitivity to antigens (allergens). Pathochemical stage: the antigen-antibody complex disrupts metabolic processes in cells, which are destroyed with the release of allergy mediators histamine, serotonin, leukotrienes, etc. As a result, capillary permeability increases, inflammatory edema is formed. Pathophysiological stage: biochemical processes caused by the antigen-antibody complex lead to functional and structural changes in the state of various organs – bronchospasm, edema, skin hyperemia, decreased blood pressure, up to the death

of tissue and even the entire organism. Disorders develop in the circulatory system, respiration, nervous system, etc. [3].

Upon first contact with an allergen, the body produces specific antibodies (IgE), which are fixed on the surface of mast cells. This process is called sensitization. When the allergen enters the body again, an antigen-antibody reaction develops, the permeability of mast cells increases and mediators of allergy and inflammation are released and stimulate the corresponding receptors in organs and tissues. This is how an allergic reaction develops. This is how an allergic reaction develops. It provokes the development of a runny nose, nasal congestion, sneezing, coughing, red eyes, and breathing problems. Over time, an allergy can occur within a few minutes, or it can last for several days or weeks [41].

Allergic reactions develop in three main ways: immediate-type hypersensitivity, delayed-type hypersensitivity; late-type allergic reactions. Immediate-type hypersensitivity develops no later than 2 hours after repeated contact with the allergen against the background of previous sensitization. It is caused by antibodies belonging to the IgE subclass of immunoglobulins. These antibodies circulate in the blood and diffuse into the tissues, where they are fixed on the surface of cells. The decisive introduction of an allergen into the body is accompanied by immediate anaphylaxis with extreme manifestations in the form of anaphylactic shock with loss of consciousness, a sharp decrease in blood pressure, shortness of breath and a high probability of death. Delayed-type hypersensitivity (basophilic type) combines manifestations of immediate-type and delayed-type hypersensitivity, develops mainly with the participation of basophils, neutrophil granulocytes and partly Ig. Characteristic for manifestations of transplantation immunity, parasitic, tick-borne, viral infections. Delayed (tuberculin) type hypersensitivity is caused by most microbial antigens. Various subpopulations of T- and B-lymphocytes, basophils, mast cells, macrophages participate in its formation. Late-type allergic reactions develop with the participation of mast cells, eosinophilic granulocytes, neutrophilic granulocytes and lymphocytes, manifest at

the time of disappearance of immediate-type hypersensitivity in the form of erythema and blisters, are characterized by edema, redness, induration, resolve after 24–48 hours with subsequent formation of petechiae [38].

According to the classification proposed in 1969 by P. Jell and R. Coombs, depending on the mechanism of the immune reaction, 4 main types of allergic reactions are distinguished. The first type of reaction (anaphylactic) is based on the reagent mechanism of tissue damage, which occurs with the participation, as a rule, of IgE, less often - of the IgG class, on the surface of the membranes of basophils and mast cells. The second type –(cytotoxic) develops with the participation of immunoglobulins of classes G and M, as well as with the activation of the complement system, which leads to damage to the cell membrane. The third type of reaction (immune complex (Arthus phenomenon)) is associated with tissue damage by immune complexes circulating in the bloodstream, occurs with the participation of immunoglobulins of classes G and M. The damaging effect of immune complexes on tissues occurs through the activation of complement and lysosomal enzymes. The fourth type of allergic reaction (cell-mediated or delayed, tuberculin) occurs after 24–48 hours, occurs with the participation of sensitized lymphocytes. Hypersensitivity according to type V – allergic reactions of autoantibodies, autoallergy. Most often, allergic reactions develop according to type I hypersensitivity [41].

Modern medicine cannot unequivocally determine the causes that provoke the occurrence of allergies. But it is only known for sure that they are associated with heredity. Factors that contribute to the development of allergic reactions are an unfavorable ecological situation in the region of residence, stress, uncontrolled use of medications, unhealthy diet, household allergens, work at a harmful enterprise, parasitic diseases [41].

There are different forms of allergic reactions.

Respiratory form: allergic rhinitis, rhinosinusitis, asthma, which is the most dangerous type of respiratory allergy. The main symptoms of allergic rhinitis are clear nasal discharge, sneezing, itching and burning in the nose, a

feeling of nasal congestion, snoring, hoarseness. Sometimes a cough joins (due to irritation of the back wall of the pharynx with mucus), a decrease in smell is possible, redness of the skin of the wings of the nose and above the upper lip.

Contact (cutaneous) form: urticaria, atopic dermatitis, eczema, Quincke's edema (angioedema). Often skin damage occurs with repeated use of hair dye, detergents and other household chemicals. At the site of contact, swelling, itching, blistering is possible, after opening which weeping erosions appear, which are then covered with crusts. Due to its rapid development, especially in the larynx, Quincke's edema is extremely dangerous, as it makes breathing difficult and can lead to death without qualified medical care [42].

Food allergy: a reaction to food products or their individual components. The most pronounced allergens are fish, milk, chicken protein, nuts. In addition, food additives, preservatives and dyes can provoke allergic reactions. Food allergies are characterized by diarrhea, the presence of blood in the feces, vomiting, lethargy, as well as skin symptoms in the form of urticaria, atopic dermatitis, oral allergy syndrome (itching, mild swelling of the oral cavity).

Insect bite allergy: a reaction to insect venom that enters the body after a bite or after contact with the waste products of insects such as wasps, bees.

Drug allergy: manifests itself very quickly after starting medication. It is especially common when taking chemotherapeutic drugs. To avoid severe allergic reactions, the introduction of a new drug should be started with small doses, gradually increasing them, constantly monitoring the body's reaction, especially in children. People who are allergic to medications should remember the name of the substance that provokes an allergic reaction, the characteristics of the body's response to it (symptoms), and inform medical professionals about the presence of an allergy [42].

Allergy to vaccination: the catalyst for the reaction is the components of the vaccine. They enter the blood directly, so the reaction can be either slow or quite severe.

Anaphylactic shock: the most aggressive type of allergic reaction. It develops rapidly, occurs with repeated exposure to drugs, food products, chemicals, insect venom. Characteristic symptoms are tinnitus, chills, weakness, dizziness, nausea, numbness, a lump in the throat, cold sweat, sharp pallor or the appearance of hives with severe itching, breathing problems, cough, increased or decreased heartbeat, changes in heart rhythm, convulsions, loss of consciousness.

Allergy during pregnancy: associated with hormonal changes in the woman's body. Since it is forbidden to take antihistamines during this period, it is impossible to treat allergies without consulting a doctor so as not to harm the baby [4].

The severity of symptoms and their variety depends on the clinical type of allergy, and even on the severity of the disease. Among the nonspecific symptoms of any allergy, weakness, irritability, mood swings, impaired concentration, sleep disturbances, headaches and pain are distinguished [41, 42].

Currently, the term "allergy" usually describes reactions of the first type - allergic reactions of immediate or anaphylactic type. Typical clinical examples of allergic reactions of immediate type are vasomotor rhinitis, urticaria, anaphylactic shock, atopic asthma, false croup.

According to WHO, allergic diseases occupy one of the first places in the structure of morbidity. Various allergic reactions are manifested in 20% of the European population, and in some environmentally unfavorable regions their number reaches 40-50%. According to forecasts of the European Commission on Allergy, in the 21st century about half of the world's population may suffer from allergies.

### 1.2. Modern directions of therapy of allergic diseases

The constant increase in the incidence of allergies is attracting more and more attention and is accompanied by a high frequency of relapses. The pathogenesis of allergic diseases is complex and includes many factors, including

the maternal and fetal environment, the living environment, genetics, epigenetics and the immune status of the organism. With the rapid development of immunology, molecular biology and biotechnology, therapeutic methods and drugs have been developed, the use of which expands the possibilities of treating allergic diseases.

Rational pharmacotherapy of allergic diseases is based on four basic principles:

1) elimination of the allergen from the patient's body;

2) use of drugs that nonspecifically suppress allergic reactions without taking into account the characteristics of a particular allergen;

3) immunosuppressive therapy;

4) specific hyposensitization or specific immunotherapy.

Today, modern methods of treating allergic diseases include elimination measures, if possible, pharmacotherapy and allergen-specific immunotherapy (ASIT) [19].

Pharmacotherapy includes immunosuppressants (cytostatics, glucocorticosteroids); mast cell activation and degranulation blockers; receptor blockers (histamine, leukotriene) and enzyme blockers (proteolysis inhibitors); anticytokine drugs. The introduction of histoglobulin stimulates the synthesis of antibodies against histamine in the body, which are able to neutralize it. Methods of treating allergic diseases include hemosorption, plasmapheresis (removal of antibodies and interleukins from the blood), as well as physiotherapy, spa therapy, etc. The correct choice and rational use of antiallergic drugs in the complex therapy of allergic diseases allow to relieve acute manifestations of allergy, achieve high treatment effectiveness and prevent its re-exacerbation.

The role of histamine in the development of allergic diseases is associated with its ability to increase the secretion of cytokines (interleukin (IL)-4, IL-5, IL-10 and IL-13) and reduce the secretion of Th1 cytokines (IL-2, IL-12, etc.). Histamine is able to modulate the cytokine network in various ways: through enhanced release of prostaglandin E2 and nitric oxide. It can also affect cytokine

production through $H_2$-histamine receptors and through the activation of protein kinase A. But 1st generation antihistamines are characterized by side effects such as drowsiness, anticholinergic effects, development of tachyphylaxis, dryness of mucous membranes, therefore it is recommended to use antihistamines II (loratadine, cetirizine) and metabolites II generation (desloratadine, levocetirizine), which are characterized by greater safety, including a significant reduction or absence of side effects. In physiological concentrations, antihistamines effectively suppress histamine-dependent pro-inflammatory cytokines (interleukins IL-6 and IL-8), which are released from endothelial and mast cells, basophils. These interleukins stimulate the secretion of pro-inflammatory mediators (tumor necrosis factor (TNF) and colony-stimulating factor from mast cells). The anti-inflammatory effect obtained in this way is similar to the action of dexamethasone [34].

WHO recommends allergen immunotherapy – etiological treatment of type I allergic diseases caused by specific allergens, which is achieved by increasing the body's immune tolerance to allergens, as the only etiological method of treating allergic diseases that effectively controls allergy symptoms, modifies the natural course of allergic rhinitis and reduces the risk of developing new allergic reactions.

Numerous studies have proven that allergen immunotherapy significantly reduces the severity of symptoms in patients, changes the course of the disease and improves the quality of life of patients with allergic diseases. However, in order to increase the safety profile and convenience for patients, it is also worth considering the methods of drug delivery – in addition to subcutaneous and sublingual immunotherapy, oral immunotherapy is a promising method [13].

For example, acalabrutinib, approved by the US Food and Drug Administration for the treatment of lymphomas by inhibiting Bruton's tyrosine kinase, may be a potential tool for preventing anaphylaxis in people with food allergy to peanuts [20].

ASIT is one of the main methods of pathogenetic treatment of IgE-mediated allergic diseases. It is the only method that can affect not only the symptoms of

allergy, but also its cause. It is a treatment method, the essence of which is to introduce patients to a causally significant allergen with a gradual increase in its dose in order to develop immunological tolerance to this allergen. ASIT was introduced into medical practice by Leonard Noon in 1911, but it remained an empirical treatment method for a long time [13, 20].

The effectiveness of ASIT is expressed in the reduction or complete absence of clinical symptoms in the event of natural exposure to the allergen. After ASIT, there is a reduction in the duration of exacerbation, a decrease in the need for drugs for both basic and symptomatic therapy. ASIT allows you to prevent the transformation of allergic rhinitis into asthma and expand the spectrum of allergens to which the patient is hypersensitive.

The method acts on both the early and late phases of the allergic response, leading to inhibition of not only the allergen-specific reaction, but also to suppression of tissue hyperreactivity. Under the action of ASIT, the migration of effector cells into the area of allergic inflammation is inhibited, and regulatory T-lymphocytes are formed, which contribute to the induction of immunological tolerance, characterized by suppression of the proliferative and cytokine response to causative allergens [8].

The first controlled study of ASIT was published in 1954. The method has been continuously studied, improved, and new scientific evidence has accumulated, demonstrated by a number of meta-analyses. Until the 1980s, the only way to administer allergens in ASIT was by injection (subcutaneously). However, the emergence of new biologically potent allergen extracts on the market raised the issue of safety due to a number of fatal systemic reactions in Europe and the USA.

Other routes of administration, such as oral and topical nasal, have been investigated to improve safety. However, the former was found to be ineffective despite the administration of very high doses of allergen, while the latter demonstrated clinical efficacy but had many side effects. The sublingual method was first proposed as an alternative route of allergen administration in 1986, and in

the following years the method was thoroughly studied, accumulating an evidence base that demonstrated its efficacy and safety.

### 1.3. Pharmacological characteristics of modern antiallergic drugs

Currently, pharmacotherapy remains one of the most common methods of treating allergic diseases and includes the use of intranasal glucocorticoids, oral and intranasal $H_1$-antihistamines, and leukotriene receptor antagonists. Unfortunately, pharmacotherapy controls symptoms only during long-term use, but does not provide sustained effectiveness after discontinuation of the drugs[17].

Modern approaches to the treatment of exacerbations of allergic diseases are based on the following provisions: the use of antihistamines for exacerbations of allergic rhinitis, atopic dermatitis, hay fever, urticaria, allergic edema; the preferential use of inhaled bronchodilators, $\beta_2$-adrenomimetics, M-cholinoblockers, inhaled GCS for asthma; infusion therapy with aminophylline for severe exacerbations of asthma; the appointment of systemic GCS (prednisolone, dexamethasone, methyl prednisolone, etc.) for life-threatening allergic conditions of the patient, taking into account the circadian rhythm and gradual withdrawal. Pathogenetic therapy of allergic diseases, aimed at reducing the activation of T-helper (Tx)2 and increasing the activity of Tx1, is impossible without understanding how various drugs affect the cytokine balance in the body. Since histamine plays a significant role in the development of IgE-dependent allergic disease, antihistamines play an important role in treatment. Antihistamines have an effect on the cytokine balance in the patient's immune system [5, 14].

The classification and nomenclature of modern AADs is given in table. 1.1.

$H_1$-histamine and serotonin receptor blockers are also classified by chemical structure: ethanolamines – diphenhydramine, clemastine, dimenhydrinate; ethylenediamines – chlorphenamine, quifenadine; phenothiazines – promethazine; piperazines – hydroxyzine, cetirizine, levocetirizine; piperidines (butyrophenones) – cyproheptadine, terfenadine, fexofenadine; azatidines – loratadine, desloratadine;

Table 1.1

**Classification and nomenclature of antiallergic drugs**

<table>
<tr><td colspan="4">H1-histamine, serotonin* receptor blockers</td></tr>
<tr><td colspan="2">I generation</td><td>II generation</td><td>III generation</td></tr>
<tr><td>Diphenhydramine (Diphenhydramine)<br>Clemastine (Tavegil)<br>Chloropyramine (Suprastin)<br>Promethazine (Pipolfen)<br>Mebhydroline (Diazolin)<br>Sexifenadine (Gistafen)</td><td>Levocabastine (Histimet)<br>Cyproheptadine* (Peritol)<br>Ketotifen (Zaditen)<br>Dimetinden (Fenistil)</td><td>Quifenadine (Fenkarol)<br>Cetirizine (Allertec)<br>Terfenadine (Trexil)<br>Loratadine (Claritin)<br>Ebastine (Kestin)<br>Azelastine (Allergodil)<br>Astemizole (Gismanal)<br>Acrivastine (Semprex)</td><td>Levocetirizine (Xyzal)<br>Fexofenadine (Telfast)<br>Desloratadine (Erius, Edem)<br>Norastemizole (Seprakor)</td></tr>
<tr><td>Membrane stabilizers, anti-mediator agents*</td><td colspan="2">Glucocorticosteroids</td><td>Leukotriene receptor antagonists</td></tr>
<tr><td>Cromoglycic acid (Lecrolin)<br>Ketotifen (Zaditen)<br>Nedocromil (Tayled)<br>Fenspiride*</td><td colspan="2">Prednisolone<br>Budesonide (Pulmicort)<br>Hydrocortisone butyrate (Solu-Cortef)<br>Triamcinolone acetonide (Kenalog)<br>Mometasone furoate (Asmanex)<br>Dexamethasone</td><td>Zafirlukast (Acolate)<br>Montelukast (Singular)</td></tr>
</table>

oxypiperidines – ketotifen; phthalazinones – azelastine; alkylamines – chlorpheniramine, dimethindene, acrivastine; pyridindoles – mebhydrolin;

quinuclidines – quifenadine; piperidine-carboxylic acids – levocabastine; piperidinimidazoles – astemizole, norastemisole; triprolidines – acrivastine [18].

The mechanism of action of AADs is associated with their influence on various links in the pathogenesis of allergy. Antihistamines by the type of competitive antagonism with histamine block histamine receptors and thereby eliminate the increased sensitivity of cell membranes of smooth muscles to free histamine: I generation drugs block $H_1$- and $H_2$-histamine receptors, II-III generation – mainly $H_1$-histamine receptors. Quifenadine also activates histaminase; ketotifen, azelastine stabilize mast cell membranes. Cyproheptadine simultaneously blocks histamine and serotonin receptors, reduces cytokine production. Vibrocil blocks $H_1$-histamine receptors, and also due to the $\alpha_1$-adrenomimetic that is part of it, reduces swelling of the nasal mucosa [19].

Membrane stabilizers block the entry of $Ca^{2+}$ into mast cells, inhibit their degranulation and stimulate their excretion, thereby preventing the release of mediators of allergy and inflammation. Inhibit phosphodiesterase of mast cells, which leads to the accumulation of cAMP in them and stabilization of membranes. Antimediator agents reduce the production of various pro-inflammatory mediators: cytokines, arachidonic acid derivatives, free radicals. At the same time, there is a moderate blockade of $H_1$-histamine receptors and a papaverine-like antispasmodic effect [42].

GCS, by increasing the content of cAMP, potentiate the action of catecholamines, which prevent bronchospasm; due to a decrease in the activity of cGMP, inhibit the cholinergic effect; reduce the synthesis of histamine (which depends on the ratio of cAMP/cGMP), serotonin and other mediators of allergy; prevent the interaction of IgE with the Fc-receptor on the surface of mast cells and basophils; inhibit the outflow of plasma and granulocytes from capillaries; reduce the content of leukocytes, eosinophils, neutrophils, lymphocytes in the focus of inflammation; inhibit phospholipase A2, reducing the release of arachidonic acid and the formation of its pro-inflammatory metabolites (PG, LT). GCS are the most

effective antiallergic drugs, but their use is limited by numerous side effects [41, 42].

Selective leukotriene receptor antagonists are competitive antagonists of LTC4-, LTD4- and LTE4-receptors (a component of the slow-reacting substance of anaphylaxis). The drugs reduce the content of cellular and extracellular factors of the inflammatory reaction in the respiratory tract, suppress the contractile activity of the smooth muscles of the respiratory tract [29, 43].

The main indications for the use of AADs are given in table 1.2.

Table 1.2

**Indications for use and interchangeability of antiallergic agents**

| Drug group | Indications for use |
|---|---|
| $H_1$-histamine receptor blockers | A conditions that requires desensitization of the body, treatment of immediate allergies: urticaria, allergic dermatitis and conjunctivitis, asthmatic bronchitis, quincke's edema, serum sickness, capillary toxicosis, etc. in anaphylactic shock, ba is ineffective, since histamine release and its interaction with $H_1$-histamine receptors have already occurred |
| Glucocorticosteroids | All allergic reactions, but due to pronounced side effects, it is used only for severe (anaphylactic shock) and moderate (serum sickness, Quincke's edema) allergic reactions, as well as for severe progressive autoimmune diseases (collagenosis), prevention of transplant rejection reactions |
| Anti-mediator agents, membrane stabilizers | Prevention of BA, allergic rhinitis |
| Leukotriene receptor antagonists | Prevention and therapy of BA (including "aspirinic"), especially with insufficient effectiveness of $\beta_2$-adrenomimetics |

II and III generation H1-histamine blockers have a higher affinity for H1-histamine receptors than I generation drugs, so they do not affect other types of receptors. In addition, these drugs do not penetrate the BBB in therapeutic doses and do not cause tachyphylaxis [1, 2, 23].

I generation of antihistamines are effective for hay fever, allergic rhinitis, sneezing, and ocular symptoms of allergies; less effective for nasal congestion and symptoms of bacterial/viral rhinitis not associated with endogenous histamine release. II generation of antihistamines are the first-line treatment for urticaria; III generation drugs are used to treat allergic rhinoconjunctivitis, rhinorrhea, itching, and sneezing, and have a prolonged effect.

**Conclusions to chapter 1**

Thus, based on literature data, it is relevant to analyze the range of AADs on the pharmaceutical market of Ukraine and, based on the analysis of evidence-based medicine data, determine the conditions for their rational choice and clinical aspects of application.

# CHAPTER 2
# MATERIALS AND RESEARCH METHODS

The object of the study was a group of drugs for the treatment of allergic diseases. We investigated antiallergic drugs available on the pharmaceutical market of Ukraine. Specific antiallergic drugs were selected for analysis, namely, $H_1$-histamine blockers, mast cell membrane stabilizers and leukotriene receptor antagonists. The State Register of Medicines of Ukraine and the Compendium of Medicines were used to analyze the assortment of drugs [40, 43].

At the first stage of the study, we determined the number of AADs among all drugs registered in Ukraine as of March 1, 2025, and found out their place in the structure of the pharmaceutical market.

In the second stage of the work, we analyzed the assortment of antiallergic drugs by international non-proprietary (INN) and trade names. We found out which groups of AADs are most in demand by the number of brands, which manufacturers' drugs (domestic and foreign) are represented on the market, and determined which domestic and foreign pharmaceutical companies produce the largest number of drugs of this group registered in Ukraine. Also, according to the analysis conducted, we will find out which AADs (by number of brands) are the most popular in the treatment of allergic diseases.

In the third stage of the study, we provided a comparative description of different groups of antiallergic drugs, using data from literature sources. To analyze the clinical aspects of use, determine the conditions for optimal selection and rational prescription of the selected drugs, we used information from well-known evidence-based medicine databases: Cochrane Library, Trip Database, Medline, PubMed, MedlinePlus and others [39].

## Conclusions to chapter 2

Thus, we have determined the test system and the object of the study. In accordance with the purpose of the work, we have chosen an adequate set of

methods that allow us to maximally analyze the assortment, conditions for rational choice and rational use of the object of the study - drugs for the treatment and prevention of allergic diseases, registered in Ukraine as of March 2025. Relevant methods for analyzing the results are proposed.

# CHAPTER 3
# OBTAINED RESULTS AND DISCUSSION

## 3.1. Determining the place of antiallergic drugs on the pharmaceutical market in Ukraine

The first stage of our study was devoted to determining the place of antiallergic drugs among all drugs present on the pharmaceutical market of Ukraine as of March 2025. To conduct the study, we used the State Register of Medicines of Ukraine and the Compendium of Medicines [40, 43]. We analyzed the assortment of specific AAPs, namely, $H_1$-histamine blockers, mast cell membrane stabilizers, and leukotriene receptor antagonists. We did not analyze the range of glucocorticosteroids and immunosuppressants.

It was determined that as of March 1, 2025, 11,784 drugs were registered in Ukraine. Of these, 4,014 were drugs of domestic manufacturers, 7,770 were drugs of foreign companies. In Ukraine, 22 international non-proprietary names (INN) of antiallergic drugs were registered, 221 were trade names. The share of AAP drugs is approximately 1.9% of the entire assortment of drugs registered in Ukraine.

## 3.2. Analysis of the assortment of antiallergic drugs

The results of the study revealed that as of the beginning of March 2025, 221 drugs for the treatment of allergic diseases, 22 INNs, were registered on the pharmaceutical market of Ukraine. Of these, $H_1$-histamine blockers – 20 INNs, 190 trade names; membrane stabilizers – 2 INNs (3 drugs); leukotriene receptor antagonists – 1 INN (25 trade names), 3 combined drugs (see Fig. 3.1, Table 3.1).

From Fig. 3.1. it is clear that the undisputed market leaders among different groups of antiallergic drugs are $H_1$-histamine blockers. They account for 86% of all antiallergic drugs registered in Ukraine.

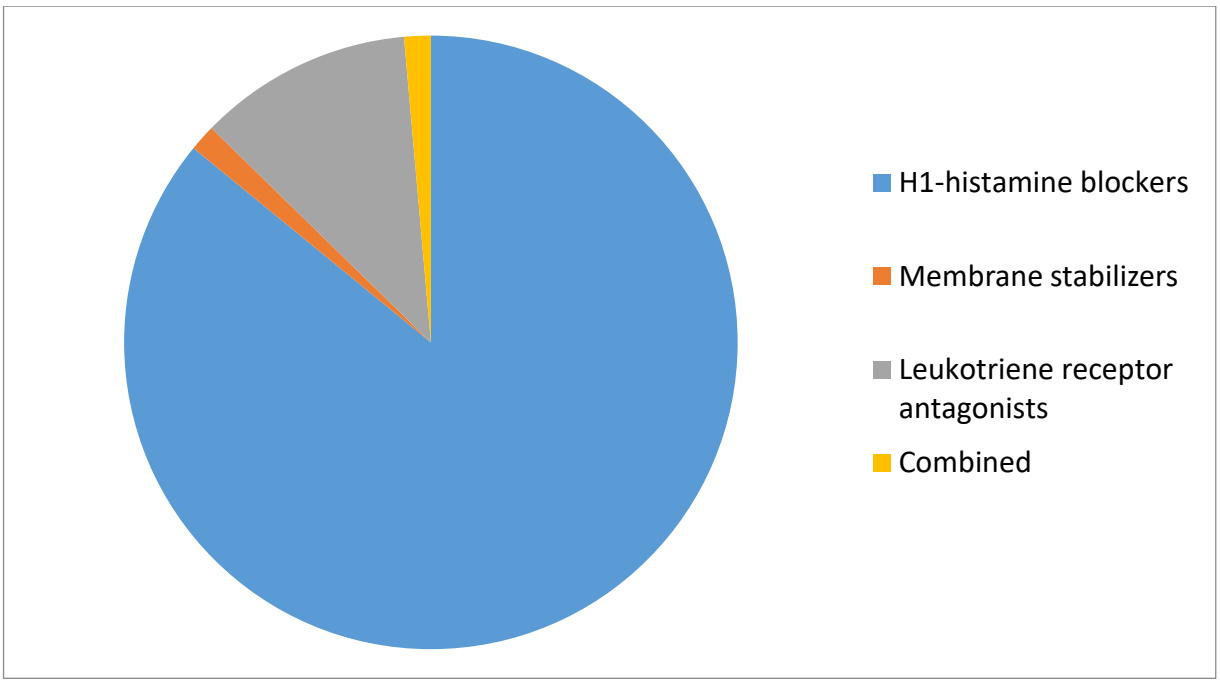


Fig. 3.1. Distribution of different groups of antiallergic drugs on the pharmaceutical market of Ukraine as of 1.03.2025

Today, representatives of all three generations of $H_1$-histamine blockers are available in Ukraine. I generation $H_1$-histamine receptor blockers are registered – 33 drugs (8 INN), II generation antihistamines – 59 drugs (8 INN), III generation $H_1$-histamine receptor blockers – 98 drugs (3 INN). Thus, the majority of modern antihistamines in Ukraine are representatives of the II and III generations, drugs with a selective mechanism of action that do not depress the CNS, have a prolonged effect and a high level of safety. First-generation drugs, unlike the above-mentioned antihistamines, penetrate well through the BBB, depress the CNS, have a non-selective mechanism of action, are able to block not only $H_1$-, but also $H_2$-histamine receptors. Cyproheptadine simultaneously blocks histamine and serotonin receptors, reduces cytokine production. Ketotifen also has a dual mechanism of action, blocking histamine receptors and at the same time stabilizing mast cell membranes. The distribution of different generations of antihistamines is shown in Fig. 3.2.

Table 3.1

**Assortment of different groups of antiallergic drugs on the pharmaceutical market of Ukraine as of March 1, 2025**

| Drug groups | International non-proprietary names | Number of trade names |
|---|---|---|
| $H_1$-histamine blockers | Diphenhydramine | 4 |
| | Clemastine | 1 |
| | Dimethindene | 5 |
| | Chloropyramine | 6 |
| | Cetirizine | 11 |
| | Levocetirizine | 41 |
| | Cyproheptadine | 1 |
| | Loratadine | 24 |
| | Mebhydroline | 9 |
| | Ketotifen | 6 |
| | Acrivastine | 1 |
| | Ebastine | 3 |
| | Fexofenadine | 7 |
| | Desloratadine | 50 |
| | Rupatadine | 3 |
| | Quifenadine | 3 |
| | Sequifenadine | 1 |
| | Bilastine | 7 |
| | Olopatadine | 7 |
| Leukotriene receptor antagonists | Montelukast | 25 |
| Mast cell membrane stabilizers | Cromoglycic acid | 2 |
| | Ketotifen | 1 |
| Combined drugs | Montelukast + levocetirizine | 3 |

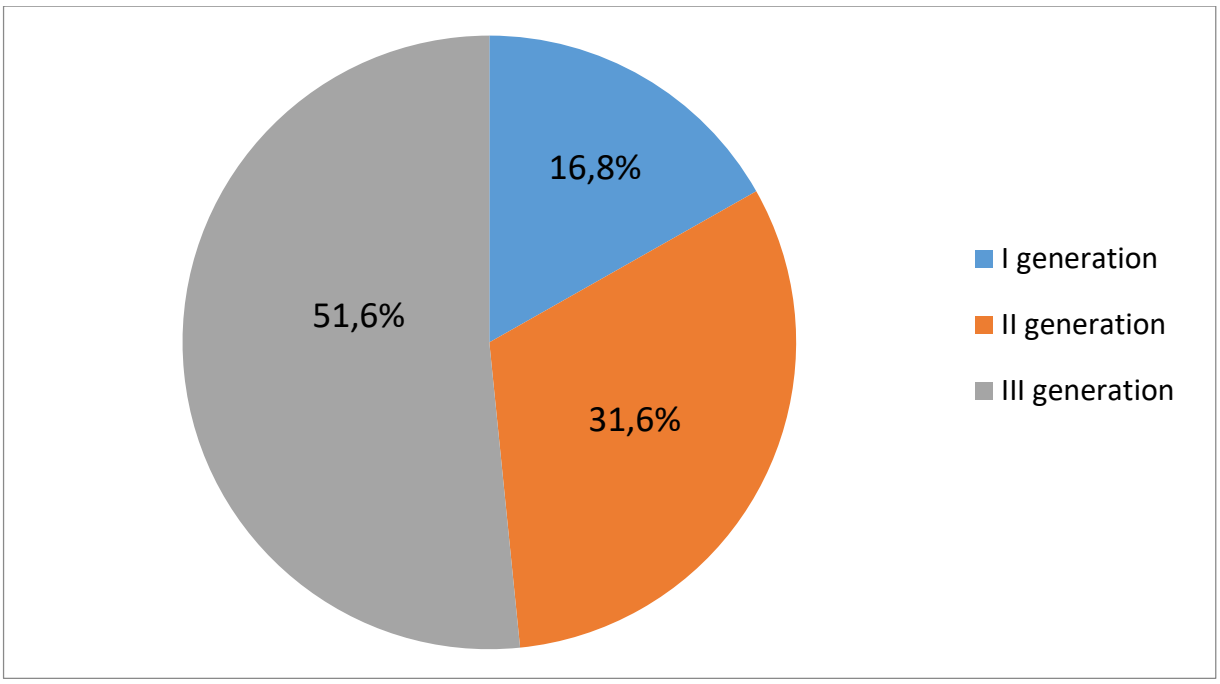


Fig. 3.2. Distribution of different generations of $H_1$-histamine blockers on the pharmaceutical market of Ukraine as of 1.03.2025

Blockers of $H_1$-histamine and serotonin receptors differ in chemical structure: ethanolamines – diphenhydramine, clemastine; ethylenediamines – chlorphenamine; piperazines – cetirizine, levocetirizine; piperidines (butyrophenones) – cyproheptadine, fexofenadine, bilastine; azatidines – loratadine, desloratadine, rupatadine; oxypiperidines – ketotifen; alkylamines – dimethindene, acrivastine; pyridindoles – mebhydroline; quinuclidines – hifenadine, sequifenadine; dibenzoxepines – olopatadine.

The second place is occupied by the youngest AADs – leukotriene receptor antagonists (11.3%). Despite the fact that only montelukast is available on the pharmaceutical market of Ukraine, as of the beginning of March 2025, 25 drugs based on it and three combination drugs containing a combination of montelukast and levocetirizine were registered.

Thus, the most popular antiallergic drugs in Ukraine today are third-generation $H_1$-histamine receptor blockers (98 trade names based on 3 INNs). The leaders in terms of the number of trade names are desloratadine (50 drugs) and levocetirizine (41 drugs). They are slightly inferior to the second-generation

antihistamine loratadine (24 drugs) and the leukotriene receptor antagonist montelukast (25 drugs). Combined drugs (3 drugs) contain a fixed combination of active ingredients, namely, montelukast and levocetirizine.

The majority of drugs for the treatment of allergic diseases are systemic drugs (92.8%), 10 drugs (4.5%) are available in eye drops, 6 (2.7%) in topical dosage forms (gels, ointments and emulsions). The majority of antiallergic drugs available on the modern Ukrainian pharmaceutical market are presented in oral dosage forms, and primarily in tablets (coated tablets, chewable tablets, dispersible tablets) - 156 drugs (70.6%), in dragees - 4 drugs (1.8%), as well as in syrups - 22 drugs (10.0%), in drops and solutions for p/o - 16 drugs (7.2%), 6 drugs (2.7%) are available in injection solutions, 2 drugs (0.9%) - in granules (Fig. 3.3). H1-histamine receptor blockers are available in tablets (coated tablets, chewable tablets, dispersible tablets) – 126 drugs (66.3%), in dragees – 4 drugs (2.1%), in syrups – 22 drugs (11.6%), in drops and solutions for p/o – 16 drugs (8.4%), 6 drugs (3.2%) are available in solutions for injection, 6 (2.7%) – in topical dosage forms (gels, ointments and emulsions) (Fig. 3.3). Only first-generation drugs are available in solutions for injection, namely, diphenhydramine (diphenhydramine) – 3 drugs and chloropyramine (suprastin, chloropyramine g/x and antihistamine) – 3 drugs. Drugs containing montelukast are available in tablets (including chewable ones) and granules.

Among the registered AADs in Ukraine, 91 (41.2%) are drugs of foreign manufacturers, 130 (58.8%) are foreign drugs. Pharmaceutical companies "Farmak" (20 drugs) and "Zdorovya" (14 drugs) are leaders in Ukraine in the production of antiallergic drugs. Among foreign companies, the leaders are "Adamed" (Poland) (9 drugs), "World Medicine" (Turkey) (8 drugs). Indian pharmaceutical companies ("Micro Labs Ltd", "Hetero Labs Limited", "Dr. Reddy's Laboratories", "Genom Biotech Pvt Ltd", "Sun Pharmaceutical Industries" and others) produce 35 drugs, which is equal to 15.8% of the entire Ukrainian market of antiallergic drugs.

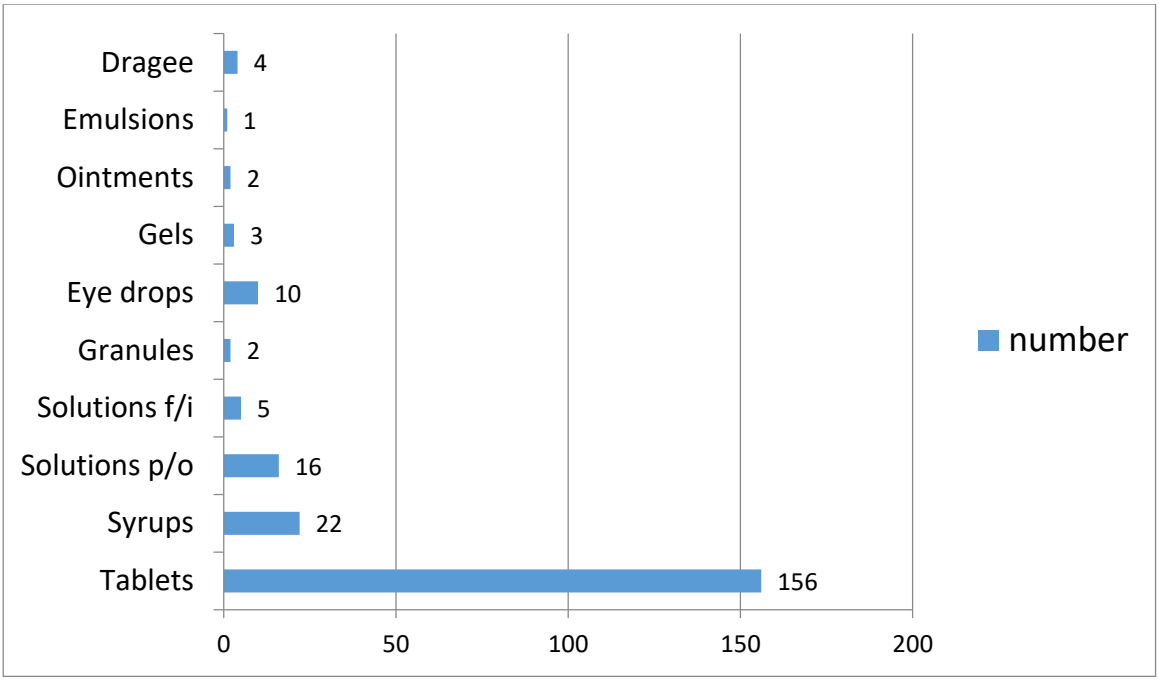


Fig. 3.3. The ratio of different medicinal forms of antiallergic drugs

So, the assortment of drugs for the treatment of allergic diseases on the modern pharmaceutical market of Ukraine is quite wide. 221 drugs based on 22 INNs are registered on the Ukrainian market. The leader is desloratadine, there are 50 drugs based on it on the market. Levocetirizine is in second place (41 drugs).

The assortment of products of foreign manufacturers is 1.4 times greater than the number of domestic drugs. That is, it can be assumed that both foreign drugs and products of domestic pharmaceutical companies are in demand.

### 3.3. Comparative characteristics of antiallergic drugs

Most antiallergic drugs on the Ukrainian market are $H_1$-histamine receptor blockers. I generation of antihistamines are non-selective histamine receptor blockers, the action lasts for 4–8 hours (diphenhydramine, promethazine), chloropyramine, mebhydrolin, clemastine, sequifenadine, cyproheptadine, ketotifen; dimethindene and clemastine – up to 12, mebhydroline – up to 24 hours). They block M-cholinergic receptors in peripheral tissues, which leads to a decrease in the secretion of exocrine glands, an increase in the viscosity of secretions, including bronchial secretions, dryness of the mucous membranes of

the oral cavity, a decrease in gastrointestinal motility and urinary tract tone, impaired accommodation, increased intraocular pressure and heart rate. Antiemetic and antiparkinsonian effects may develop, and some drugs exhibit antidopaminergic, antitussive, and anxiolytic effects. Side effects from the GIT may include nausea, vomiting, diarrhea, decreased or increased appetite. They penetrate into the blood-brain barrier (BBB) and block $H_1$-histamine receptors in the CNS, which is manifested by a sedative effect, drowsiness, decreased psychomotor activity, increased appetite, a feeling of lethargy, impaired coordination of movements, decreased ability to learn and concentrate. The greatest effect on the CNS is caused by diphenhydramine drugs. The sedative effect is enhanced by alcohol and other substances that depress the central nervous system. Dizziness, tinnitus, apathy, fatigue, decreased visual acuity, diplopia, nervousness, insomnia, tremor are possible. With prolonged use of I generation antihistamines, addiction develops. A significant disadvantage is the appointment of these drugs several times a day. Restrictions for the clinical use of I generation antihistamines are the first 3 months of pregnancy, astheno-depressive syndrome, glaucoma, benign prostatic hyperplasia, BA, spastic phenomena from the GIT, intestinal and bladder atony, all types of activity that require high attention and quick reaction, elderly patients [3, 44].

II generation antihistamines, such as terfenadine, astemizole, loratadine, acrivastine, cetirizine, ebastine, have high affinity for $H_1$-receptors, have limited penetration through the BBB, do not exhibit sedative and potentiating effects, do not affect choline and serotonin receptors, and are not habit-forming with prolonged use. These drugs are prescribed 1–2 times a day. However, terfenadine and astemizole have a significant side effect – an effect on the cardiovascular system (ventricular arrhythmias with prolongation of the Q–T interval on the ECG, tachycardia, which develops due to the blockade of potassium channels that control the repolarization of myocardial membranes) [26]. All second-generation antihistamines (except cetirizine and acrivastine) are prodrugs, the action of which is due to active metabolites formed in the liver by the CYP 3A4 isoenzyme of the

cytochrome P450 system. They should not be used with drugs that are metabolized by the same enzyme systems: macrolide antibiotics (erythromycin, clarithromycin, oleandomycin, azithromycin), antifungal drugs (ketoconazole, itraconazole), some antiarrhythmic drugs (quinidine, procainamide, disopyramide), antidepressants (fluoxetine, sertraline, paroxetine), as well as in cases of impaired liver function, which may increase the risk of cardiotoxic effects (for terfenadine and astemizole) [22, 28, 30]. Of the II generation drugs, bilastine has the highest affinity for $H_1$-receptors. At the same time, due to its low penetration through the BBB, bilastine is characterized by the lowest level of binding to $H_1$-receptors in the brain, which minimizes the risk of its adverse effects on the CNS [11, 31].

III generation antihistamines are active metabolites of second-generation drugs (fexofenadine is the active metabolite of terfenadine, norastemizole is astemizole, desloratadine is loratadine). All drugs are highly selective blockers of $H_1$-histamine receptors, which have antiallergic and anti-inflammatory effects, do not penetrate the BBB, do not exhibit sedative, hypnotic, cardiotoxic and some other undesirable effects, therefore they have a significantly better safety profile. They are rapidly absorbed in the gastrointestinal tract, are characterized by prolonged action and are prescribed once a day. They inhibit mediators of systemic allergic inflammation, including cytokines and chemokines, and reduce the expression of adhesion molecules, inhibit chemotaxis, activation of eosinophil granulocytes and the formation of superoxide radicals; reduce bronchial hyperreactivity. The use of III generation antihistamines is most rational in long-term therapy of allergic diseases (perennial allergic rhinitis, seasonal allergic rhinitis or rhinoconjunctivitis, chronic urticaria, atopic and allergic contact dermatitis). The safety of using these drugs in pregnant women has not been studied sufficiently, so their use is currently not recommended for this category of patients [16, 21, 25].

Classic indications for the use of antihistamines are allergic rhinitis, conjunctivitis, hay fever, urticaria, angioedema, and atopic dermatitis [42].

A comparative analysis of the main side effects of different groups of AADs is given in Tables 3.2-3.3.

Table 3.2

**Main side effects of antiallergic drugs of different groups**

| Side effects | 1st generation $H_1$-histamine blockers, montelukast | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | diphenhydramine | chloropyramine | clemastine | cyproheptadine | mebhydroline | ketotifen | dimethindene | sequifenadine | montelukast |
| Dizziness, CNS depression | + | + | + | + | + | + | + | + | + |
| General weakness | + | + | + | + | + | + | + | | + |
| Decreased attention, slowing down of reactions | + | + | + | + | + | + | | | |
| ↓ BP | + | + | | + | | | | | |
| ↑ heart rate | + | + | + | | | | | | + |
| Hematopoiesis suppression | | | | + | + | | | + | |
| Dry mouth | + | + | + | + | + | + | + | | + |
| Anorexia | + | | | + | | | | | |
| Increased appetite, weight gain | | + | | + | | + | | + | |
| Dyspepsia | + | + | + | + | + | + | + | + | + |
| Diarrhea | + | + | | + | | | | | + |
| Constipation | + | + | + | + | + | + | | | |
| Urinary retention | + | + | | + | + | | | | |

Table 3.3

**Main side effects of antiallergic drugs of different groups**

| Side effects | 1st, 2nd generation $H_1$-histamine blockers, cromoglycic acid | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | loratadine | cetirizine | acrivastine | ebastine | quifenadine | levocetirizine | fexofenadine | desloratadine | cromoglycic acid |
| Dizziness, CNS depression | + | + | | + | + | + | + | | + |
| General weakness | + | + | + | + | + | + | + | + | |
| Decreased attention, slowing down of reactions | | | + | | | | | | |
| ↓ BP | | | | | | | | | + |
| ↑ heart rate | + | | | + | | + | + | | |
| Hematopoiesis suppression | | | | | | | | | |
| Dry mouth | + | + | + | + | + | + | + | + | + |
| Anorexia | | | | | | | | | |
| Increased appetite, weight gain | + | + | | + | | + | | | |
| Dyspepsia | + | + | + | + | + | + | + | | + |
| Diarrhea | + | | | | | + | | | |
| Constipation | + | | | | | + | | | |
| Urinary retention | | | | | | + | | | |

The main advantages of drugs of II and III generation compared to 1st generation $H_1$-histamine blockers are:

• high specificity and high affinity for $H_1$-receptors;

• rapid onset of action when administered orally (except for astemizole);

• sufficient duration of antihistamine action (up to 24 hours) and the possibility of a single dose during the day;

• lack of blockade of other types of receptors, which is associated with the side effects of 1st generation $H_1$-blockers;

• impassability through the BBB when used in therapeutic doses and lack of sedative effect;

• lack of connection of drug absorption with food intake;

• lack of tachyphylaxis.

Mast cell membrane stabilizers prevent the release of allergy mediators (histamine, LT, etc.) from mast cells and thereby reduce the intensity of allergic inflammatory reactions. These drugs are used exclusively to prevent allergic reactions. Cromoglycic acid prevents the development of the early and late phases of allergen-induced bronchoconstriction, reduces bronchial hyperreactivity, and prevents the development of bronchospasm. However, cromoglycic acid does not have bronchodilator and antihistamine properties. The main mechanism of action of the drug is the inhibition of the release of allergy mediators from target cells, the prevention of the early and late stages of the allergic reaction in response to immunological and other stimuli in the lungs. Cromoglycic acid acts on the receptor apparatus of the bronchi, increases the sensitivity and concentration of β-adrenergic receptors, blocks reflex bronchoconstriction by inhibiting the activity of C-fibers of sensitive endings of the vagus nerve in the bronchi, which leads to a decrease in the release of substance P and other neurokinins. Prophylactic use of cromoglycic acid suppresses reflex bronchospasm caused by stimulation of sensitive C-fibers. The pharmacological effect develops gradually – after 2 weeks or more. Ketotifen, in addition to preventing mast cell degranulation, has antihistamine activity, is a calcium antagonist, and eliminates β-adrenoceptor tachyphylaxis. Reduces airway hyperreactivity associated with platelet activating

factor or allergens; inhibits the accumulation of eosinophils in the airways; also blocks $H_1$-histamine receptors [44].

The action of mast cell membrane stabilizers extends to a large number of cells involved in the allergic reaction, they slow down both the early and late phases of the allergic process. The spectrum of action of nedocromil sodium is wider than that of cromoglycic acid. Possessing high therapeutic efficacy in mild and moderate asthma, allergic rhinitis, conjunctivitis, drugs of this group are practically devoid of side effects. Mast cell membrane stabilizers are used only for the purpose of prevention, so taking the drugs is started 3–4 weeks before the probable contact with the allergen. The persistent effect of mast cell membrane stabilizers develops within 10–12 weeks of taking the drugs.

Montelukast belongs to the leukotriene receptor antagonists, it is used for the prevention of asthma attacks. By blocking receptors for biologically active cysteinyl LTs, montelukast reduces bronchial hyperreactivity in asthma, prevents excessive secretion in the bronchi and swelling of the respiratory tract mucosa, and thus prevents the development of allergic inflammation. Its use allows to reduce the severity of asthma and the frequency of asthma attacks. The broncholytic effect of montelukast develops slowly from 1 to several days, so therapy should be regular, constant, long-term and continued during exacerbations. Side effects: abdominal pain, headache, allergic reactions, nausea, vomiting, lethargy, apathy, flu-like syndrome, hepatomegaly, increased liver transaminases [28, 29].

The pharmacological effects of I generation antihistamines are determined by their extremely high lipophilicity and ability to block receptors of various types: antiallergic action (blockade of histamine receptors); anticholinergic action (reduction of exocrine secretion, increase in viscosity of secretions); central anticholinergic activity (sedative and hypnotic action); enhancement of the action of CNS depressants; potentiation of the effect of catecholamines (fluctuations in blood pressure); local anesthetic action. The pharmacodynamics of I generation antihistamines includes a large number of side effects [30, 41].

### 3.4. Determining the clinical aspects of the use of antiallergic drugs

To analyze the clinical aspects and conditions of rational use of drugs for the treatment of allergic diseases, we used the Cochrane Library, Trip Database, Medline, PubMed, MedlinePlus, and others. These databases contain systematic information on the effectiveness and safety of various medical technologies. The results of the analysis of the AADs evidence base are presented in the table 3.4.

Table 3.4

**Results of the analysis of the evidence base of clinical efficacy and safety of antiallergic drugs according to systematic reviews**

| № | Title of the study, year of publication | Research results presented in systematic reviews |
|---|---|---|
| 1 | Efficacy and Safety of Bilastine in the Treatment of Allergic Rhinitis: A Systematic Review and Meta-analysis, 2022 [27]. | *The aim:* to determine the efficacy and safety of bilastine in the treatment of AR. The primary outcomes assessed were total symptom score (TSS), nasal symptom score (NSS), and non-nasal symptom score (NNSS). Secondary outcomes were rhinitis discomfort, quality of life (QOL), and adverse events. Risk of bias and quality of evidence were assessed for all studies. *Results obtained:* Bilastine was superior to placebo in improving TSS, NSS, NNSS, rhinitis discomfort score, and quality of life. It had fewer cases of drowsiness compared to cetirizine. Bilastine was effective and safe in treating the general symptoms of AR. Although bilastine was as effective as cetirizine, drowsiness was significantly less with bilastine. |

Continuation of Table 3.4

| | | |
|---|---|---|
| 2 | Efficacy and safety of rupatadine in Japanese adult and adolescent patients with chronic spontaneous urticaria: a double-blind, randomized, multicenter, placebo-controlled clinical trial / Cochrane Database of Systematic Reviews, 2019 [9, 10]. | *The aim:* To conduct a prospective, multicenter, randomized, placebo-controlled, double-blind study in adolescent and adult CSU outpatients aged 12 to < 65 years (JAPIC-CTI No. 152786). Overall, 94, 91, and 92 eligible patients orally received placebo, rupatadine 10 mg, and 20 mg once daily for 2 weeks, respectively.<br>*Results obtained:* The primary and secondary efficacy endpoints consistently favored rupatadine 10 and 20 mg doses over the placebo. No noteworthy dose-related increase in the incidence of adverse drug reactions was observed. Rupatadine is safe and effective at a dose of 10 mg once daily, and can be safely increased to 20 mg once daily, as necessary. |
| 3 | Antihistamine effects and safety of fexofenadine: a systematic review and Meta-analysis of randomized controlled trials / Cochrane Database of Systematic Reviews, 2019 [12]. | *The aim:* However, there is still a lack of collective evidence regarding the antihistamine effects and safety profiles of fexofenadine relative to other antihistamine drugs and placebo. Therefore, we aimed to systematically evaluate the antihistamine effects and safety of fexofenadine.<br>*Results obtained:* Fexofenadine has a positive antihistamine effect, which is probably no worse than the II generation antihistamines. Fexofenadine probably has a favorable safety profile, which is more likely better than that of the I generation of antihistamines. |

Continuation of Table 3.4

| | | |
|---|---|---|
| | | There is lack of data to support that fexofenadine has a better overall safety profile compared to the second-generation antihistamines, however, some presently available evidence on sedative effects and certain aspects of cognitive/psychomotor function favors fexofenadine. Therefore, fexofenadine may be worthy of recommendation for safety related workers. |
| 4 | The Efficacy and Safety of High Dose (10 mg) of Desloratadine (Dazit® 10) in the Treatment of Chronic Spontaneous Urticaria in India: A Phase III, Multicentric, Open-Label, Single-Arm Study / Cochrane Database of Systematic Reviews, 2024 [15]. | *The aim:* We evaluated the efficacy and safety of 10 mg desloratadine (OD) in 256 nonresponsive patients with moderate to severe CSU. The primary outcome was the change in Urticaria Activity Score (UAS7) from baseline to four weeks. Additionally, change in Chronic Urticaria Quality of Life (CU-Q2oL) scores during the course of treatment was also evaluated. *Results obtained:* Results indicated improvements in the disease severity as well as its positive impact on participants' QoL. This study confirms the efficacy and safety of daily use of a twofold dose of desloratadine in nonresponsive moderate to severe patients. |
| 5 | The efficacy and safety of high-dose nonsedating antihistamines in chronic spontaneous urticaria: a systematic review and meta-analysis | *The aim:* to evaluate the efficacy and safety of high doses of antihistamines compared to standard doses in the treatment of chronic spontaneous urticaria. *Results obtained:* It has been determined that a high dose of antihistamine (twice the standard |

Continuation of Table 3.4

| | | |
|---|---|---|
| | of randomized clinical trials, 2023 [37]. | dose) may be more effective than a standard dose in treating chronic spontaneous urticaria. High and standard doses of the drugs showed similar side effects, with the exception of drowsiness, where the incidence appeared to be dose-dependent in some studies. |
| 6 | Evidence-based use of antihistamines for treatment of allergic conditions, 2023 [18]. | *The aim:* to provide a comprehensive overview of evidence-based use of $H_1$-antihistamines for mainly allergic rhinitis (AR) while also discussing urticaria, anaphylaxis, and BA aimed at the practicing physician.<br>*Results obtained:* II generation antihistamines are first-line therapy for AR and urticaria. I generation compounds are not recommended for clinical practice in the allergic conditions described in this review. In fact, I generation antihistamines are frequently used for other indications such as bronchitis, motion sickness, nausea, and vomiting. For anaphylaxis, BA, antihistamines are adjunctive therapies that can be used at the physician's discretion after close consideration of the patient's symptoms. Antihistamines are generally safe and can be used in combination with other therapies for better disease management. |

Continuation of Table 3.4

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|---|---|---|
| 7 | Current status of antihistamine drugs repurposing for infectious diseases / *Medicine in Drug Discovery*, 2022 [36]. | *The aim:* to gather information on the potential role of antihistamines as anti-infective agents. *Results obtained:* Only five antihistamines had in vivo evaluations in rodents, while one study utilized a wax moth model to determine astemizole's anti-Cryptococcus sp. activity when combined with fluconazole. In vitro studies showed that clemastine was active against Plasmodium, Leishmania, and Trypanosoma, while terfenadine suppressed Candida spp. and Staphylococcus aureus growth. In vitro assays found that SARS-coV-2 was inhibited by doxepin, azelastine, desloratadine, and clemastine. Different antihistamines inhibited the Ebola virus (diphenhydramine, chlorcyclizine), Hepatitis C virus (chlorcyclizine), and Influenza virus (carbinoxamine, chlorpheniramine). Generally, in vitro activity (IC50) of antihistamines was in the low to sub-μM range, except for Staphylococcus epidermidis (loratadine MIC = 50 μM) and SARS-coV-2 (desloratadine 70% inhibition at 20 μM). |
| 8 | Anti-Inflammatory Activities of an Anti-Histamine Drug, Loratadine, by Suppressing TAK1 in AP-1 Pathway / *Int. J. Mol*, 2022 [14]. | *The aim:* to investigate whether Loratadine can be utilized as an anti-inflammatory drug through a series of in vitro and in vivo experiments. *Results obtained:* The expression of c-Jun and c-Fos, AP-1 subunits, was repressed by Loratadine and, correspondingly, the expression of p-JNK, p-MKK7, and p-TAK1 was also inhibited. |

Continuation of Table 3.4

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| 8 | | In addition, Loratadine was able to reduce gastric bleeding in acute gastritis-induced mice; Western blotting using the stomach samples showed reduced p-c-Fos protein levels. Loratadine was shown to effectively suppress inflammation by specifically targeting TAK1 and suppressing consequent AP-1 signaling pathway activation and inflammatory cytokine production. |
| 9 | Pro-Arrhythmic Potential of Oral Antihistamines (H1): Combining Adverse Event Reports with Drug Utilization Data across Europe / PLOS ONE, 2015 [26]. | *The aim:* To investigate the pro-arrhythmic potential of antihistamines by combining safety reports of the FDA Adverse Event Reporting System (FAERS) with drug utilization data from 13 European Countries. *Results obtained:* Some second-generation antihistamines are associated with signal of torsadogenicity and largely used in most European countries. Although confirmation by analytical studies is required, regulators and clinicians should consider risk-minimisation activities. Also antihistamines without signal but with peculiar use in a few Countries (e.g., levocetirizine) or with increasing consumption (e.g., rupatadine) deserve careful surveillance. |

Continuation of Table 3.4

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| 10 | New antihistamines – perspectives in the treatment of some allergic and inflammatory disorders Arch Med Sci, 2019 [33]. | *The aim:* It is suggested that in some disorders in which classic antihistamines (i.e. drugs antagonizing histamine effects at $H_1$ receptors) were not effective, it might be possible to control them using novel histamine receptor ligands acting at $H_3$ and/or $H_4$ receptors.<br>*Results obtained:* The $H_4$ receptor is a novel, attractive drug target for a range of conditions, in particular in disorders associated with inflammation or allergies. $H_4$ receptor antagonists presented high efficacy and relative safety in animal models and currently several clinical trials involving them are being conducted or were recently completed. There is still much to be examined. The full therapeutic potential of $H_3$ receptor and $H_4$ receptor ligands is far from understood. There are many remaining questions, especially with regard to the characterization of the latest discovered $H_4$ receptor. |
| 11 | Efficacy of Montelukast in Allergic Rhinitis Treatment: A Systematic Review and Meta-Analysis. Drugs, 2020 [29]. | *The aim:* to assess the effectiveness of montelukast in treating allergic rhinitis.<br>*Results obtained:* Montelukast is more effective than placebo in treating the overall symptoms of allergic rhinitis while the combined therapy of montelukast and an oral antihistamine is superior to either montelukast or an oral antihistamine alone. |

Continuation of Table 3.4

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| 12 | Evaluation of Neuropsychiatric Effects of Montelukast-Levocetirizine Combination Therapy in Children with Asthma and Allergic Rhinitis. Children (Basel), 2023 [29]. | *The aim:* to evaluate the neuropsychiatric effects of montelukast-levocetirizine combination therapy in children. *Results obtained:* This descriptive study was conducted with children aged 2-5 years, diagnosed with asthma and allergic rhinitis, who began to receive montelukast and levocetirizine combination therapy. The respiratory and asthma control test for children (TRACK), Rhino Conjunctivitis Scoring System (RCSS), and common neuropsychiatric effects (irritable behavior, hallucinations, headaches, nightmares, sleep disorders, behavioral and mood disorder, restlessness, depression) were ascertained by the questionnaire applied before and 4 weeks after the treatment. Parents answered on behalf of their children. The most common finding before and after treatment was irritable behavior. While irritable behavior was observed in 82.4% of children before the treatment, this percentage was 63.2% after the treatment ($p = 0.004$). The percentage of children who developed at least one neuropsychiatric symptom after treatment was 22.1%. There was no significant effect of age, gender, RCSS, TRACK, or allergy test positivity on the development of neuropsychiatric symptoms ($p > 0.05$). |

Continuation of Table 3.4

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| | | According to the results, at least one neuropsychiatric finding developed in approximately one in five children. |

Analysis of evidence-based medicine databases allowed us to identify certain features and clinical aspects of the use of AADs.

Diphenhydramine is a reference "night" antihistamine of the 1st generation. In addition to sedative and hypnotic activity, it exhibits weak ganglioblocking, anti-inflammatory, local anesthetic, spasmolytic, antiemetic, potentiating and hypothermic effects. Clemastine is more active than diphenhydramine and acts for 8-12 hours, strongly suppresses the CNS. The inhibitory effect on the CNS in chloropyramine is less pronounced than in diphenhydramine. Promethazine, in comparison with diphenhydramine, exhibits a strong and long-lasting antiallergic, hypothermic, antinausea, antiemetic, potentiating and antitussive effect, which, however, develops slowly. Its local anesthetic effect is more pronounced than that of procaine. Blocks α-adrenoreceptors, therefore it can provoke the development of orthostatic hypotension. Mebhydrolin is a standard "daytime" antihistamine of the 1st generation. Unlike diphenhydramine and chloropyramine, it does not have a hypnotic effect. Cyproheptadine exhibits anticholinergic and sedative properties, stimulates appetite, blocks the secretion of adrenocorticotropic hormone in Itsenko-Cushing syndrome and hypersecretion of somatotropin in acromegaly. Ketotifen is effective for the prevention of sunburn [17, 18, 41, 43].

Levocabastine, azelastine are effective in seasonal allergic rhinitis, allergic conjunctivitis. Hifenadine has a more selective anti-inflammatory effect compared to other antihistamines. It does not have a depressing effect on the CNS.

Cetirizine has a long-term selective effect on $H_1$-histamine receptors. Terfenadine is a fast-acting selective $H_1$-histamine blocker. Acrivastine has an anti-inflammatory effect that lasts up to 12 hours. Dimetinden, loratadine have antipruritic effects. Dimetinden slightly suppresses the CNS. Astemizole does not

have a sedative and anticholinergic effect. In ebastine, due to the action of the active metabolite, the antiallergic effect lasts for 48 hours. Bilastine has less pronounced sedative properties compared to cetirizine [11, 35].

Fexofenadine, levocetirizine, desloratadine are the primary active metabolites. They selectively block $H_1$-histamine receptors, have antiallergic and anti-inflammatory effects, do not penetrate the BBB, do not exhibit sedative, hypnotic, cardiotoxic and some other undesirable effects, have a high level of safety, are characterized by prolonged action and are prescribed once a day [35].

Levocetirizine is the levorotatory (active) isomer of cetirizine. The affinity of levocetirizine for $H_1$-receptors is twice as high as that of cetirizine and 30 times higher than that of the S-enantiomer dextrocetirizine. Levocetirizine is twice as active as cetirizine in antiallergic action. It causes less pronounced sedative effects and is more active than desloratadine [31, 32].

Cromoglycic acid obtained from the fruits of Ammi tooth, is a specific drug for the prevention of asthma attacks in young patients without signs of pneumosclerosis. It is used prophylactically to prevent the development of an asthma attack, but not to relieve acute attacks. The new membrane stabilizer nedocromil sodium blocks the activity of chloride channels of mast cells, and thereby inhibits the release of allergy mediators [28].

Montelukast sodium reduces bronchial reactivity to inhaled allergens, thus preventing the development of bronchospasm and reducing the content of cellular and extracellular inflammatory factors in the respiratory tract.

Antihistamines are incompatible with anticoagulants, trimeperidine, emetics, M-cholinomimetics, tricyclic antidepressants, streptomycine, neomycine, kanamycine, alcohol.

Diphenhydramine, chloropyramine, clemastine, cyproheptadine are incompatible with CNS depressants. Terfenadine, loratadine – with ketoconazole, itraconazole (risk of cardiomyopathy), cisapride, hepatotoxic drugs. Diphenhydramine potentiates the effects of hypnotics, narcotics and neuroleptics, local anesthetics, alcohol, sedatives, incompatible with vitamin C [3].

In kidney diseases, antihistamines should be used with caution. If long-term use of $H_1$-histamine and serotonin receptor blockers is necessary, preference is given to drugs of the II-III generation or alternate with drugs of the I generation, changing every 5 days. Antihistamines of the II generation selectively act on $H_1$-receptors, therefore they have less neurotoxicity and a less sedative effect. Local use of antihistamines can cause irritation and sensitization, so it is better to prescribe them perorally [35]. The appointment of diphenhydramine during breastfeeding can cause paradoxical stimulation of the central nervous system in children. Dimenhydrinate can mask the clinical picture of appendicitis. Terfenadine is used with caution in patients with arrhythmias, coronary heart disease. Young children must strictly follow the recommendations for the dosage of mebhydrolin (psychomotor agitation is possible). Clemastine solution cannot be administered intraarterially. Inhalation of cromoglycic acid makes it possible to gradually reduce the doses of corticosteroids and bronchodilators. In asthma of physical exertion, to prevent an attack, inhalation of cromoglycic acid is performed immediately before physical exertion and 20-30 minutes after inhalation of the bronchodilator [41].

The solution of cromoglycic acid should not be inhaled in a mixture with solutions of bromhexine and ambroxol, but can be used in combination with bronchodilators and GCS. With a single administration of ketotifen with oral hypoglycemic agents, thrombocytopenia may occur. Ketotifen should be prescribed with caution to people whose work requires concentration of attention. It potentiates the effect of hypnotics and sedatives. At the beginning of treatment with ketotifen, anti-asthmatic drugs, especially systemic corticosteroids, should not be abruptly discontinued, since the development of adrenal insufficiency is possible. Ketotifen should be discontinued gradually in patients with BA and bronchoobstructive syndrome.

Dimenhydrinate, dimethindene, zafirlukast are taken before meals; during meals – chloropyramine, ketotifen; after meals – mebhydrolin, quifenadine, cyproheptadine, promethazine.

It is suggested that some diseases in which current $H_1$-histamine blockers are not effective may be treated with new histamine receptor ligands that act on $H_3$- and/or $H_4$-histamine receptors. $H_4$-histamine receptor blockers are new, promising drugs for a number of inflammatory and allergic diseases. $H_4$-histamine receptor antagonists have demonstrated high efficacy and relative safety in preclinical studies in experimental models, and several clinical trials with their participation are currently underway or have recently been completed [33]. However, the full therapeutic potential of $H_3$-receptors and $H_4$-receptor ligands is still far from being fully understood. Many questions remain, especially regarding the characterization and physiological role of $H_4$-receptors. But, taking into account all of the above, the creation and study of $H_3$- and $H_4$-histamine receptor blockers is a promising direction in the therapy and prevention of allergic diseases.

**Conclusions to chapter 3**

1. There are 221 antiallergic drugs registered on the pharmaceutical market of Ukraine, 22 INN. $H_1$-histamine blockers account for 86% of all antiallergic drugs registered in Ukraine.

2. In terms of the number of trademarks, the most popular is the third-generation antihistamine desloratadine, with 50 drugs based on it on the market. Levocetirizine is in second place (41 drugs).

3. Among the antiallergic drugs registered in Ukraine, 41.2% are drugs of foreign manufacturers, 58.8% are foreign drugs. Pharmaceutical companies "Farmak" and "Zdorovya" are leaders in Ukraine in the production of antiallergic drugs. Among foreign companies, the leaders are the companies "Adamed" (Poland), "World Medicine" (Turkey).

4. Based on the results of the analysis of literature data, a comparative pharmacological characteristic of different classes of antiallergic drugs was provided. It was established that antihistamines of the II and III generations are safer.

5. Based on the analysis of evidence-based medicine data, it was determined that antihistamines of the III generation are the most in demand today (by frequency of prescription).

6. Clinical aspects and conditions for the rational use of antiallergic drugs of different groups were established.

# CONCLUSIONS

1. There are 221 antiallergic drugs registered on the pharmaceutical market of Ukraine, 22 international non-proprietary names. The market leaders among various groups of antiallergic drugs are $H_1$-histamine blockers. They account for 86% of all antiallergic drugs registered in Ukraine.
2. In terms of the number of trademarks, the most popular is the III generation antihistamine desloratadine, with 50 drugs based on it on the market. Levocetirizine is in second place (41 drugs). They are slightly inferior to the II-st generation antihistamine loratadine (24 drugs) and the leukotriene receptor antagonist montelukast (25 drugs).
3. Among the antiallergic drugs registered in Ukraine, 91 (41.2%) are drugs of foreign manufacturers, 130 (58.8%) are foreign drugs. Pharmaceutical companies "Farmak" and "Zdorovya" are leaders in Ukraine in the production of antiallergic drugs. Among foreign companies, the leaders are the companies "Adamed" (Poland), "World Medicine" (Turkey). The assortment of drugs from foreign manufacturers exceeds the number of domestic drugs by almost one and a half times.
4. Based on the results of the analysis of literature data, we provided a comparative pharmacological characteristic of different groups of antiallergic drugs. The main advantages and disadvantages of drugs of each group were determined.
5. Based on data from 12 systematic reviews, the conditions for rational use and certain clinical aspects of antiallergic drugs of different groups were determined, namely, attention to rational choice of drug, assessment of drug interactions, etc.
6. The creation, study and implementation of selective $H_3$- and $H_4$-histamine receptor blockers into clinical practice is one of the perspective directions of therapy and prevention of allergic diseases.

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# APPLICATIONS

APPLICATION A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
КАФЕДРА БІОТЕХНОЛОГІЇ

MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
DEPARTMENT OF BIOTECHNOLOGY

# ПРОБЛЕМИ ТА ДОСЯГНЕННЯ СУЧАСНОЇ БІОТЕХНОЛОГІЇ

# PROBLEMS AND ACHIEVEMENTS OF MODERN BIOTECHNOLOGY

**Матеріали**
**V міжнародної науково-практичної**
**конференції**

**Materials**
**of the V International Scientific and Practical**
**Conference**

**ХАРКІВ**
**KHARKIV**
**2025**

**Analysis of the assortment of antiallergic drugs in Ukraine**

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Allergic diseases are an important clinical problem of medicine. Modern epidemiological data show that today allergic diseases are one of the most common groups of diseases in the world. The incidence is more than 150 million people, and this figure continues to grow. At the same time, the prevalence of allergic diseases in European countries reaches 30%, and about 10% of patients have chronic diseases of allergic genesis.

Currently, pharmacotherapy remains the mainstay of treatment for allergic diseases and includes intranasal glucocorticoids, oral and intranasal antihistamines, and leukotriene receptor antagonists. Mast cell membrane stabilizers are used to prevent certain allergic diseases.

The aim of the study was to analyze the assortment of antiallergic drugs on the pharmaceutical market of Ukraine. The State Register of Medicinal Products of Ukraine and the Compendium of Medicinal Products were used to analyze the assortment of antiallergic drugs. Specific antiallergic drugs were selected for the analysis, namely, $H_1$-histamine blockers, mast cell membrane stabilizers, and leukotriene receptors antagonists.

It was determined that as of March 1, 2025, 11,784 drugs were registered in Ukraine. Of these, 4,014 were drugs of domestic manufacturers, 7,770 were drugs of foreign companies. 22 international non-patented names (INN) of antiallergic drugs, 221 trade names were registered in Ukraine. Of these, $H_1$-histamine blockers - 20 INNs, 190 trade names; membrane stabilizers - 2 INNs (3 drugs); leukotriene receptors antagonists - 1 INN (25 trade names), 3 combined drugs. The share of antiallergic drugs is approximately 1.9% of the entire assortment of drugs registered in Ukraine. The leaders among various groups of antiallergic drugs are $H_1$-histamine

blockers. They account for 86% of all antiallergic drugs registered in Ukraine. Today, representatives of all three generations of $H_1$-histamine blockers are available in Ukraine. First-generation $H_1$-histamine receptor blockers are registered – 33 drugs (8 INN), second-generation antihistamines – 59 drugs (8 INN), third-generation $H_1$-histamine receptor blockers – 98 drugs (3 INN). Thus, the majority of modern antihistamines in Ukraine are representatives of the second and third generations, drugs with a selective mechanism of action that do not suppress the CNS, have a prolonged effect and a high level of safety. The second place is occupied by the youngest antiallergic drugs – leukotriene receptors antagonists (11,3%). It was found that the most popular antiallergic drugs in Ukraine today are third-generation $H_1$-histamine receptors blockers (98 trade names based on 3 INNs). The leaders in terms of the number of trade names are desloratadine (50 drugs) and levocetirizine (41 drugs). They are slightly inferior to the second-generation antihistaminic drug loratadine (24 drugs) and the leukotriene receptors antagonist montelukast (25 drugs). Combined drugs (3 drugs) contain a fixed combination of active ingredients, namely, montelukast and levocetirizine.

Among the antiallergic drugs registered in Ukraine, 91 (41.2%) are drugs of foreign manufacturers, 130 (58.8%) are foreign drugs. Pharmaceutical companies "Farmak" (20 drugs) and "Zdorovya" (14 drugs) are leaders in Ukraine in the production of antiallergic drugs. Among foreign companies, the leaders are "Adamed" (Poland) (9 drugs), "World Medicine" (Turkey) (8 drugs). Indian pharmaceutical companies ("Micro Labs Ltd", "Hetero Labs Limited", "Dr. Reddy's Laboratories", "Genom Biotech Pvt Ltd", "Sun Pharmaceutical Industries" and others) together produce 35 drugs, which is equal to 15.8% of the entire Ukrainian market of antiallergic drugs.

Thus, the range of drugs for the treatment of allergic diseases on the modern pharmaceutical market of Ukraine is quite wide. 221 drugs based on 22 INNs are registered on the Ukrainian market. The market leader is desloratadine (50 drugs based on it). Levocetirizine is in second place (41 drugs). The range of products of foreign manufacturers exceeds the number of domestic drugs by 1.4 times.

APPLICATION B

*Ф А 2.2.1-32-366*

**National University of Pharmacy**

Faculty pharmaceutical
Department of Pharmacology and Clinical Pharmacy
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

**APPROVED**
**The Head of Department Pharmacology and Clinical Pharmacy**

**Sergii SHTRYGOL**
«02» September 2024

**ASSIGNMENT**
**FOR QUALIFICATION WORK OF AN APPLICANT FOR HIGHER EDUCATION**

**Saad Eddine LAMFANNAN**

1. Topic of qualification work: "Analysis of the range of anti-allergic drugs in Ukraine and their comparative characteristics",
supervisor of qualification work: Anna KONONENKO, PhD, assoc. prof.
approved by order of NUPh from "27" of September 2024 № 237

2. Deadline for submission of qualification work by the applicant for higher education: May 2025.

3. Outgoing data for qualification work: domestic and foreign recommendations on modern approaches to pharmacotherapy of allergic conditions, based on the principles of evidence-based medicine, scientific literary sources on the rational and safe use of medicines for the symptomatic treatment of allergies.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): to conduct a literature review on the etiology, pathogenesis, classification, clinical manifestations and modern approaches to pharmacotherapy of allergic conditions; to analyze the range of antiallergic drugs; to study the clinical and pharmacological characteristics and conduct a comparative analysis of different groups of antiallergic drugs; to determine the features and aspects of the clinical application of modern AAs based on the analysis of evidence-based medicine data.

5. List of graphic material (with exact indication of the required drawings):
- 6 tables, 4 figures

6. Consultants of chapters of qualification work

| Signature | **Name, SURNAME, position of consultant** | **Signature, date** | |
|---|---|---|---|
| | | **assignment was issued** | **assignment was received** |
| 1 | Anna KONONENKO, associate professor of higher education institution of Pharmacology and Clinical Pharmacy department | 02.09.2024 | 02.09.2024 |
| 2 | Anna KONONENKO, associate professor of higher education institution of Pharmacology and Clinical Pharmacy department | 03.03.2025 | 03.03.2025 |
| 3 | Anna KONONENKO, associate professor of higher education institution of Pharmacology and Clinical Pharmacy department | 17.03.2025 | 17.03.2025 |

7. Date of issue of the assignment: “02” September 2024

**CALENDAR PLAN**

| **№** | **Name of stages of qualification work** | **Deadline for the stages of qualification work** | **Notes** |
|---|---|---|---|
| 1. | Writing Chapter 1 "Literature Review" | December 2024 | **done** |
| 2. | writing Chapter 2 "Research Methods" | March 2024 | **done** |
| 3. | Writing Chapter 3 "Research Results" | March 2024 | **done** |
| 4. | Finalization of qualification work and preparation of documents | May 2024 | **done** |

An applicant of higher education_____Saad Eddine LAMFANNAN

Supervisor of qualification work_____Anna KONONENKO

**ВИТЯГ З НАКАЗУ № 237**

По Національному фармацевтичному університету

**від 27 вересня 2024 року**

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу Фм20(4,10д) 2024-2025 навчального року, освітньо-професійної програми – Фармація, другого (магістерського) рівня вищої освіти, спеціальності 226 – Фармація, промислова фармація, галузь знань 22 Охорона здоров'я, денна форма здобуття освіти (термін навчання 4 роки 10 місяців), які навчаються за контрактом (мова навчання англійська та українська) згідно з додатком № 1.

| Прізвище, ім'я здобувача вищої освіти | Тема кваліфікаційної роботи | | Посада, прізвище та ініціали керівника | Рецензент кваліфікаційної роботи |
|---|---|---|---|---|
| **по кафедрі фармакології та клінічної фармації** | | | | |
| Ламфаннан Саад Еддін | Аналіз асортименту антиалергічних засобів в Україні та їх порівняльна характеристика | Analysis of the range of antiallergic drugs in Ukraine and their comparative characteristics | Доц. Кононенко А.В. | Доц. Щербак О.А. |

**Ректор** Віріно Секретар

ФА2.8-03-317

# ВИСНОВОК

**експертної комісії про проведену експертизу**
**щодо академічного плагіату у кваліфікаційній роботі**

**здобувача вищої освіти**

«26» квітня 2025 р. № 331058564

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Ламфаннан Саад Еддін, групи Фм20(4.10) англ-03, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Аналіз асортименту антиалергічних засобів в Україні та їх порівняльна характеристика / Analysis of the range of antiallergic drugs in Ukraine and their comparative characteristics», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

**Голова комісії,**
**проректор ЗВО з НПР,**
**професор** **Інна ВЛАДИМИРОВА**

*Ф А 2.2.1-32-353*

**REVIEW**

**of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy**

**Saad Eddine LAMFANNAN**

**on the topic: «Analysis of the range of anti-allergic drugs in Ukraine and their comparative characteristics»**

**Relevance of the topic.** Allergic diseases are an important clinical problem of medicine. Modern epidemiological data indicate that today allergic diseases are one of the groups of the most common chronic diseases in the world, affecting more than 150 million people. According to forecasts of the European Commission on Allergy, in the 21st century about half of the world's population may suffer from allergies.

**Practical value of conclusions, recommendations, and their validity.** The conclusions and recommendations formulated in the qualification work correspond to the objectives of the study. The results of the obtained studies can be used by practicing physicians, pharmacists and health care organizers to optimize the use of antiallergic drugs. The obtained research results were highlighted by the author in the abstracts and tested at a scientific and practical conference.

**Assessment of work**. The qualification work is a completed research, designed in accordance with all requirements. It is recommended to conduct an additional check of spelling errors.

**General conclusion and recommendations on admission to defend.** The work is performed in full, designed in accordance with the current requirements for the qualification works at the National University of Pharmacy, and can be recommended for submission to the Examination Commission for further defense.

Scientific supervisor _____ Anna KONONENKO

«9» May 2025

**REVIEW**

**of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy**

**Saad Eddine LAMFANNAN**

**on the topic: «Analysis of the range of anti-allergic drugs in Ukraine and their comparative characteristics»**

**Relevance of the topic.** Allergic diseases are one of the most common causes of general morbidity in the world and cause a significant burden on health care and the medical system of different countries. At least 30% of the population suffers from diseases such as BA, allergic rhinitis, atopic dermatitis, urticaria and life-threatening cases of food, drug, and insect venom allergies, and their prevalence continues to grow worldwide. These diseases are a current "disease of civilization". According to statistics, every fifth person in the world suffers from allergies. Today, modern methods of treating allergic diseases include elimination measures, if possible, pharmacotherapy and allergen-specific immunotherapy (ASIT). Pharmacotherapy includes immunosuppressants (cytostatics, glucocorticosteroids); mast cell activation and degranulation blockers; receptor blockers (histamine, leukotriene) and enzyme blockers (proteolysis inhibitors); anticytokine drugs. The correct choice and rational use of antiallergic drugs in the complex therapy of allergic diseases allow to relieve acute manifestations of allergy, achieve high treatment effectiveness and prevent its re-exacerbation.

**Theoretical level of work.** The author theoretically substantiated the relevance of the topic, formulated the goals and objectives of the work. In the work submitted for review, the author reviewed a large volume of scientific sources on the relevant topic. The data was systematized and the range of antiallergic drugs available on the Ukrainian market was analyzed. The evidence base of clinical effectiveness and safety of drugs for the treatment of allergies was analyzed based on data from international clinical guidelines, systematic reviews and results of clinical studies. The main directions for increasing the level of safety were established and the conditions for the

rational use of antiallergic drugs were determined. The results obtained made it possible to determine the conditions for the rational use of drugs for the treatment of allergies. The conclusions and provisions of the qualification work made by the author are based on a sufficient number of studies.

**Author's suggestions on the research topic.** Based on the results obtained, the author identified the main directions for minimizing side effects and the conditions for the rational use of antiallergic drugs.

**Practical value of conclusions, recommendations, and their validity.** The results of the work and the conclusions drawn on their basis are of high practical importance for the implementation of methods to increase the effectiveness of the pharmacotherapy of allergy with the participation of both doctors and pharmacists.

**Disadvantages of work.** There are grammatical and punctuation errors, unsuccessful stylistic turns in the work.

**General conclusion and assessment of the work.** The work meets the requirements for qualification work in National University of Pharmacy and can be recommended for defense.

Reviewer _____ Olena SHCHERBAK

«14» May 2025

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ**
**НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ**
**ВИТЯГ З ПРОТОКОЛУ № 19**
**засідання кафедри фармакології та клінічної фармації**

15 травня 2025 р. м. Харків

**Голова:** завідувач кафедри, доктор мед. наук, професор Штриголь С. Ю.
**Секретар:** кандидат фарм. наук, доцент Вєтрова К. В.

**ПРИСУТНІ:** зав. каф., проф. Штриголь С.Ю., проф. Деримедвідь Л.В., доц. Бєлік Г.В., доц. Вєтрова К.В., доц. Жаботинська Н.В., доц. Кононенко А. В., доц. Матвійчук А.В., доц. Отрішко І.А., доц. Очкур О.В., доц. Рябова О.О., доц. Савохіна М.В., доц. Степанова С. І., доц. Таран А.В., ас. Верховодова Ю.В., ас. Підгайна В.В. та здобувачі вищої освіти.

**ПОРЯДОК ДЕННИЙ:**
1.Розгляд кваліфікаційних робіт здобувачів вищої освіти для подання робіт до Екзаменаційної комісії.

**СЛУХАЛИ:**
1.Здобувача вищої освіти Ламфаннана Саада Едділа зі звітом про проведену наукову діяльність за темою кваліфікаційної роботи: «Аналіз асортименту антиалергічних засобів в Україні та їх порівняльна характеристика» («Analysis of the range of anti-allergic drugs in Ukraine and their comparative characteristics»).

**УХВАЛИЛИ:**
1. Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Ламфаннан Саад Еддін допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

**Голова**
Завідувач кафедри, проф. Штриголь С. Ю.

**Секретар**, доц. Вєтрова К. В.

*Ф А2.2.1-32-042*

# НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

## ПОДАННЯ
## ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
## ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Саад Еддін ЛАМФАННАН до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньо-професійною програмою Фармація
на тему: «Аналіз асортименту антиалергічних засобів в Україні та їх порівняльна характеристика».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Микола ГОЛІК /

**Висновок керівника кваліфікаційної роботи**

Здобувач вищої освіти Саад Еддін ЛАМФАННАН у повному обсязі виконав кваліфікаційну роботу. За актуальністю, методичним рівнем, теоретичним та практичним значенням, об'ємом виконаних досліджень кваліфікаційна робота відповідає вимогам і допускається до захисту в Екзаменаційній комісії.

Керівник кваліфікаційної роботи

_____ Анна КОНОНЕНКО

«09» травня 2025 р.

**Висновок кафедри про кваліфікаційну роботу**

Кваліфікаційну роботу розглянуто. Здобувача вищої освіти Саад Еддін ЛАМФАННАН допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри
фармакології та клінічної фармації

_____ Сергій ШТРИГОЛЬ

«15» травня 2025 року

Qualification work was defended

of Examination commission on

« __ » June 2025

with the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____/ Volodymyr YAKOVENKO /