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QUALIFICATION WORK

on the topic:

RATIONALE FOR THE EXTEMPORANEOUS CREAM COMPOSITION AND BASE CHOICE WITH LEVOCETIRIZINE

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ANNOTATION

The qualification work is dedicated to the theoretical justification of the composition, technology development and experimental studies on the extemporaneous cream and with levocetirizine.

The work is presented on 45 pages of printed text, consists of an introduction, 3 chapters, general conclusions, a list of used sources, appendices. The list of used sources contains 32 items. The work is illustrated with 4 table and 6 figures.

Key words: cream, extemporaneous, technology, levocetirizine.

АНОТАЦІЯ

Кваліфікаційна робота присвячена теоретичному обґрунтуванню складу, розробці технології та експериментальним дослідженням екстемпорального крему з левоцетиризином.

Робота викладена на 45 сторінках друкованого тексту, складається зі вступу, 3-х розділів, загальних висновків, списку використаних джерел, додатків. Перелік використаних джерел містить 32 позицій. Роботу ілюстровано 4 таблицями та 6 рисунками.

Ключові слова: крем, екстемпоральний, технологія, левоцетиризин.

CONTENTS

LIST OF USED ABBREVIATIONS

API - Active pharmaceutical ingredients;

EAACI - European Academy of Allergology and Clinical Immunology;

GCs – glucocorticosteroids;

HVA - Hereditary vibrational angioedema;

SPU – State Pharmacopoeia of Ukraine;

INTRODUCTION

Actuality of theme. The actuality of the theme is demonstrated by the following evidence. The skin represents one of the most significant immunological organs, susceptible to a multitude of external and internal influences, in addition to innate adaptive immune responses. A number of dermatological conditions, including atopic dermatitis, contact dermatitis, urticaria, angioedema, psoriasis and autoimmune blistering disorders, are associated with immune processes. The majority of these diseases are chronic, inflammatory, and proliferative, with both genetic and environmental factors exerting a significant influence. These immunological mechanisms may have implications for potential future therapeutic targets [3, 10].

Urticaria is finally recognised as an independent disease, but a complete understanding of the mechanisms of its occurrence still eludes researchers. Furthermore, over the past five years, additional evidence has accumulated indicating that patients with urticaria have a significantly impaired quality of life. Consequently, these patients merit the focused attention of medical professionals.

Hives are defined as an inflammatory dermatological condition that arises when the immune system releases histamine. This results in the leakage of small blood vessels, which, in turn, causes the skin to swell. The term "angioedema" is used to describe swelling in the deep layers of the skin.

Two distinct forms of urticaria have been identified: acute and chronic. Acute urticaria may manifest subsequent to the ingestion of a specific foodstuff or contact with a particular trigger. Additionally, non-allergic causes may be responsible, including elevated temperature, exogenous or endogenous exposure, the use of drugs or certain foods, insect bites, or infections. Chronic urticaria is rarely caused by specific triggers, rendering allergy tests an ineffective diagnostic tool. Chronic urticaria can persist for an extended period, ranging from months to years. According to the literature, urticaria is observed during the lifetime of 15% to 25% of individuals. While the majority of these cases are readily treatable, approximately 30% of patients experience symptoms for a duration exceeding six weeks. In such

instances, urticaria is regarded as a chronic condition [2, 9].

The utilisation of novel pharmaceutical agents for the localised management of urticaria will result in a reduction of bothersome symptoms and a concomitant reduction in the overall duration of treatment. Furthermore, the incidence of adverse effects will be diminished, and the costs associated with the use of expensive, industrially produced pharmaceuticals will be significantly reduced.

The purpose of the study. The objective of study is to provide a theoretical justification of extemporaneous cream composition, base choice, technology development and to conduct experimental properties studies of extemporaneous cream with Levocetirizine for skin allergic diseases treatment.

Research tasks:

- to conduct an analysis of literature data on types of allergic diseases and mechanisms of its development;
- to carry out analysis of modern approaches to the treatment of allergic skin diseases;
- to chow the range of medicines for the treatment of allergic skin diseases, in particular urticaria;
- theoretically substantiate the composition and develop the technology of the extemporaneous cream with Levocetirizine, taking into account the physical and chemical properties of the ingredients;
- the stability of the developed cream during storage investigate.

The subject of research. A study was conducted to examine the development of extemporaneous cream with Levocetirizine, with a particular focus on its composition and technology.

Research objects. Levocetirizine, purified water, Olivem 1000, Peach oil.

Research methods. Physical, chemical, technological and organoleptic.

Practical significance of the obtained results. Extemporaneous cream with Levocetirizine for skin allergic diseases treatment was suggested.

Elements of scientific research. The research methodology included an investigation of the scientific literature on the subject, as well as laboratory-based

experiments. Based on the findings of these studies, extemporaneous cream for the symptomatic therapy of skin allergic diseases was offered, developed and tested.

Approval of research results and publication. The results of this research have been peer-reviewed and published. The findings can inform the further development of the cream's composition, potentially expanding the range of modern drugs for urticaria treatment. “Current issues of creating new medicines: XXIX international scientific and practical conference of young scientists and students” (April 19-21, 2023, Kharkiv). Publication on the topic “Rationale of the cream composition for the urticaria treatment” was represented.

The work is presented on 45 pages of printed text, consists of an introduction, 3 chapters, general conclusions, a list of used sources, appendices. The list of used sources contains 32 items. The work is illustrated with 4 table and 6 figures.

CHAPTER 1.
ALLERGIC DISEASES

1.1. Allergic diseases characteristics

It is now relatively commonplace to encounter individuals who exhibit allergic reactions to specific products or who suffer from allergic rhinitis. Indeed, this pathology affects approximately one-third of the global population, ranking as the fifth most prevalent chronic disease worldwide. The risk of developing allergic diseases is increased by a number of factors, including the deterioration of the ecological situation and the emergence of new allergens. The prevalence of disinfectants is also a significant contributing factor, as is acute and chronic stress, which is particularly relevant in our modern, turbulent times.

It is noteworthy that in developed countries, approximately 90% of the population experiences severe stress. For instance, the 2012 global population survey indicated that the average stress level was 4.9 out of 10, with a score of 1 indicating low stress. Furthermore, it is notable that approximately 20% of the population perceives their stress levels to be at an extreme (8-10 points). This is particularly pertinent given the additional stressors that individuals face in the current context, including concerns about the future of the state and their own circumstances [3, 10].

The field of psychosomatic relationships represents a significant challenge in modern medicine. Despite centuries of research into the interconnection between mental and physical health, beginning with the works of Hippocrates and Aristotle, this area of study remains a complex and multifaceted one.

In accordance with the contemporary nomenclature of the European Academy of Allergology and Clinical Immunology (EAACI), allergy is defined as a hypersensitivity reaction initiated by immune mechanisms (allergos – other, ergos – action) [3, 16].

The significant prevalence, rapid growth rates, variety of clinical forms, chronic relapsing course and large number of complications associated with allergic diseases make them a priority interdisciplinary problem in modern medicine.

Allergy is a disease characterised by an increased sensitivity of the body to certain environmental influences, referred to as allergens, which elicit a reaction from the immune system in the form of various symptoms.

An allergic reaction is defined as a hypersensitivity reaction of the first type, which develops in response to the introduction of an allergen into the body. Concurrently, the production of antibodies, namely immunoglobulin E, occurs in response to the introduction of specific proteins. The reaction that develops during the production of immunoglobulins is referred to as an allergic reaction and is manifested only in the case of hypersensitivity of the body.

Given the varying degrees of sensitivity to different immunoglobulins, allergic reactions can manifest with mild symptoms or have serious consequences for the body as a whole.

Allergic diseases can manifest in any individual, irrespective of age or gender. They may present as transient symptoms that abate with the disappearance of the allergen, or they may manifest in an acute form [1, 8, 10].

All allergens can be classified into two principal categories.

Exoallergens are environmental factors that act as a catalyst for the onset of an allergic reaction. Endoallergens, on the other hand, are intrinsic elements of the body's internal milieu that accompany the progression of an allergic response.

It is becoming increasingly evident that the term "allergy" is being applied to a growing number of conditions that, in principle, cannot be of an allergic nature. A lack of understanding of the nature and cause of the disease leads to the use of a variety of drugs, which temporarily alleviate the symptoms. However, once the medication is discontinued, the symptoms recur. Furthermore, the administration of pharmaceutical agents may result in the emergence of drug resistance, and in instances where the use of such agents is justified, the desired therapeutic effect may not be achieved.

While all individuals are susceptible to allergic reactions, some experience them to a greater extent than others. This is due to the fact that the body's sensitivity is influenced not only by immunoglobulins, which are produced in response to an

allergen, but also by genetic predisposition. Consequently, in numerous instances, allergy diagnoses take into account family history to facilitate a more precise diagnosis [3, 12, 15].

Recently, medical practitioners have increasingly observed that allergic reactions manifest as a consequence of excessive adherence to hygiene regulations. This results in the immune system receiving an inadequate load, a reduction in the body's resistance, and an increase in sensitivity to the most prevalent allergens. Additionally, the frequency of allergic reactions may lead to the frequent consumption of products derived from the chemical industry.

Allergic diseases classification:

Allergic rhinitis: this disease is characterised by the following symptoms: frequent sneezing, watery nasal discharge, nasal congestion, scabies in the pharyngeal cavity, and in the majority of patients, scabies and redness of the eyes (allergic conjunctivitis).

Seasonal allergic rhinitis, which may manifest at any time of year, is typically triggered by allergens present in the domestic environment. These include house dust mites (which secrete a protein called Der p 1), mould spores and allergens excreted by the saliva or mammary glands of cats and dogs.

Conversely, seasonal sensitivity to the pollen of trees, plants, or grasses manifests as allergy symptoms exclusively during the flowering seasons of these plants. Seasonal allergies, also known as hay fever, typically manifest in the spring (when flowers and trees are in bloom) or in the autumn (when other plants are in seasonal bloom) [7, 16, 21].

Allergic inflammation of the conjunctiva of the eye. This type of allergy presents with lacrimation, redness and crusting of the eyes or eyelids, and frequently co-occurs with an allergic runny nose.

Allergic (bronchial) asthma is characterised by the presence of symptoms such as shortness of breath, cough and a sensation of suffocation. These symptoms are the result of inflammation of the respiratory tract. The swelling of the airways, which is a consequence of inflammation, results in respiratory difficulty.

Inhalation of allergens can result in allergic inflammation of the airways. However, the implementation of appropriate treatment and prevention strategies can effectively mitigate or alleviate the symptoms associated with asthma.

Approximately 70% of individuals with asthma are affected by the disease as a result of allergic sensitivity, with approximately 50% of these individuals also exhibiting symptoms of allergic rhinitis. In children, asthma is more frequently caused by allergies than in adults. Indeed, in 90% of cases of asthma in children and in 50% of cases in adults, this disease is caused by allergies.

Atopic dermatitis (atopic eczema) is also referred to as "skin asthma."

The condition in question pertains to dermatological inflammation, which typically manifests in a recurrent pattern. The condition is characterized by the presence of scabies and dry skin, as well as a red rash. In some cases, the presence of dandruff or skin roughness at the site of inflammation may be observed [5, 10, 23].

This disease is more prevalent among infants and young children.

The typical rash manifests in different locations on the body, depending on the age of the patient. In children and adolescents, it most frequently appears on the elbows and behind the knees, while in adults, it is most common on the palms and neck.

Atopic dermatitis in young children is typically the initial presentation of a constellation of atopic disorders precipitated by allergic responses, which the individual will subsequently experience, including atopic dermatitis, food sensitivities, allergic rhinitis, and asthma.

Urticaria (also known as nettle fever or hives) is an itchy rash characterised by red spots with a raised, swollen centre that appears in various places on the body.

The rash is typically pruritic, but typically resolves within a few hours of onset. Recurrences are often transient and occur in different locations. Additionally, the colour of the rash remains unchanged and there is no scarring to the skin. Furthermore, 40% of patients present with subcutaneous oedema (angioedema), which typically occurs on the lips, hands, eyelids, and other areas.

Urticaria may manifest acutely, lasting from several hours to six weeks. In such instances, a systemic/cutaneous reaction may ensue.

Chronic urticaria persists for a minimum of six weeks, with some cases lasting for months or even years. In the majority of cases, chronic urticaria is not a manifestation of an allergic reaction, but rather the consequence of an immunological response that results in the activation of mast cells and the release of histamine [16, 31, 42].

Food allergies are marked by a swift allergic response, which can sometimes be life-threatening, such as in the case of an anaphylactic reaction triggered by certain foods.

The most common food allergens include:

- Dairy products (milk)
- Eggs
- Fish
- Crustaceans and mollusks
- Nuts: almonds, Brazil nuts, cashews, chestnuts, hazelnuts, macadamia nuts, pecans, pine nuts, pistachios, walnuts
- Peanuts
- Grains: wheat, rye, barley, oats
- Soy
- Sesame seeds

The prevalence of food allergies is increasing globally, with an estimated 3-5% of children under six years of age and 1-2% of school-age children affected. It is predicted that the majority of individuals with food allergies will continue to experience allergic reactions into adulthood. It is crucial to highlight that individuals with food allergies are at risk of developing a severe anaphylactic reaction following the consumption of even a small amount of a particular food product. Asthma is identified as a significant risk factor for anaphylaxis [6, 11, 21].

Allergy to medicines. Adverse reactions to drugs, including allergic reactions to them, represent a significant cause of morbidity and mortality in the modern world.

Drug allergy represents one of the most common causes of anaphylactic reactions. In some cases, repeated exposure to a single drug (and, in other instances, to another drug belonging to the same class or group) can prove to be life-threatening. The diagnostics carried out in the allergy clinic have enabled the diagnosis of drug sensitivity and the prevention of dangerous allergic reactions.

Conversely, misdiagnosis of allergies is a prevalent phenomenon, resulting in many patients receiving inadequate treatment. The utilisation of alternative medicinal therapies in the absence of confirmed allergies to the requisite pharmaceuticals may result in the patient being compelled to resort to less efficacious and more costly interventions. It is therefore imperative that an accurate diagnosis of drug allergy is made. It should be noted that in certain cases, it may be possible to allow the taking of vital drugs (for example, chemotherapy in the case of cancer or treatment with antibiotics, which have no substitute), even if the patient is sensitive to them. This requires a procedure performed by an allergist, known as desensitization [7, 13, 22].

It is important to note that there are other forms of allergy that are more prevalent than others. One such example is bee venom allergy. In the case of this potentially fatal form of allergy, a treatment involving an allergy shot (immunotherapy) has been developed which provides 99% protection against an anaphylactic reaction caused by a repeated sting.

Another form of allergy that markedly impairs the quality of life of individuals with underlying health conditions is contact dermatitis, a type of allergic inflammation of the skin caused by exposure to an allergen. The subject under discussion is an itchy skin infection accompanied by an eczematous rash that appears after prolonged contact of the skin with a foreign substance (for example, with nickel, cosmetics, rubber, gloves, etc.). The accurate identification of the allergen

responsible for the allergic reaction enables the avoidance of further contact and facilitates the healing process of the affected skin [9, 12].

Given its high prevalence, the lack of unified approaches to its diagnosis and treatment, the financial costs associated with therapy and rehabilitation for patients, and the reduction in their quality of life, urticaria represents a significant medical and social problem. In accordance with the findings of various authors, urticaria is estimated to affect approximately 30% of the global population. Allergists and dermatologists, to whom patients with urticaria most often turn, are particularly aware of the significance of this issue.

Epidemiological Characteristics of Urticaria:

Urticaria is a common condition, affecting 15-25% of the population at least once in their lifetime. It presents in varying forms:

- 49% of patients experience both urticaria and angioedema.
- 40% experience only urticaria.
- 11% have isolated angioedema.

In most cases (70-75%), urticaria follows an acute course, resolving within a few weeks, while in 25-30% of patients, it becomes chronic, persisting for six weeks or longer.

Urticaria can manifest at any age, though it is most prevalent in individuals aged 14-40 years, where the peak incidence is observed. However, in recent years, there has been an increase in the number of cases among preschool and younger children. Among children and adolescents, the prevalence of urticaria is around 7%.

It is important to note that urticaria can be triggered by a variety of factors, including infections, medications, food, and environmental allergens, making it a condition that may require individualized management depending on the cause and severity of the symptoms [1, 11, 14].

It is widely acknowledged that acute forms of urticaria are more prevalent in children. Therefore, in children under the age of two, only acute forms of urticaria are typically observed, with a duration of no more than six weeks. In children between the ages of two and twelve, both acute and chronic forms are present, with

the former being the predominant form. In children older than 12 years, chronic forms of urticaria are more prevalent than acute forms. In infants and young children (aged 1 to 36 months), acute urticaria can result in urgent situations that require inpatient treatment, accounting for 0.4% of all hospitalisations. The prevalence of acute urticaria is higher among children with atopic diseases. Accordingly, the ETAC study estimated the prevalence of urticaria among young children to be 16.2% over a 18-month period. It is estimated that over 50% of patients with acute urticaria also have other allergic diseases[1, 3, 11, 14].

1.2 Urticaria etiology and pathogenesis

Urticaria is a group of diseases that are characterised by the development of blisters and/or angioedema. It should be noted that conditions in which blisters are a symptom, such as skin tests, auto-inflammatory syndromes, diseases caused by mutations in protein-coded genes that play a leading role in the regulation of the inflammatory response, anaphylaxis, and hereditary angioedema, are not classified as urticaria.

It is noteworthy that a universally accepted classification of urticaria has yet to emerge. In practice, however, it is more often divided into allergic and non-allergic categories. In accordance with the "Official Conclusions of the Problem Commission on EAACI Nomenclature," urticaria is regarded as an allergic condition, with its pathogenesis mediated by immunological mechanisms. If there is evidence that it is caused by IgE-dependent mechanisms, it is designated as "IgE-mediated urticaria" [3, 16, 22].

The clinical classification of urticaria is based on the following criteria:

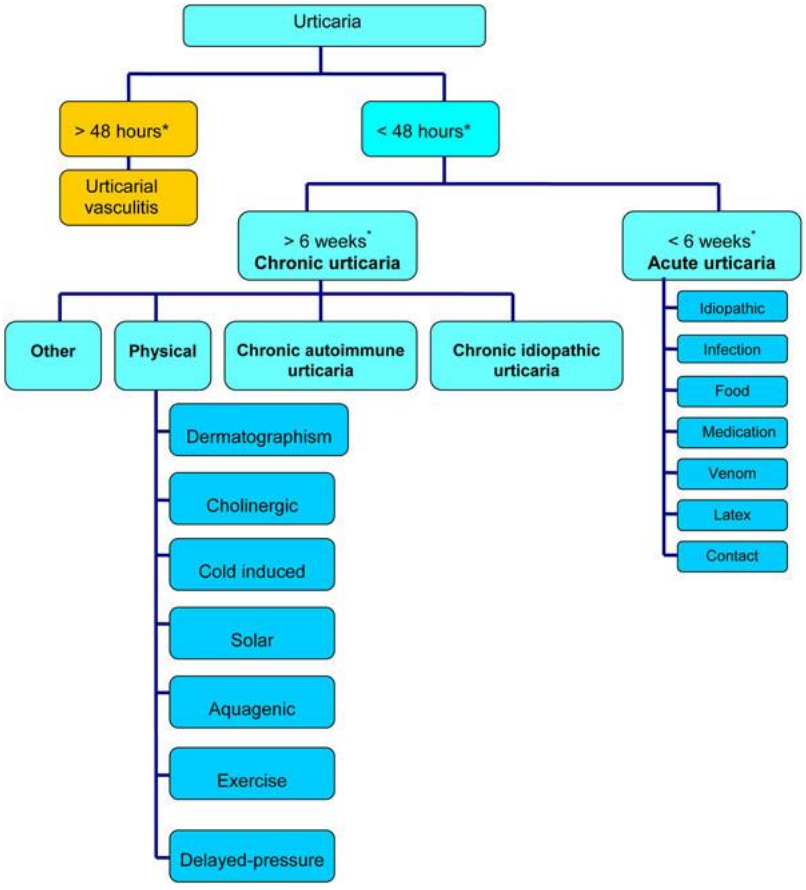
1) The duration of the disease can be classified as acute (less than six weeks) or chronic (more than six weeks).

2) The pathogenetic mechanisms can be divided into immunological or allergic, anaphylactoid or pseudoallergic, physical, or other types. It is notable that urticaria can also be caused by physical factors, which account for 17% of cases. Of all cases of chronic urticaria, the following types may be distinguished:

dermographic, pressure-induced, vibrational, solar, cholinergic, adrenergic, thermal, cold, aquagenic, contact, pigmentary, hereditary vibrational oedema.

In addition, other types of urticaria may be identified, including papular, infectious, vasculitis, paraneoplastic, psychogenic, and endocrine. 4) Hereditary forms of urticaria: hereditary ANO, disorder of protoporphyrin metabolism, Schnitzler syndrome (urticaria, amyloidosis, deafness), hereditary cold urticaria, deficiency of C3b-inactivator [3, 11, 21].

At present, the classification system outlined in the European consensus document on urticaria and angioedema, published in 2009, is the most commonly employed by medical practitioners. Diseases that have historically been associated with urticaria, but which do not meet the criteria for urticaria, and syndromes involving urticaria/angioedema are considered separately.



Pic. 1.1. European Classification of Urticaria

Classification and diagnosis of urticaria

The etiology of urticaria is complex due to the various diseases that can manifest with this symptom. This complexity affects the classification, diagnosis, and therapy of urticaria. The most common causes of urticaria are as follows:

Common Triggers of Urticaria

1) Food Products

Certain foods are known histamine liberators or contain high levels of histamine, which can trigger urticaria. These include:

- Fish, seafood
- Eggs
- Nuts
- Legumes
- Citrus fruits
- Tomatoes, eggplants
- Smoked products
- Chocolate, cheese
- Alcohol
- Confectionery with food dyes (e.g., tartrazine)

2) Acute Urticaria

- Urticaria can develop in patients with pollinosis after consuming foods with cross-reactive properties with pollen.

For instance:

- People allergic to tree pollen may react to stone fruits, berries, and nuts.
- Individuals sensitized to birch pollen may experience allergic reactions when eating apples or carrots [2, 10, 16].

3) Medications

Common drugs associated with urticaria include:

- Antibiotics, sulfonamides
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Opiates
- B vitamins

- Protein-based preparations (e.g., blood products, insulin)
- Anticonvulsants
- Radiopaque iodine-containing agents
- Muscle relaxants
- Angiotensin-converting enzyme (ACE) inhibitors

4) Parasitic Invasions

- Infections caused by helminths or protozoa can trigger urticaria.

5) Insect Venoms

- Venom from Hymenoptera insects (e.g., bees, wasps, hornets) can cause allergic reactions, including urticaria.

6) Infections

- Bacteria, viruses, and fungi can act as triggers.
- Common culprits include:
  - *Helicobacter pylori* (linked to gastrointestinal issues)
  - Intestinal dysbacteriosis (dysbiosis)
  - Chronic viral infections such as hepatitis, herpesvirus, and frequent acute respiratory viral infections (ARVI).

7) Physical Factors

- Environmental conditions such as:
  - Temperature changes
  - Pressure
  - Vibration
  - Sun exposure (insolation)
  - Exercise
  - Swimming

8) Psychogenic Factors

- Stress and emotional triggers can also play a role in exacerbating or triggering urticaria episodes[7, 9, 10].

The development of acute urticaria is more often associated with a number of different factors, including drugs, food products, infectious agents, pollen, epidermal

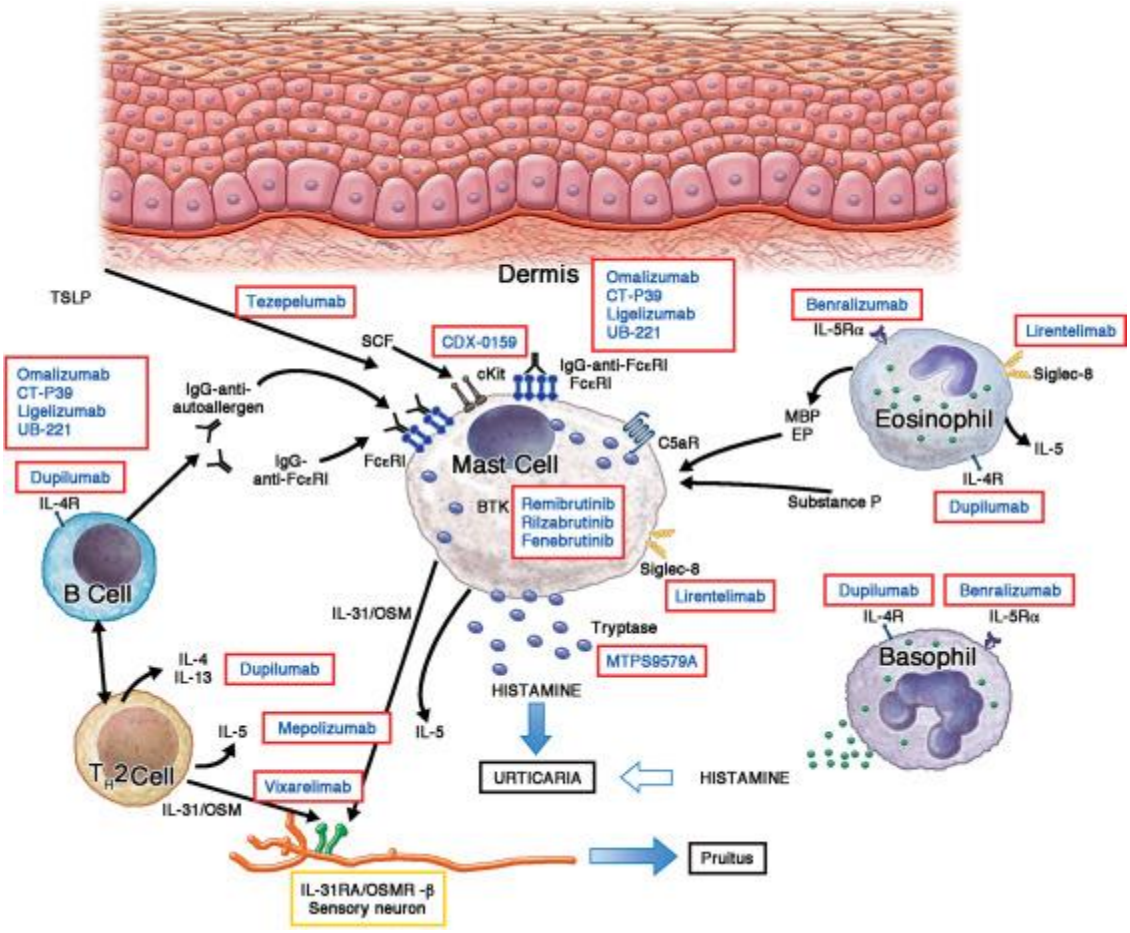
allergens, household allergens and insect allergens. It is frequently the case that chronic recurrent urticaria is caused by a number of different physical factors.

The pathogenesis of urticaria is a complex process. In the majority of cases, this is due to the development of IgE-dependent allergic reactions. A significant number of studies have demonstrated a high prevalence of acute urticaria in individuals with atopic conditions. A review of clinical symptoms in patients with food allergies revealed that acute urticaria, either isolated or in conjunction with Quincke's oedema, is the most prevalent clinical manifestation of food allergies, occurring in 75% of cases. It is estimated that 50% of patients with acute urticaria also have concomitant allergic diseases, such as hay fever or bronchial asthma.

Urticaria can result from a number of different pathogenic mechanisms, which can be broadly classified into two main categories: allergic and non-allergic. It should be noted that in both cases, the primary chemical mediator of acute urticaria is histamine, which is released from mast cell granules due to the influence of both non-immunological and immunological factors[5, 7, 9, 16].

Immunological (allergic) mechanisms are mediated by specific receptors on the cell membrane. The following specific receptors are present on the surface of mast cells and contribute to the activation of these cells: high-affinity receptors for IgE antibodies, C3a and C5a receptors, receptors for cytokines, and so on. Activation of mast cells through these receptors immediately releases preformed mediators of mast cells (the "early phase" of the inflammatory response). This then causes various inflammatory cells, including eosinophils, neutrophils, and basophils, to become involved after a few hours.

This inflammatory response is characterized as a "late phase" response, typically occurring hours after the initial allergen exposure. In allergic urticaria, the release of histamine is primarily mediated by immunological reactions. The process begins with the synthesis of specific IgE antibodies in response to the first exposure to an allergen. These IgE antibodies then bind to high-affinity IgE receptors on the surface of mast cells [2, 3, 5, 7].



Pic. 1.2. Biologics and sites of action for chronic inducible urticaria

This initial stage of sensitization is clinically asymptomatic, meaning that the individual does not experience noticeable allergic reactions at this point. However, sensitization can be identified through various allergy testing methods, including skin prick tests (in vivo) and specific IgE tests (in vitro), which can confirm the presence of allergen-specific IgE in a child [2, 16].

Upon subsequent exposures to the same allergen, the previously formed antigen-antibody complexes become fixed on the smooth cell membrane of the mast cells. This binding activates the mast cells, leading to their degranulation, which involves the release of histamine and other inflammatory mediators, such as leukotrienes and prostaglandins. These substances are responsible for the clinical manifestations of allergic urticaria, including skin wheals, redness, and itching.

The late-phase response can contribute to sustained inflammation, potentially leading to chronic urticaria if the individual continues to be exposed to the allergen.

Understanding these mechanisms is crucial for developing effective treatment strategies and managing allergic reactions in patients.

Once released, histamine acts on a number of different receptor types. H1, H2 and H3 receptors. In addition to histamine, other mediators, including prostaglandins, bradykinin, and leukotrienes, are involved in the occurrence of oedema in urticaria. The syndrome of hyperemia, which occurs as a result of vasodilation, is mediated by such mediators as histamine, platelet-activating factor, and bradykinin. The pruritus associated with urticaria is caused by the stimulation of nerve endings, with the direct involvement of histamine. The activation of C-fibres by histamine and prostaglandin D2 results in the secretion of neuropeptides, additional vasodilation and degranulation of mast cells [2, 3, 16].

In a non-allergic (non-immunological) reaction, mediators are released as a result of the influence of a factor or substance that does not involve the participation of IgE. The degranulation of mast cells in the skin, which is caused by certain substances (e.g., codeine), can result in the development of urticaria. The non-immunological factors that activate mast cells include neuropeptides (such as substance P and vasoactive intestinal polypeptide) and hormones (such as estrogen and ACTH). Additionally, drugs (such as aspirin, NSAIDs, codeine, and polymyxin B) and physical effects (such as high and low temperatures and pressure) can also cause mast cell degranulation. Furthermore, substances of animal origin and radiopaque substances can also induce this process.

In the case of acute urticaria, it is typically the case that immunological IgE-mediated mechanisms of stem cell activation exert a dominant influence. In chronic urticaria, immunological mechanisms of mast cell activation may also be involved, potentially representing an autoimmune form of the disease. Studies have demonstrated that 40-60% of patients with chronic urticaria exhibit autoantibodies (IgG1, IgG3, IgG4) to the high-affinity IgE receptor in their blood. This interaction results in the degranulation of mast cells and basophils. This process is facilitated by the activation of the complement system, which results in the release of anaphylatoxin C5a. The formation of autoantibodies appears to be influenced by

genetic factors. Concurrently, the impact of established non-specific triggers of chronic urticaria (emotional distress, premenstrual syndrome, alcohol, pharmaceuticals, physical factors, etc.) is achieved through the non-immunological activation of stem cells [3, 8, 21].

The clinical manifestations of urticaria vary depending on the type. Urticaria can manifest at any age, from infancy onwards. The disease manifests abruptly with the emergence of urticarial elements (blisters) of varying dimensions on any portion of the skin, accompanied by pruritus. Upon applying pressure to the urticarial element or slight stretching of the skin, white centres become visible. The duration of the elements of the rash varies considerably, from a few minutes to three hours or more, with some cases extending up to 24–48 hours. The rash subsequently vanishes without a trace, only to reappear in other areas of the skin. Hives may present in a variety of forms, including the whimsical outlines of islands and continents (urticaria geographica), arcs or rings (urticaria figurata or urticaria girata). The elements of the rash are typically red or pink in colour, though in severe cases they may assume a cyanotic hue. The dimensions of the urticarial elements can range from 1-2 cm in diameter to an impressive scale, with areas of tens or even hundreds of square centimetres.

Mucous membranes may be implicated in the pathogenesis of the disease, as evidenced by the appearance of symptoms of oedema of the hard and soft palate, larynx, oesophagus, and stomach.

In cases of severe severity, in addition to the typical symptoms of urticaria, there may also be observed breathing difficulties, vomiting and diarrhoea. The severity of urticaria may result in a change in the general condition, from satisfactory to severe, with an increase in body temperature, the onset of symptoms indicative of intoxication, and a worsening of well-being [5, 7, 10, 16].

It is estimated that approximately 50% of individuals with urticaria will develop subcutaneous oedema or allergic angioedema. The aetiology and pathogenesis of this condition are similar to those of allergic urticaria. In clinical practice, oedema of the eyelids and lips is the most frequently observed presentation.

Furthermore, Quincke's oedema may manifest on the face, trunk, extremities, and genitals. In 85% of cases, the face and limbs are affected [9, 10, 16].

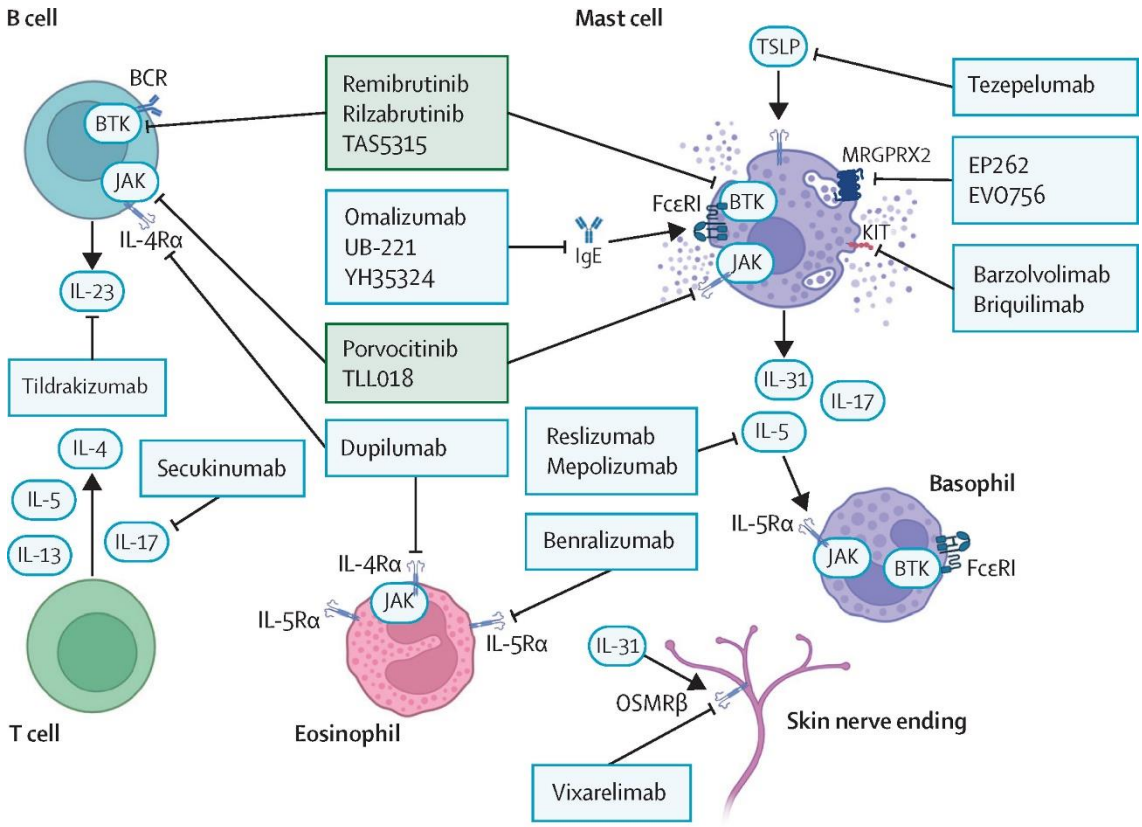
In infants, papular urticaria may manifest, with the delayed type of reaction playing a pivotal role in its pathogenesis. The condition is characterised by cellular perivascular infiltration and the appearance of papules, measuring between 10 and 20 mm in diameter, surrounded by a zone of hyperaemia measuring between 2 and 4 mm. The rash persists for up to 10 to 14 days. The most common aetiological factor is the bite of domestic fleas.

In cases of physical urticaria, the presence of life-threatening systemic lesions is frequently observed. It is possible for a single patient to present with a combination of different physical urticaria types. This is the most common form of dermographic physical urticaria. The condition manifests as pruritus and dermatological eruptions in areas of pressure or friction, predominantly in regions of close contact between the skin and various forms of clothing, including undergarments, footwear, accessories such as belts and wristwatches, and other materials. The occurrence and duration of urticaria elements can be classified into three categories: immediate (lasting 2–5 minutes to half an hour), delayed (30–120 minutes to 3–9 hours), and delayed (4–6 hours to 24–48 hours). In some cases, it may manifest as a secondary symptom of acute urticaria due to the use of certain medications, scabies, insect bites, mastocytosis, and in some instances, as a familial dermatographia [14, 22].

Cold urticaria is defined by the onset of urticaria, pruritus, erythema and hereditary warm angioedema (HWA) in areas of the skin and mucous membranes that have undergone cooling, including exposure to cold air, water, food and drinks. The clinical presentation of cold-induced cholinergic urticaria is characterised by the typical elements that manifest when the body is cooled or when physical activity is undertaken in cold environments.

Additionally, isolated cases of aquagenic urticaria, a form of urticaria that develops when in contact with water, have been documented.

Solar urticaria is defined by the onset of pruritus within seconds of exposure to light, with the typical urticarial rash appearing 2–3 minutes later and persisting for up to 3–4 hours. Delayed solar urticaria is less common, with the onset of symptoms occurring 18 to 72 hours after exposure to sunlight. Localised heat application to the skin can result in the development of either immediate (onset within 5 minutes) or delayed (onset after 4 to 6 hours) limited heat urticaria.



Pic. 1.3. Available and novel therapies under development for chronic urticaria

Cholinergic urticaria is one of the most prevalent forms, particularly among adolescents and young adults. The condition is characterised by the presence of small, point-like cells, measuring between 1 and 3 mm in diameter, which cause a significant degree of pruritus. The initial presentation of the rash is observed on the face and neck, subsequently disseminating to other regions of the body, ultimately manifesting as generalized urticaria. Additionally, the disease may manifest in a systemic manner, presenting with symptoms such as suffocation, headache, and loss

of consciousness. Such urticaria is frequently precipitated by a hot shower, a sudden change in temperature, physical exercise, increased sweating, stress, consumption of hot food and drinks, and alcohol. Once the body has been cooled, the clinical manifestations will dissipate within a period of 30 to 60 minutes [3, 5, 10, 16].

A distinctive feature of adrenergic urticaria (a variant of cholinergic urticaria) is the appearance of a white halo around a small papule. It can be reproduced internally with each injection of norepinephrine and is brought about by the administration of beta-blockers.

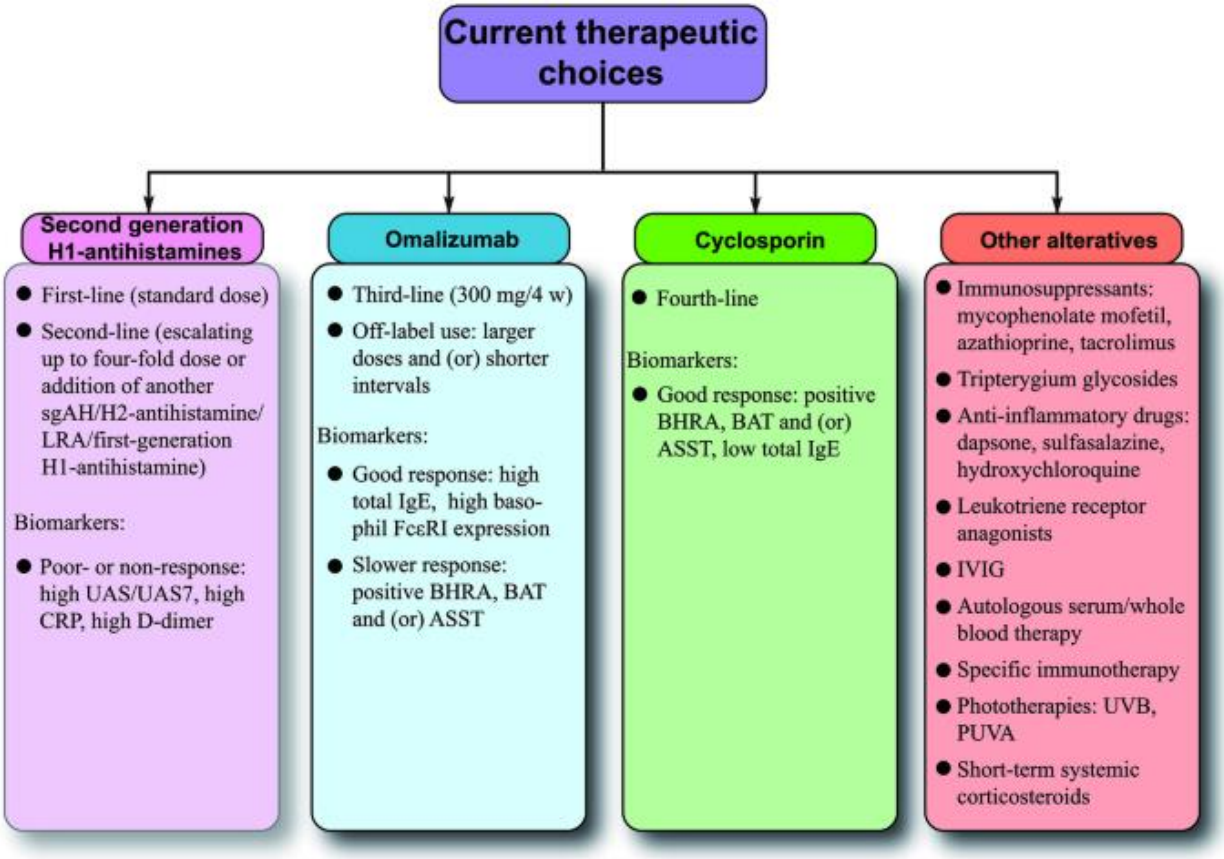
Hereditary vibrational angioedema is characterised by the development of swelling and local itching of the skin in areas exposed to vibration, including the hands and face when riding a horse, motorcycle, using massage devices, or working with a jackhammer. The itching and blisters typically appear a few minutes after exposure to vibration and resolve within a day. Systemic reactions are also possible. This form of urticaria is typically hereditary and develops in childhood.

Papular urticaria is typified by the presence of erythematous, intensely pruritic papules of varying dimensions, frequently situated on regions of the body not covered by clothing, and which persist for an extended period. The emergence of this form of urticaria is frequently linked to hypersensitivity to insect saliva (fleas, lice, gnats, mosquitoes) [5, 7, 9, 16].

1.3. Treatment of urticaria

The treatment of urticaria is dependent upon the form of the disease and the underlying causative factors. Nevertheless, the fundamental tenets of therapy remain consistent, encompassing the following stages. The treatment of various types of urticaria employs the use of medicinal products belonging to different pharmacological groups, which are utilized in varying combinations and dosages (Table 1.1.).

Table 1.1.



In order to eliminate the causative and provoking factors, patients with urticaria must adhere to certain rules, depending on the form of the disease.

A hypoallergenic diet should be followed, which excludes food allergens and histamine liberators. Contact with other exoallergens should be avoided, as should the influence of physical factors such as physical activity and temperature. The use of photoprotective measures is also recommended. Furthermore, patients should refrain from carrying heavy objects, wearing belts, tight clothing or shoes, bathing in cold water, eating cold food and drinks, and so on.

It is recommended that patients with urticaria and Quincke's oedema refrain from taking acetylsalicylic acid and other non-steroidal anti-inflammatory drugs, as these agents have been observed to exacerbate existing urticaria in approximately 50% of cases. It is also imperative to refrain from the utilisation of angiotensin-converting enzyme inhibitors, as these pharmaceutical agents have been identified as a potential precipitating factor for the development of Quincke's oedema. This

assertion is supported by a substantial body of evidence, as evidenced by references [3, 13, 22].

Patients with urticaria must undergo remediation of chronic foci of infection, deworming, and a course of treatment for concomitant diseases that can cause exacerbation of urticaria. In cases of allergic urticaria, specific immunotherapy or allergy vaccination with the causative allergens may be an effective treatment option.

Although the role of histamine in all forms of urticaria remains unproven, antihistamines continue to represent the primary avenue for symptomatic therapy and the management of its clinical course.

In cases of mild urticaria, oral administration of non-sedating antihistamines (desloratadine, cetirizine, fexofenadine, levocetirizine) is recommended for a period of three to four weeks. Sedative antihistamines (e.g., clemastine, chloropyramine) are employed for the treatment of urticaria of moderate severity via parenteral administration for a period of 2-3 days, after which a transition to non-sedating antihistamines is initiated for a duration of 1 month. In cases of severe urticaria, parenteral administration of antihistamines for a period of 5-7 days, in conjunction with glucocorticosteroids for a duration of 2-5 days, is recommended. Additionally, detoxification therapy may be a viable option. Subsequently, oral administration of non-sedating antihistamines is indicated for a period of one month. Glucocorticosteroids are more frequently prescribed for urticaria in medium doses (1-2 mg/kg, according to prednisolone) [5, 21].

In certain instances, the utilisation of antihistamine membrane-stabilising pharmaceuticals for a period of two to three months has been demonstrated to be an efficacious approach.

Furthermore, the literature also presents data on the efficacy of leukotriene receptor antagonists (montelukast) and 5-lipoxygenase inhibitors (zileuton) in the long-term management of chronic urticaria. Additionally, the use of M-cholinergic blockers (belataminal, belaspon, beloid) and anxiolytics (hydroxyzine) may be recommended for patients with cholinergic urticaria. Beta-blockers have been

demonstrated to be effective in the treatment of adrenergic urticaria. In the case of cold urticaria, intravenous immunoglobulin administration may be a viable option. A range of therapeutic agents, including pancreatic enzymes, anti-Helicobacter drugs, agents for correcting intestinal dysbiosis, histaglobulin, and anthelmintic drugs, may be employed as part of a symptomatic therapy for chronic idiopathic urticaria, in accordance with the relevant indications. Antibacterial (antibiotic), antiviral (acyclovir), and antifungal therapies may also be considered.

The literature also contains data on the successful use of cyclosporine A, methotrexate, non-steroidal anti-inflammatory drugs, plasmapheresis, and thyroxine (in the presence of antithyroid autoantibodies). A distinctive approach is necessary for patients with hereditary angioedema. In the event of an exacerbation of this form of urticaria, the administration of fresh or fresh-frozen native plasma or a 5% solution of aminocaproic acid intravenously is recommended as a source of C1-inactivator. The subsequent administration of a 5% solution of aminocaproic acid intravenously is advised at four-hour intervals or until the exacerbation subsides. As an alternative to aminocaproic acid, tranexamic acid may be employed as an internal treatment. The treatment of facial and neck swelling comprises the administration of native plasma, a 5% solution of aminocaproic acid, furosemide, and dexamethasone. In the event of laryngeal oedema, the administration of an inhalation solution comprising 0.1% adrenaline and 5% ephedrine hydrochloride is recommended [3, 12, 21].

In cases of severe autoimmune chronic urticaria, treatment with plasmapheresis, intravenous immunoglobulin, and cyclosporine is indicated and should be conducted in a specialized setting. The use of plasmapheresis is an effective and pathogenetically justified treatment for chronic autoimmune urticaria. In cases of severe autoimmune chronic urticaria where conventional therapy has been unsuccessful, the use of non-specific immunotherapy methods, including cyclosporin A and intravenous immunoglobulin, is also a justifiable course of action. The efficacy of intravenous immunoglobulin in the management of autoimmune chronic urticaria is attributed to its capacity to activate T-suppressors and stimulate

the production of anti-idiotypic antibodies directed against functional antibodies that activate mast cells. The use of cyclosporine in the treatment of chronic urticaria is justified by its ability to suppress the degranulation of mast cells and basophils, as well as the production of cytokines. This is of particular importance in preventing the "late phase" reaction.

The term "external," "local," or "topical" is used to describe a form of therapy that involves the application of agents to the surface of the skin. In patients presenting with any form of urticaria, whether allergic or non-allergic, this approach to treatment serves an auxiliary role. Ointments can achieve a number of effects, including:

The application of topical agents has been demonstrated to result in a reduction of itching, a decrease in the severity of oedema and an acceleration of the regression of the rash [5, 7, 9, 10].

Blisters (urticaria) are the result of swelling of the papillary layer of the skin, which occurs as a consequence of the action of a special substance, namely histamine. It is only possible to halt the pathological process with drugs of systemic action, that is to say, general-action tablets, capsules and injections.

Local treatments for urticaria are available in various dosage forms and contain active substances with antipruritic, anti-inflammatory, hormonal, and antihistamine properties.

Glucocorticoid-based preparations are reserved for the most severe cases, as they have pronounced side effects. However, they are highly effective in halting the symptoms of the disease, with examples including Lokoid, Akriderm, Komfoderm, Triderm, Advantan, Elocom, Uniderm, and Celestoderm. Topical glucocorticosteroids (GCs) are the most efficacious treatment for allergic conditions. They are typically employed as a second-line therapy when other pharmacological agents have proven ineffective. The use of GCs in itching is justified only when there is a pronounced inflammatory process. Hydrocortisone has the weakest anti-inflammatory effect of all glucocorticosteroids [5, 7, 10, 16].

Synthetic derivatives, in which fatty acid esters or halogens are introduced into the molecule, have a markedly more potent anti-inflammatory effect. However, they also have a more pronounced local effect, which can include destructive effects on the skin, drying, and even the appearance of irreversible atrophic bands and telangiectasias. These effects can occur with long-term application and systemic effects. For instance, fluorinated derivatives are absorbed from the surface of the skin into the bloodstream in accordance with the principle of feedback, thereby enabling the suppression of their own hormone production and exerting a pronounced hormonal effect on the patient's body. The recently developed non-halogen-containing preparations for external use are free from the aforementioned disadvantages. Such medications include budesonide, mometasone furoate, and methylprednisolone aceponate, among others. In the case of external use (in conjunction with other GCS), a number of rules must be adhered to:

1. It is inadvisable to utilise these pharmaceuticals on the face and flexor surfaces for a period exceeding four weeks.

2. The application of hydrocortisone preparations with a concentration exceeding 1% to the face is contraindicated.

3. GCS should not be used for the treatment of bacterial, viral, fungal infections, tuberculosis, or syphilis. Furthermore, drugs should not be used for the management of adverse cutaneous reactions to vaccination.

5. The use of GCS has been demonstrated to impede the normal healing processes associated with wounds.

6. It is imperative that the dosage form of the drug recommended by the physician is utilised, and that the prescribed amount is applied to the skin exclusively. It is imperative that the prescribed dosage of the drug is not exceeded.

7. In cases of concomitant bacterial and fungal infection, it is necessary to select combined agents with antifungal and antimicrobial activity [2 - 4, 22].

To enhance the absorption of glucocorticosteroid (GCS) preparations from the skin surface, salicylates are often included in the composition of the dosage form. Salicylates have keratolytic properties, meaning they help dissolve the outer layer of

the skin (stratum corneum). This action facilitates the penetration of GCS into the deeper layers of the skin, improving the medication's effectiveness.

Topical antihistamines are indicated for the treatment of urticaria. Antihistamines relieve itching, which has a negative impact on quality of life. They allow patients to obtain sufficient rest, avoid emotional distress, and experience reduced excitement at home and at work. Psilo-balsam is manufactured by the pharmaceutical industry in the form of a gel for external use, packaged in tubes containing 1% diphenhydramine. It should be noted that the drug is contraindicated for use in children under the age of two and in cases where extensive application is required.

The use of antihistamines is indicated for the reduction of pruritus and oedema. This pharmacological group encompasses a variety of external therapeutic agents, predominantly non-hormonal ointments. In traditional treatment, antihistamine drugs are prescribed for the purpose of soothing itching. Examples of such drugs include lotions, creams, ointments (such as Topikrem, Emolium, Skin-cap, and Skin-active) and cool compresses. In the form of tablets, the following drugs are available: The antihistamines cetirizine (marketed as Cetrin, Cetirizine-Teva, and Cetirizine-Akrihin), levocetirizine (Zodak Express, Ksyzal, and Suprastinex), loratadine (Claritin, Lomilan, Loratadine-Teva, and Loratadine-Akrihin), desloratadine (Clarinex and Aerius), and Suprastin are available. Tavegil is also a relevant option. The external use of antihistamines may permit the cessation or reduction of systemic antihistamine therapy, which has the potential to enhance the efficacy and safety of systemic treatment. This is particularly relevant in the context of first-generation antihistamines. In the event of inadequate efficacy of local antihistamine therapy, it is advisable to consider systemic antihistamine or glucocorticosteroid administration [2, 5, 7, 9, 16].

Conclusions to chapter 1

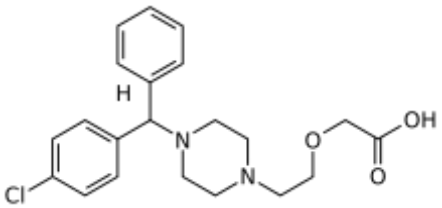
It can be observed that urticaria presents itself in a multitude of forms and variants with regard to its clinical course. Frequently, urticaria is a symptom of non-allergic diseases, which necessitates the input of allergists and dermatologists, in addition to other practising doctors, in order to select the most appropriate approaches to the diagnosis, treatment and prevention of urticaria. Local therapy of urticaria plays an important role in systemic therapy, with the objective of combating the symptoms. There is no single scheme for the treatment of urticaria, with the therapy being selected on an individual basis. It is recommended that creams of pharmaceutical production are used, which can combine active pharmaceutical ingredients with the properties required for the treatment.

CHAPTER 2
RESEARCH OBJECTS AND METHODS

The extemporaneous cream developed for local urticaria therapy was formulated using the following active pharmaceutical ingredients: Levocetirizine, peach oil, Olivem 1000 and purified water. It was recommended that a cream base be used. The specified medicinal and auxiliary substances were found to comply with the requirements of the regulatory documentation with reference to qualitative and quantitative indicators [17, 20, 27, 28].

2.1. Objects of research

Levocetirizine is a synthetic drug that is a piperidine derivative and belongs to the group of third-generation antihistamines. In terms of chemical structure, it is a left-rotating isomer of cetirizine, which in turn is a metabolite of hydroxyzine, a representative of the first generation of antihistamines - piperidine derivatives.



2-(2-{4-[(R)-(4-chlorophenyl)(phenyl)methyl]piperazin-1-yl}ethoxy)acetic acid

Pic. 2.1. Levocetirizine chemical and structure formula

The mechanism of action of the drug is selective blocking of histamine H1 receptors, prevention of smooth muscle spasms caused by histamine, including bronchoconstriction in patients with obstructive pulmonary disease, dilation of capillaries and increased permeability, development of angioedema, erythema and itching of the skin and mucous membranes. In allergic rhinitis, the drug reduces sneezing, lacrimation, nasal discharge, and itching of the nasal mucosa [17, 18].

Levocetirizine is used for seasonal and year-round allergic rhinitis, pollinosis, allergic conjunctivitis, urticaria, Quincke's edema, pruritus, as well as in the complex therapy of atopic dermatitis, chronic eczema and bronchial asthma in both adults and children.

The following side effects may occur when using levocetirizine:

- Allergic reactions - very rarely (less than 0.01%) skin rash, itching, Quincke's edema, urticaria, anaphylactic reactions.

- Digestive system: often (1-10%) dry mouth; infrequently (0.1-1%) abdominal pain; very rarely (less than 0.01%) nausea [17, 18].

- From the nervous system - often (1-10%) headache, drowsiness, increased fatigue; rarely (0.01-0.1%) migraine, dizziness, in case of overdose in children - increased excitability.

- Other side effects: very rarely (less than 0.01%) weight gain, dyspnea.

- Changes in laboratory tests - increased activity of liver enzymes.

Levocetirizine is contraindicated in case of hypersensitivity to the drug and severe renal failure. The drug is not used in children under 2 years of age. Levocetirizine is not recommended during pregnancy and lactation [17, 18].

Peach oil (Oleum persicorum) is a fatty oil obtained by cold pressing the seeds of plants belonging to the olive subfamily, Prunoideae, namely the common peach (Percica vulgaris Mill.), the common apricot (Armeniaca vulgaris Lam.), the domestic plum (Prunus domestica L.) and the plum (Prunus divaricata, Ledeb.).

Peach oil is a transparent, oily liquid with a light yellow colouration. It is odourless or possesses a weak, distinctive odour, and has a pleasant, oily taste. It does not become desiccated in the air. At a temperature of -10°C, the oil should remain in a liquid state and retain its transparency. The formation of a thin film on the surface of the oil is permitted. The oil is soluble in 60 parts of absolute alcohol, readily soluble in ether and chloroform. Its density is 0.914–0.920, its refractive index 1.470–1.473, its acid value no more than 2.5, its number of saponification 185–195, and its iodine number 96–103 [26, 31].

Pic. 2.2. Peach oil

It is employed as a solvent in the production of injection solutions (e.g., chrysanol, sinestrol, testosterone propionate), as well as suspensions (e.g., bioquinol, bismoverol). It is a constituent of spermacetate ointment, emulsions, tetracycline ointment, and dental paste. It is also a gentle laxative medicinal substance [35, 37].

Olivem 1000 is a PEG-free, self-emulsifying, olive-based, non-ionic oil-in-water multifunctional ingredient. Chemically similar to the lipid composition of the skin surface, it is a combination of fatty acids. It has the ability to form liquid crystal structures that mimic the organisation of the stratum corneum. The emulsifier Olivem® 1000 provides a deep moisturising effect [20, 26, 31].

Pic. 2.3. Olivem 1000

Olivem 1000 is ideal for use in skin care as well as in hair care formulations such as cream rinses and leave-in conditioners. In hair care products it improves wet combability. It is also effective as an emulsifying base for more traditional hair conditioner formulations using cationic ingredients, extending its range of applications. Olivem 1000 allows emulsification of various polar oils such as liquid esters, certain waxes, triglycerides and vegetable oils.

Typical applications include Olivem 1000:

Sensitive skin products

Night creams

Daily moisturisers

Sensitive skin products

After-sun creams and lotions

Baby care creams and lotions

Hair conditioning creams

Recommended amount: 1.5 to 3% for lotions, serums, gels or tonic and 3.5 to 8.5% for creams [20, 26, 31].

Purified Water

The solution is a colourless, transparent liquid with no discernible odour or taste. Its pH range is 5.0-7.0 (potentiometrically determined). All excipients employed in the study comply with the requisite specifications set forth in the relevant documentation. The reagents utilized during the physico-chemical investigations were prepared in accordance with the methodologies outlined in [19, 24].

2.2. Research methods

Description. The following section outlines the research methods employed in this study. The appearance and organoleptic properties of the samples (colour, smell, consistency) were subjected to rigorous control. The model samples were subjected to a detailed examination to ascertain whether any indications of physical

instability were present, such as delamination or discolouration.

Appearance, color and smell.

The appearance, colour and odour properties were ascertained by subjecting samples of the ointment to examination on a glass slide.

The stability of the ointment was determined using the stratification-centrifugation method [25, 31].

The determination method is as follows: Five samples of the ointment are placed in test tubes, which are installed in the centrifuge holder.

The initial centrifugation stage lasts for 10 minutes at a rotation speed of 500 rpm. Once this period has elapsed, the test tubes must be removed and the ointment samples examined for delamination. Should the samples exhibit a change in homogeneity, resulting in separation into distinct components, the height of the separated fractions is measured and their appearance described.

Subsequently, centrifugation is conducted for a period of 10 minutes at a speed of 1000 rpm. Subsequently, the identical measurements and determinations as those conducted in the initial stage are performed. In subsequent stages, the number of revolutions is incrementally increased, starting at 2000 rpm and continuing with higher values, such as 3000 rpm. The number of revolutions is increased until delamination occurs in all samples of ointments. The results of these studies are used to draw conclusions regarding the comparative stability or instability of ointments.

The objective is to determine the thermal stability of the samples. To conduct the test, five to six test tubes (diameter: 15 mm; height: 150 mm) are required. A volume of 10ml of the test samples is introduced into test tubes and subjected to a thermostat at a temperature range of 40-40°C for a period of 1 week. Thereafter, the samples are transferred to a refrigerator at a temperature range of 10-12°C for an additional week. Following this, an additional 3-day period is allotted for the samples to be stored at room temperature, during which the stability of the samples is determined through the observation of the absence of delamination [24, 25, 32].

It is essential to ascertain the pH of ointments in order to regulate the behaviour of medicinal substances and bases during the storage period. A change in

pH is indicative of a change in the physical and chemical properties of the substance in question. To ascertain the pH of an ointment, a portion of the product is combined with 50ml of purified water at a temperature of 50-60°C and agitated on a vibrator for 30 minutes. The resulting extract is filtered, and a potentiometric titration is performed in accordance with the SPU method [24, 25, 31].

Conclusions to chapter 2

The characteristics of the active pharmaceutical ingredient (API), auxiliary substances, and the range of methods necessary for the rational selection of the composition and cream base for the treatment of urticaria were presented.

CHAPTER 3.
COMPOSITION AND TECHNOLOGY SUBSTANTIATING OF THE EXTEMPORANEOUS CREAM WITH LEVOCETIRIZINE

3.1. Justification of the Levocetirizine and base choice

As indicated in the literature, the cream being developed should ideally possess a multifaceted topical effect, encompassing antipruritic, anti-inflammatory, and regenerative properties. In order to achieve the aforementioned specifications, it was proposed that the following active components be introduced, thereby conferring the desired set of actions upon the drug.

In recent years, due to changes in weather and environment, a variety of harmful gases, dusts and other pollutants have appeared in many places, causing people to produce various anaphylactoid sensitinogens. Seasonal changes, field work, hypersensitivity to pollen, ingestion of noxious gases and sand, etc., cause an increasing number of people to suffer from various anaphylactic diseases, such as allergic rhinitis, urticaria, asthma, which causes skin redness, itching, flushing, and anaphylactogenesis, etc. are very important diseases.

Drugs for external use, directly on the affected areas, are usually used to treat all skin diseases. They use gels, creams, ointments belonging to a group of drugs - soft dosage forms [4, 29, 30, 32].

Olivem 1000 is ideal for skin care applications. Olivem 1000 makes it possible to emulsify various oils of different polarity. Its recommended quantity for cream is from 3.5 to 8.5% [20].

It was necessary to select the components of the base and determine their amounts experimentally in the first stage of research.

On the basis of the above, it was proposed to prepare cream bases with the following compositions (Table 3.1). Peach oil was used in concentrations of 3%, 10%, 15%, 20% and Olivem 1000 in concentrations of 3%, 5%, 7%.

Table 3.1.

COMPOSITIONS OF CREAM BASES

Component	Amount, %			
	1	**2**	**3**	**4**
Olivem 1000	3 %	3 %	3 %	3 %
Peach oil	5 %	10 %	15 %	20 %
Water purified	92 %	87 %	82 %	77 %

Component	Amount, %			
	5	**6**	**7**	**8**
Olivem 1000	5 %	5 %	5 %	5 %
Peach oil	5 %	10 %	15 %	20 %
Water purified	90 %	85 %	80 %	75 %

Component	Amount, %			
	9	**10**	**11**	**12**
Olivem 1000	7%	7%	7%	7 %
Peach oil	5 %	10 %	15 %	20 %
Water purified	88 %	83 %	78 %	73 %

Technique for preparing cream base samples: heat both phases in a water bath. Without removing from the water bath, add the aqueous phase to the fatty phase and mix for a few minutes. Then emulsify with a mini blender for a few minutes and mix again until the emulsion has cooled down completely.

The cream bases obtained were evaluated according to organoleptic indicators including colour, homogeneity, consistency. The results are shown in Table 3.2.

From the results of the table it can be seen that cream base samples 1-3 with 3% Olivem 1000 content have the same liquid consistency as 5% sample 5; 7% sample 9 and uneven consistency 3, 4, therefore they cannot be used for cream preparation.

The 3% Olivem 1000 content does not give the desired creamy consistency. Using Olivem 1000 at 5% and 7% with 10%, 15% and 20% oil, cream bases with satisfactory organoleptic indicators were obtained.

Table 3.2.

Organoleptic quality indicators of cream bases

Indicator	Sample					
	1	2	3	4	5	6
Color	White	White	White	White	White	White
Homoge-neity	like homo-geneous	like homo-geneous	non-homo-geneous	non-homogeneous	like homo-geneous	like homo-geneous
Consis-tency	fluid	fluid	fluid	creamy	fluid	creamy

Indicator	**Sample**					
	7	**8**	**9**	**10**	**11**	**12**
Color	White	White	White	White	White	White
Homoge-neity	like homo-geneous	like homo-geneous	like homo-geneous	like homo-geneous	like homo-geneous	like homo-geneous
Consis-tency	creamy	creamy	fluid	creamy	creamy	creamy

Therefore, base sample 7 with peach oil 15% and Olivem 1000 5% was selected for further research.

3.2. Extemporaneous cream composition and technology with Levocetirizine

The cream compositions under investigation have been prepared in consideration of the physico-chemical properties of the active and excipient

ingredients [27, 28, 32].

Characteristic:

The given drug is a cream (ointment emulsion) containing, soluble in water API Levocetirizine, emulsifier Olivem-1000 peach oil and purified water.

Cream composition:

Levocetirizine 2,5 %.

Peach oil 15 %.

Olivem 1000 5 %.

Purified water 77,5 %.

Levocetirizine is a water-soluble substance which is added to the cream partly as a water solution.

Stages of the technological process

1. Preparatory work:

1.1. Pharmaceutical expertise

1.2. Calculations

1.3. Preparation of excipients, active and additional substances

2. Cream technology:

2.1. Weighing peach oil 3.0 in a porcelain cup.

2.2. Weigh out Olivem 1000 1.0.

2.3. Heat the peach oil to 75°C on water bath and add the emulsifier Olivem 1000. Mix.

2.4. Measure out 13.5 ml of purified water and transfer to an auxiliary glass bottle.

2.5. Add hot purified water to peach oil, Olivem 1000 and mix for 1-2 min.

2.6. Remove the cream from the water bath and homogenise for 2 minutes.

2.7. Weigh out 0.5 Levocetirizine and dissolve in 2 ml of water

2.8. Add Levocetirizine solution to the cream in a mortar and mix until completely cooled.

3. Quality control: written control, physical control (weight deviation), organoleptic control, questionnaire control.

4. Packaging. Marking (labelling).

5. Delivery control.

3.3. Terms of storage investigations

The following indicators: appearance, colour, odour, application, pH and stability were determined in the prepared cream samples for 32 days. The creams were stored in a refrigerator at 2-8°C (Table 3.3.).

Table 3.3.

ORGANOLEPTIC QUALITY INDICATORS OF THE EXTEMPORANEOUS CREAM WITH LEVOCETIRIZINE

Research term	Appearance	Color	Odor	Stratification (thermostability)	pH
1 day	uniform soft cream	white	specific	no observation	5.2
5 days	uniform soft cream	– "–	– « –	no observation	5.2
32 days	uniform soft cream	– "–	– « –	no observation	5.3

The results of the study of the organoleptic characteristics of the cream, shown in Table 3.3, show that the samples remain stable when stored in the refrigerator for 32 days. On the basis of the research carried out, it is possible to set a storage period of up to 30 days in a refrigerator at 2-8°C.

Conclusions to chapter 3

1. Theoretically proven active ingredient selection for cream for symptomatic treatment of urticaria.

2. The composition of the cream base, containing peach oil, Olivem 1000 and purified water, was chosen experimentally.

3. For the formation of a stable emulsion phase of the O/V type cream, an emulsifier (Olivem 1000) and its concentration were chosen experimentally.

3. It has been demonstrated that the organoleptic, physico-chemical and pH properties of the cream of the selected composition do not change significantly after 30 days of storage in the refrigerator (2-8 °C). 4.

5. Suggested efficient technology for the cream of the selected composition.

GENERAL CONCLUSIONS

1. Theoretical justification of extemporaneous cream composition, base choice, technology development was provide and experimental properties studies of extemporaneous cream with Levocetirizine for skin allergic diseases treatment was conducted.

2. Literature analysis of allergy types and mechanisms of their development was performed.

3. Modern approaches to the treatment of allergic skin diseases, especially urticaria, were analysed.

4. On the basis of extensive research, the composition of the cream base for the treatment of urticaria was selected.

5. Taking into account the physical and chemical components of the cream, its composition and technology were theoretically and experimentally substantiated.

6. The shelf life of 30 days in the refrigerator has been demonstrated.

7. Extemporaneous cream with Levocetirizine for skin allergic diseases treatment was conducted has been proposed.

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APPENDICES

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ

МАТЕРІАЛИ
XXIX МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ

19-21 квітня 2023 року
м. Харків

Харків
НФаУ
2023

Continuation of Appendix A

УДК 615.1

Редакційна колегія: проф. Котвіцька А. А., проф. Владимирова І. М.
Укладачі: Сурікова І. О., Боднар Л. А., Григорів Г. В. Литкін Д. В.

Актуальні питання створення нових лікарських засобів: матеріали XXIX міжнародної науково-практичної конференції молодих вчених та студентів (19-21 квітня 2023 р., м. Харків). – Харків: НФаУ, 2023. – 606 с.

Збірка містить матеріали Всеукраїнської науково-практичної конференції «Youth Pharmacy Science», які представлені за пріоритетними напрямами науково-дослідної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва й обігу лікарських засобів; суспільствознавства; фундаментальних та мовних наук.

УДК 615.1

Continuation of Appendix A

DEVELOPMENT OF COMPOSITION OF CAPSULES FOR THE TREATMENT OF RESPIRATORY DISEASES

Saidi Said
Scientific supervisor: Puliaiev D.S.
National University of Pharmacy, Kharkiv, Ukraine
d.s.puliaiev@nuph.edu.ua

Introduction. Respiratory diseases are one of the most important health problems due to their high prevalence, often severe with frequent complications. Treatment of these diseases to date remains a difficult problem due to the fact those respiratory diseases with different etiologies similar to clinical manifestations. Therefore, it is important in the arsenal of medicines have the effect of which will be aimed at the reduction and elimination of the main manifestations of the disease, regardless of etiology, and at the same time be safe for treatment.

In recent years, more and more recognition have herbal medicinal products. The advantage of plant-based drugs is that biologically active substances of plants more natural included in the metabolic processes of the human body, unlike synthetic drugs.

Aim. Development of composition capsules for the treatment of respiratory disease.

Materials and methods. The physicochemical, technological and biopharmaceutical methods have been used in study.

Results and discussion. The characterization and evaluation of medications used to treat respiratory diseases in literary sources has been explored. It has been demonstrated how quickly novel combination medications in capsules form based on medicinal plant materials may be developed. The research of medicinal raw materials is important for producing novel medications, according to the literature.

As active substances, a dry extracts of linden flower and licorice root is proposed, which is characterized by inflammatory, antimicrobial, diaphoretic, antipyretic antiallergic, expectorant, spasmolytic actions.

During physicochemical and technology researches it is established that dry extracts possess the low flowability, high absorbing capacity and unsatisfactory indicators of compactibility. For the purpose of rational choice of excipients properties of potato starch, microcrystallic cellulose and lactose are studied. Technical characteristics on mixes for granulation with different humidifiers are established (MC of 3%, PVP of 5%, PVP of 5% of MC 0.5%i ethanol). Based on the studies carried out, a rational composition of capsules and a technological scheme for their production are proposed.

Conclusions. Development of composition of the capsules for the treatment of the respiratory disease was conducted.

RATIONALE OF THE CREAM COMPOSITION FOR THE URTICARIA TREATMENT

Ziati Ibtissam[1], Kovalov V.M.[2]
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[1]National University of Pharmacy, Kharkiv, Ukraine
[2]Kharkiv National Medical University, Kharkiv, Ukraine
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Introduction. Significant prevalence, variety of clinical forms, chronic relapsing course, a large number of complications put allergic diseases in a number of priority interdisciplinary problems

Continuation of Appendix A

of modern medicine. The use of new extemporaneous drugs for the local treatment and manifestations of urticaria will reduce unpleasant sensations and shorten the duration of treatment, prevent the appearance of side effects, and significantly reduce the costs of expensive industrially produced drugs.

Aim. Substantiation of the cream composition for the urticaria treatment.

Materials and methods. Active pharmaceutical ingredients were used in the development of the cream composition for the urticaria treatment: menthol, fexofenadinum hydrochloride, excipients: peach oil, emulsifier Olivem 1000 and purified water. To achieve the goal, general scientific methods of research were used: analysis, synthesis, comparison, generalization, comparison, systematization for processing literary data.

Results and discussion. Menthol has weak local anesthetic properties, stimulates cold receptors of the skin and mucous membranes, is a weak antiseptic. It is widely used in the food industry and in medicine. Fexofenadine, an active metabolite of terfenadine, is a non-sedating selective H1-receptor antagonist with a rapid and long-lasting effect. It is the first antihistamine of the third generation. Peach oil is widely used in modern dermatology and cosmetics. It has an anti-inflammatory, wound-healing and toning effect on the skin. Olivem 1000 is an olive based non-ionic oil-in-water PEG-free self-emulsifying multifunctional ingredient. It is a combination of fatty acids, chemically similar to the lipidic composition of the skin surface. It has the ability to generate liquid crystal structures that mimic the stratum corneum organization. Emulsifier Olivem® 1000 provides a deep moisturizing effect.

Conclusions. Considering the above, we consider it rational and relevant to develop a cream composition with API menthol, fexofenadinum hydrochloride, the use of modern substances for the urticaria treatment will enrich the pharmaceutical market with innovative drugs, and further research in this direction will allow creating an effective drug.

Continuation of Appendix A

Appendix B

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

СЕРТИФІКАТ УЧАСНИКА

Цим засвідчується, що

Ziati Ibtissam, Kovalov V.M.
Scientific supervisor: Kovalov V.V

брав(ла) участь у роботі
XXIX Міжнародної науково-практичної конференції молодих вчених та студентів
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

В.о. ректора
Національного фармацевтичного університету Алла КОТВІЦЬКА

19-21 квітня 2023 р, м. Харків

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department pharmaceutical drug technology

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
The Head of Department
Liliia VYSHNEVSKA

_____
"_06_" May 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Ibtissam ZIATI

1. Topic of qualification work: «Emulgel technological properties for the dermatitis treatment investigation», supervisor of qualification work: Volodymyr KOVALOV, PhD, assoc. prof.,

approved by order of NUPh from "06" of February 2024 № 34

2. Deadline for submission of qualification work by the applicant for higher education: November 2024.

3. Outgoing data for qualification work: improving the composition and studying the technological properties of emulgel for the treatment of dermatitis.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): conduct an analysis of literature data on types of dermatitis and their pathogenesis (disease mechanisms); design and theoretically substantiate the composition of the dermatitis gel using ingredients with established anti-inflammatory, anti-itch, and skin-barrier-repair properties; experimentally optimize the emulgel composition, considering compatibility of ingredients, physical and chemical properties of ingredients; estimate the stability of emulgel for the treatment of dermatitis under various storage conditions; investigate technological properties of the final product.

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

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Volodymyr KOVALOV, associate professor of higher education institution of department Pharmaceutical drug technology	20.05.2024	20.05.2024
2	Volodymyr KOVALOV, associate professor of higher education institution of department Pharmaceutical drug technology	14.06.2024	14.06.2024
3	Volodymyr KOVALOV, associate professor of higher education institution of department Pharmaceutical drug technology	16.09.2024	16.09.2024

7. Date of issue of the assignment: "06" May 2024

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	The topic selection	May 2024	done
2	Analysis of literary sources	June 2024	done
3	Conducting experimental research in	September - October 2024	done
4	Designing the work	October 2024	done
5	Submission of finished work to the examination commission	October 2024	done

An applicant of higher education _____ Ibtissam ZIATI

Supervisor of qualification work _____ Volodymyr KOVALOV

ВИТЯГ З НАКАЗУ № 34
По Національному фармацевтичному університету
від 06 лютого 2024 року

1. Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу 2 циклу Фм20*(4,10д) 2024-2025 навчального року, ступінь вищої освіти «магістр», галузь знань 22 Охорона здоров'я, спеціальність 226 – Фармація, промислова фармація, освітньо-професійна програма – Фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців). Мова навчання англійська.

№ з/п	Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **по кафедрі аптечної технології ліків**					
2.	Зіаті Ібтіссам	Обґрунтування складу та вибору основи екстемпорального крему з левоцетиризином	Rationale for the extemporaneous cream composition and base choice with Levocetirizine	доцент ЗВО Ковальов В.В.	доцент ЗВО Трутаев С.І.

Ректор

Вірно. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«05» листопада 2024 р. № 328898329

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Зіаті Ібтіссам, Фм20*(4,10д)-англ-01, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Обґрунтування складу та вибору основи екстемпорального крему з левоцетиризином / Rationale for the extemporaneous cream composition and base choice with Levocetirizine», 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

Ibtissam ZIATI

on the topic: « Rationale for the extemporaneous cream composition and base choice with Levocetirizine»

Relevance of the topic. Urticaria is a very complex nosology, and the diagnosis of urticaria sounds quite mysterious to many doctors, even to specialists who deal with it. Urticaria can appear in different guises: both as a separate nosology, and as a syndrome, and as a symptom of various types of pathologies, and this is one of the difficulties of diagnosing and treating urticaria. It is known that the quality of life of a patient with chronic urticaria is equal to the quality of life of a patient with insulin-dependent diabetes. That is, such a comparison is not accidental, it suggests that this suffering really greatly changes a person's life, and requires a change in his entire way of life. Urticaria can accompany various types of other types of allergic nosologies. All of the above allows to conclude that the treatment of urticaria should be complex and an important place in it belongs to local therapy, which can be carried out using local means of both industrial and extemporaneous preparation. Master's thesis of Ibtissam ZIATI dedicated to this topical issue.

Practical value of conclusions, recommendations and their validity. During the writing of the thesis, the master's student analyzed literary data on the etiology, pathogenesis and clinical manifestations of allergic skin diseases, in particular urticaria, proved the need for the use of local drugs in complex therapy, theoretically and experimentally substantiated the composition of cream for the urticaria treatment, and proposed its technology.

Assessment of work. The master's work was completed at a high modern level. The master's student successfully solved all tasks. The results of the work are of practical interest.

General conclusion and recommendations on admission to defend. Ibtissam ZIATI master's thesis can be submitted for defense to the Examination Commission of the National Pharmaceutical University for the assignment of the educational qualification level of Master of Pharmacy.

Scientific supervisor _____ Volodymyr KOVALOV

«4» of October 2024

Ф А 2.2.1-32-356

REVIEW

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

Ibtissam ZIATI

on the topic: « Rationale for the extemporaneous cream composition and base choice with Levocetirizine»

Relevance of the topic. Urticaria is one of the most common skin diseases. According to modern research, every fifth person on Earth has at least one episode of urticaria during their lifetime, and in recent years, there has been a significant increase in the incidence, especially among the population of developed countries. Urticaria manifests as inflammatory, itchy rashes on the skin and/or angioedema (swelling of the deep layers of the skin or mucous membranes), which most often regress within 24 hours. Almost 70% of patients with urticaria experience recurrent angioedema. In 15% of cases, angioedema can occur in isolation, accompanied by rashes on the skin. Thus, the problem of urticaria is extremely urgent, as it significantly reduces the quality of life. The success of urticaria treatment is mainly determined by a well-conducted examination and a rational choice of medicines. At present, schemes for the step-by-step treatment of urticaria have been developed and are effectively used. A special place in them is occupied by means for topical therapy as industrial and extemporaneous production.

Theoretical level of work. The work carried out by Ibtissam ZIATI is devoted to analysis of the etiological factors that lead to the emergence and development of urticaria, studied the pathogenesis and approaches to its treatment. The composition of cream for the urticaria treatment is theoretically and experimentally substantiated.

Author's suggestions on the research topic. The master's student conducted theoretical and experimental studies on the justification of the choice of active and auxiliary substances of cream, studied its stability during storage, proposed a rational technology of cream.

Practical value of conclusions, recommendations and their validity. On the basis of the conducted research, a cream intended for the treatment of urticaria, is proposed for practical implementation. The obtained results can be used for the purpose of

expanding the assortment of preparations for the urticaria.

Disadvantages of work. According to the text of the work there are some typographical errors, bad expressions. However, this does not reduce the value of the work and does not call into question the results obtained.

General conclusion and assessment of the work. The qualification work of the applicant deserves high marks, meets the requirements and can be submitted for official defense to the examination commission of the National University of Pharmacy.

Reviewer _____ assoc. prof. Sergiy TRUTAIEV

«10» of October 2024

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № _2_
«_14_» _жовтня_ 2024_
року м. Харків

засідання кафедри
аптечної технології ліків
(назва кафедри)

Голова: завідувачка кафедри, професор Вишневська Л. І.
Секретар: докт. філ., ас. Зуйкіна Є.В.

ПРИСУТНІ:

проф. Половко Н.П., проф. Семченко К.В., проф. Зуйкіна С.С., проф. Левачкова Ю.В., доц. Ковальова Т.М., доц. Буряк М.В., доц. Ковальов В.В., доц. Олійник С.В., доц. Марченко М.В., доц. Живора Н.В., ас. Іванюк О.І., асп. Бондар Л.А., асп. Паливода П.В.

ПОРЯДОК ДЕННИЙ:

Про представлення до захисту кваліфікаційних робіт здобувачів вищої освіти.

СЛУХАЛИ: проф. Вишневську Л. І. – про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт здобувачів вищої освіти.

ВИСТУПИЛИ: Здобувач вищої освіти групи Phm19(4,10d) eng 04 спеціальності 226 «Фармація, промислова фармація» Ibtissam ZIATI – з доповіддю на тему «Rationale for the extemporaneous cream composition and base choice with Levocetirizine» (науковий керівник, доц. Володимир КОВАЛЬОВ).

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу.

Голова
Завідувачка кафедри, проф. _____ **Лілія ВИШНЕВСЬКА**
(підпис)

Секретар
асистент _____ **Єлизавета ЗУЙКІНА**
(підпис)

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Ibtissam ZIATI до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Rationale for the extemporaneous cream composition and base choice with Levocetirizine»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____/ Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Ibtissam ZIATI представила кваліфікаційну роботу, яка за об'ємом теоретичних та практичних досліджень повністю відповідає вимогам до оформлення кваліфікаційних робіт.

Керівник кваліфікаційної роботи

_____ Володимир КОВАЛЬОВ

«04» жовтня 2024 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Ibtissam ZIATI допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри
аптечної технології ліків

_____ Лілія Вишневська

«14» жовтня 2024 р.

Qualification work was defended

of Examination commission on

« 28 » of November 2024

With the grade _____

Head of the State Examination commission,

D.Pharm.Sc, Professor

_____ / Oleh SHPYCHAK