PROSPECTS OF THE USE OF PHYTOPREPARATIONS IN OPHTHALMOLOGY

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Summary. Ophthalmological products are presented on the pharmaceutical market in a large assortment, and are one of those few medicinal forms, as a result of the use of which, along with the therapeutic effect, an irritating effect is revealed almost immediately. Auxiliary substances are used for the ability to give medicines a certain form, convenient use, transportation and storage. Substances that contribute to the solution of this issue include excipients that to some extent affect the quality indicators of drugs and their shelf life and do not reduce the pharmacological effect. The study of auxiliary substances in ophthalmic dosage forms will provide an opportunity to ensure better indicators of the quality of medicinal products.

Key words: vision, dosage forms, eye drops, excipient.

Sight is one of the receptive senses, one of the most important sensory sensations, because through it we receive and analyze the largest percentage of information in the form of an image that comes from the environment. The eyes are exposed to a lot of stress and it is not surprising that recently various diseases and pathological conditions of the organ of vision are becoming more and more common [1]. According to the WHO, about 300 million people in the world have vision problems, of which 43% suffer from refractive errors - nearsightedness, farsightedness and astigmatism [2]. Therefore, ophthalmic products are presented on the pharmaceutical market in a large assortment. It should be noted that ophthalmic drugs are one of those few medicinal forms, as a result of the use of which, along with the therapeutic effect, an irritating effect is revealed almost immediately. The eye reacts to even minor irritation with increased lacrimation, due to which, on the one hand, visual ability is inhibited, and on the other hand, the concentration of medicinal substances decreases prematurely, as the injected solution is washed out, as a result of which the bioavailability of medicinal substances decreases. Therefore, the requirements for ophthalmic drugs for local use are quite high. Modern pharmaceutical codes, the State Pharmacopoeia of Ukraine do not make a significant difference between drugs for the treatment of eye diseases and parenteral drugs. Medicinal products for the eyes must be: sterile, stable, isotonic, contain an exact dosage of the medicinal substance, have no mechanical contamination visible to the naked eye, some must have a prolonged effect, be convenient to use [3]. To meet these requirements, eye drops require appropriate approaches, taking into account the chemical nature of medicinal substances and therapeutic purpose. These features result in a number of specific and necessary requirements for the composition, production and use of eye drops. Liquid dosage forms intended for use in ophthalmology, like almost all pharmaceutical preparations known today, contain active pharmaceutical ingredients and excipients.

The scientific works of famous scientists (M.T. Alyushin, V.M. Gretskyi, L. Zaturetskyi, H. Levy, A.I. Tintsova, G.V. Tsagareishvili, G.S. Bashura, V.A. Golovkin, T.A. Groshovyi, D.I. Dmitrievskyi, F.A. Zhoglo, V.O. Oridorog, I.M. Pertsev, B.G. Yasnytskyi and others), who determined the influence of excipients and technological techniques on the properties and effectiveness of drugs are devoted to solving this problem.

The purpose of the work was to study the nomenclature of ophthalmic dosage forms of the WORLD MEDICINE OPHTHALMICS company, and to substantiate the
choice of composition and the influence of auxiliary substances on the technological properties of medicinal products.

Materials and methods. In order to determine the range and designation of excipients, a marketing and merchandising analysis of eye drops available on the domestic pharmaceutical market was performed. The results were evaluated using correlation analysis in the STATISTIKA 6.0 software package.

Results and their discussion. The use of an auxiliary substance in the composition of a pharmaceutical preparation for the ability to give medicines a certain form, convenient for use, transportation and storage, is a prerequisite for their indifference in the chemical and pharmacological aspect [4]. However, biopharmaceutical studies confirmed the need to take into account the influence of the components of the pharmaceutical system and the type of dosage form when determining the effectiveness of pharmacotherapy [5]. The analysis of the "active substance — excipient" system made us reconsider the concept of excipients as indifferent formants. The ability of excipients to change the nature and strength of the therapeutic effectiveness of active pharmaceutical ingredients and, therefore, the pharmaceutical preparation as a whole was experimentally established [6].

One of the leading importers of ophthalmic drugs is World Medicine Ophthalmics, a pharmaceutical company that supplies high-quality drugs for the treatment of diseases in ophthalmology. In addition to becoming accessible to patients, the company's mission is to improve the quality of life of patients and return them to a full life in society. The World Medicine company has a multidisciplinary portfolio, which includes more than 350 medicines in such fields of medicine as therapy, neurology, endocrinology, cardiology, rheumatology, gastroenterology, urology, pulmonology and others.

The most used among ophthalmic dosage forms are eye drops in the form of aqueous solutions. The nomenclature of ophthalmic medicines in the form of eye drops is presented in the table 1.

**Table 1**

<table>
<thead>
<tr>
<th>No</th>
<th>The name of the medicinal product</th>
<th>Pharmaceutical form and dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Daveris</td>
<td>eye drops, solution 40 μg/ml dropper bottle 2.5 ml, No. 1</td>
</tr>
<tr>
<td>2</td>
<td>Dorzamed</td>
<td>eye drops, solution 2% dropper bottle 5 ml, No. 1</td>
</tr>
<tr>
<td>3</td>
<td>Cataxol</td>
<td>eye drops, solution 0.15 mg/ml dropper bottle 15 ml, No. 1</td>
</tr>
<tr>
<td>4</td>
<td>Clodifen</td>
<td>eye drops, solution 1 mg/ml dropper bottle 5 ml, No. 1</td>
</tr>
<tr>
<td>5</td>
<td>Latamed</td>
<td>eye drops dropper bottle 2.5 ml, No. 1</td>
</tr>
<tr>
<td>6</td>
<td>Latasopt</td>
<td>eye drops, solution 0.05 mg/ml dropper bottle 2.5 ml, No. 1</td>
</tr>
<tr>
<td>7</td>
<td>Levoximed</td>
<td>eye drops, solution 5 mg/ml dropper bottle 5 ml, No. 1</td>
</tr>
<tr>
<td>8</td>
<td>Medexol</td>
<td>eye drops, solution 1 mg/ml dropper bottle 5 ml, No. 1</td>
</tr>
<tr>
<td>9</td>
<td>Medexol</td>
<td>eye drops, suspension 1 mg/ml dropper bottle 10 ml, No. 1</td>
</tr>
<tr>
<td>10</td>
<td>Medetrom</td>
<td>eye drops, suspension dropper bottle 5 ml, No. 1</td>
</tr>
</tbody>
</table>
In the technology of ophthalmic drugs in the form of drops, materials and methods are used that ensure sterility, prevent contamination of the drug by microorganisms and products of their vital activity. Among the auxiliary substances used in the technology of eye drops, there are solvents, stabilizers, isotonic substances, extenders, preservatives, substances that regulate the pH of the environment, etc. Some excipients can perform different functions, i.e. be assigned simultaneously to several classification groups (Table 2).

### Table 2

<table>
<thead>
<tr>
<th>No</th>
<th>Group of excipients</th>
<th>The most widely used excipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Solvents</td>
<td>Water for injections, purified water</td>
</tr>
<tr>
<td>2.</td>
<td>Preservatives</td>
<td>Merthiolate, chlorobutanol hydrate, benzalkonium chloride, cytylpyridinium chloride, phenyl mercury nitrate (borate, acetate), chloramphenicol in combination with boric acid</td>
</tr>
<tr>
<td>3.</td>
<td>Stabilizers</td>
<td>Disodium edetate, sodium chlorate, chlorine dioxide</td>
</tr>
<tr>
<td>4.</td>
<td>Buffer solutions</td>
<td>Tartrate, phosphate, borate, citrate</td>
</tr>
<tr>
<td>5.</td>
<td>pH regulators</td>
<td>Sodium hydroxide, hydrochloric acid</td>
</tr>
<tr>
<td>6.</td>
<td>Prolongers</td>
<td>Hypromellose, carmellose sodium, polyvinyl alcohol, methylcellulose, hydroxyethylcellulose, carbomer 974P, povidone, mannitol, betacyclodextrin, alginic acid, carboxymethylcellulose and sodium carboxymethylcellulose (1%), polyvinylpyrrolidone, collagen</td>
</tr>
<tr>
<td>7.</td>
<td>Regulatory substances</td>
<td>Sodium chloride, potassium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate</td>
</tr>
<tr>
<td>8.</td>
<td>Osmotic pressure</td>
<td>Castor oil polyethoxylated, hydrogenated 40, polyethylene glycol</td>
</tr>
</tbody>
</table>

A necessary condition for the production of eye drops is stability, which will ensure a long shelf life of drugs in large-scale production. The main reasons for the instability of aqueous eye drops are the hydrolysis of medicinal substances, their oxidation and contamination of solutions by microorganisms. Stabilization factors include: the introduction of buffer solutions, the composition and pH of which to the greatest extent ensure not only the stability of medicinal substances, but also the detection of the maximum therapeutic effect; preservatives and antioxidants[7].
Stabilizers in eye drops perform the function of increasing chemical resistance, since the destruction of medicinal substances in drops can occur during sterilization and long-term storage, and also provide a reduction in the irritating effect of the solution on the mucous membrane of the eye. The chemical stability of the active substances is mainly ensured by the addition of disodium edetate.

The necessary pH level provides comfort in use in eye drops, and also affects the processes of activation and inhibition of the action of medicinal substances in solutions. In most cases, buffer solutions are used, as well as hydrochloric acid or sodium hydroxide [8]. It should be remembered that drops that do not contain preservatives can be potentially dangerous from the point of view of microbial contamination of the eye surface. One of the preservatives with proven effectiveness, which is included in the composition of eye drops, is benzalkonium chloride (BAC), which belongs to the quaternary ammonium compound. Benzalkonium chloride is the dominant preservative used in ophthalmic preparations over the past several decades, and is included in 70% of eye drops. The preservative has an antimicrobial effect, has limited penetration into the structures of the eye, and remains stable in solutions for a long time [9].

Today, in order to optimize the positive effect of preservatives, special balanced mixtures of preservatives have been developed for each group of drugs, which ensure their universal use[10]. The main problem here is determining the optimal concentration of preservatives. Their insufficient amount does not ensure the storage of pharmaceuticals for a given period of time, and the excess may be unacceptable due to the deterioration of the quality of the products for which they are used to protect, or for economic reasons. The composition of each pharmaceutical preparation is experimentally selected with its own concentration of preservatives.

Frequent use of eye drops wash away the tear fluid, which contains lysozyme, as a result of which it can encourage the development of infectious processes. However, the use of medicinal preparations more than once a day significantly reduces the level of patient compliance, which in turn can lead to a decrease in the effectiveness of the prescribed treatment. To prevent this, extenders are added to the composition of eye drops, the mechanism of action of which is to increase the viscosity of the solution. In our case, macrogol glycerol, mannitol (E 421), propylene glycol are used as extenders.

An important characteristic of eye drops is the amount of osmotic pressure, sodium chloride is used to regulate it in eye drops.

Therefore, the quality and shelf life of pharmaceuticals are indicators that have both economic and social significance.

Conclusions. The study of auxiliary substances in ophthalmic dosage forms will provide an opportunity to ensure better indicators of the quality of medicinal products. Substances that contribute to the solution of this issue include excipients that to some extent affect the quality indicators of drugs and their shelf life and do not reduce the pharmacological effect.

References:


