# NATIONAL UNIVERSITY OF PHARMACY

## TECHNOLOGY OF DRUGS DEPARTMENT

**Discipline: «PHARMACY-BASED TECHNOLOGY OF DRUGS»**

# Technology of ophthalmic medicines

*Lecture for students of specialty "PHARMACY FOR FOREIGN STUDENTS"*

**Lecturer: ass. prof. Kovalyov V. V.**

# THE PLAN OF THE LECTURE

1. Definition and classification of ophthalmic medicinal forms
2. Requirements of ophthalmic medicinal forms
3. Classification of ophthalmic medicinal forms
4. Definition and requirements of ophthalmic drops
5. Technology of preparing ophthalmic drops
6. Ophthalmic ointments
7. Stages of the technological process of preparing ophthalmic ointments

**Theoretical issue for self-study:**

1. Preservatives and prolongation agents in technology of ophthalmic medications, their characteristics and application.

# LITERATURE


1. Chemist's technology of drugs: The manual for students of higher schools / Tikhonov A. I., Yarnykh T. G., Yurieva A. B., Garkavtseva O. A.; Edited by A. I. Tikhonov and T. G. Yarnykh. – Kharkiv: NUPh; Original, 2011. – 424 p.
2. Dry, liquid and soft medicinal forms: A textbook for English students in specialty "Pharmacy" / A. I. Tikhonov, T. G. Yarnykh, A. B. Yurieva, L. N. Podorozhna, S. S. Zuykina; Ed. by A. I. Tikhonov. – Kharkiv: NUPh; Original, 2011. – 208 p.
3. Good Pharmacy Practice (GPP) in community and hospital pharmacy settings / World Health Organization. – 1996.
4. Guidelines on the Equipment Requirements of a Retail Pharmacy Business / To facilitate compliance with Regulations 4(1) and 4(4) of the Regulation of Retail Pharmacy Businesses Regulations 2008 (S.I. No. 488 of 2008).
5. Guidelines to prepare for the final module control and state attestation on the discipline "Chemist's Technology of Drugs": for English students of specialty "Pharmacy": Reference edition. For individual student's work / Yarnykh T. G., Rukhmakova O. A., Buryak M. V. and others. – Kharkiv: NUPh, 2014. – p 48.
6. John F Marriott, Keith A Wilson, Christopher A Langleyv, Dawn Belcher Pharmaceutical Compounding and Dispensing. - Published by the Pharmaceutical Press. – 2010. – 288 p.
7. Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Garkavtseva O.A. Chemist's Technology of Drugs: The manual for students of higher schools / Edited by A.I. Tikhonov and T.G. Yarnykh. – Kharkiv: NUPh; Original, 2011. – 424 p.
8. United State Pharmacopeia. – XXIV ed. – Rockville: The United State Pharmacopeial, Inc., 2000. – 2569 p.
9. USP Pharmacists' Pharmacopeia. – II ed. – Rockville. The United State Pharmacopeial, Inc., 2008. – 1519 p.

# DEFINITION AND CLASSIFICATION OF OPHTHALMIC MEDICINES

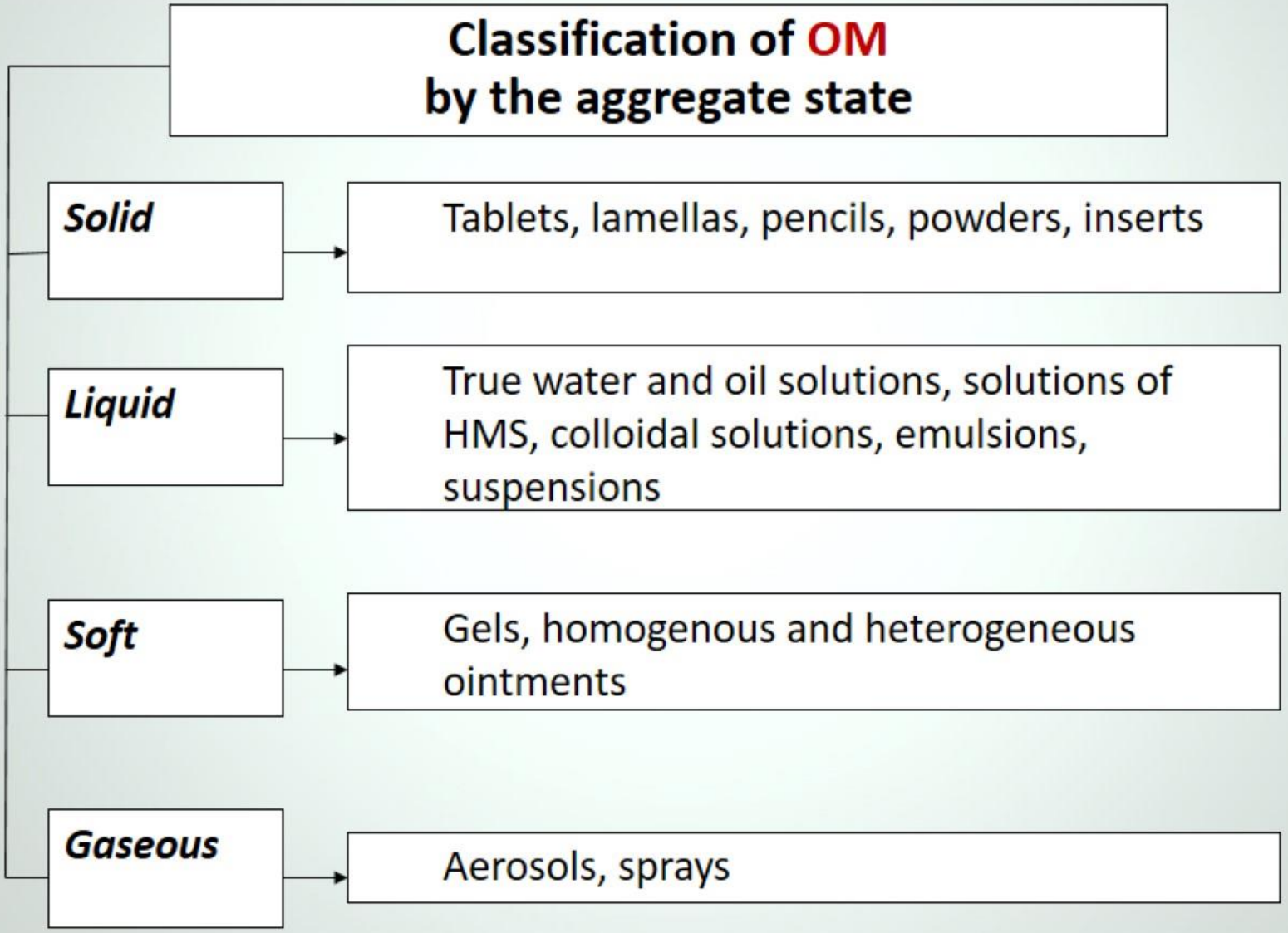
**Ophthalmic medicines (OM)** (definition by State Pharmacopoeia of Ukraine)

⇨ **are sterile liquid, soft or solid medicines intended for introduction into the eyes, conjunctiva or conjunctival sack**

**Classification of OM by the type of a medicinal form**

- Drops
- Washings
- Ophthalmic inserts
- Soft medicines
- Solutions

# CLASSIFICATION OF OPHTHALMIC MEDICINES



# REQUIREMENTS TO OPHTHALMIC MEDICINES

**Requirements to ophthalmic medicines**

1. Maximal dispersion of medicinal substances
2. Sterility
3. Stability
4. Isotonicity
5. Uniform distribution on the mucus of the eye
6. The absence of the irritant action
7. Uniform distribution, and the exact Concentration medicinal substances
8. The prolongation of action and buffer properties (in some cases)

# DEFINITION AND REQUIREMENTS OF OPHTHALMIC DROPS

**OPHTHALMIC DROPS**
(guttae ophtalmicae)

⇨ are liquid medicinal form, which are aqueous or oil solutions, thin suspensions of medicinal substances intended for instillation into eyes

**Requirements to ophthalmic DROPS**

2. **Sterility**
3. **Stability**
4. **Isotonicity**
6. **The absence of the irritant action**

**The prolongation of action and buffer properties (in some cases)**

# OPHTHALMIC DROPS

Sterilization of eye drops depends on the stability to temperature of medicinal substances in solutions.
**By the way of sterilization medicinal substances can be divided into three groups:**

| | |
|---|---|
| **Solutions of medicinal substances, which can be sterilized by thermal sterilization without adding stabilizers** | Boric acid, nicotinic acid, sodium chloride, furacillin, etc. |
| **Solutions of medicinal substances, which can be sterilized by thermal sterilization after adding stabilizers** | Sodium sulphacyl, ethylmorphine hydrochloride, phizostigmine salicylate, soluble saluside, etc. |
| **Solutions of medicinal substances, which cannot be thermally sterilized and prepared in aseptic conditions without further sterilization** | Protargol, collargol, lidase, chimopsine, tripsine, penicillin, etc. |

# TECHNOLOGY OF PREPARATION OPHTHALMIC DROPS

**Ophthalmic drops are prepared in aseptic conditions by the mass-volumetric method with the subsequent sterilization of termostable substances.**

In order to decrease the loss of medicinal substances during the preparation of ophthalmic drops two ways are used:

- Dissolve a **medicinal substance**, which is **easily soluble in water**, in a portion of water (**1/2 from the solvent's volume**), filter the solution in the bottle for dispensing **through a paper filter previously washed** by the sterile water for injections, and then **wash the filter** by the **remaining portion** of the solvent.

- If a medicinal substance is **poorly soluble in water**, dissolve it in **all the solvent's quantity** prescribed and filter in a **graduated cylinder** through a **dry filter** and cotton. **Add** the **missing quantity** of water through the same filter and cotton to **make the required volume** of the solution

# DEFINITION AND REQUIREMENTS OF OPHTHALMIC OINTMENTS

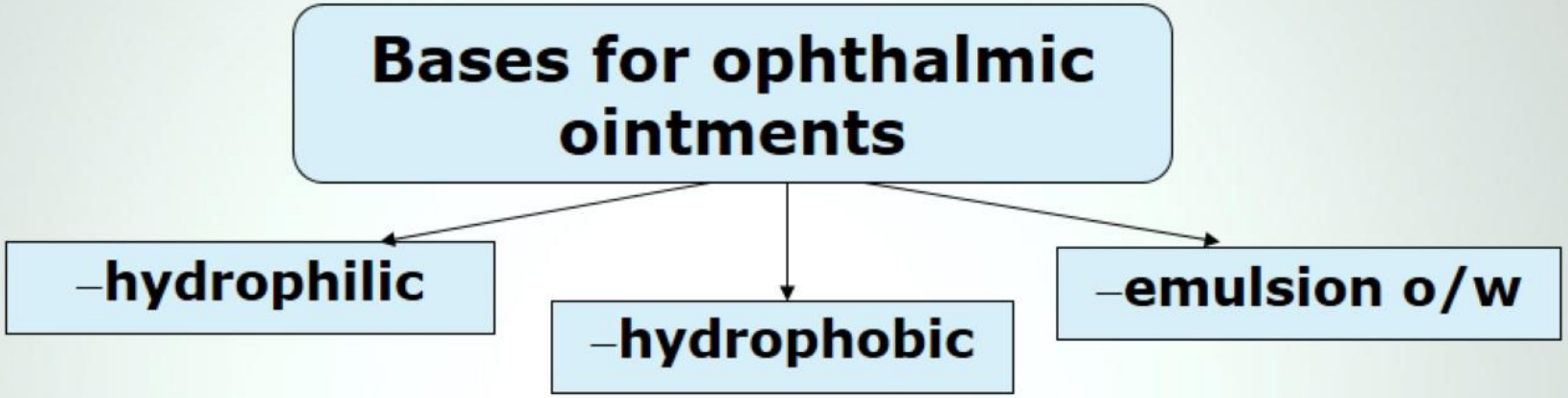
**OPHTHALMIC SOFT MEDICINES**
(State Pharmacopoeia of Ukraine)

⇨ are homogenous sterile ointments, creams or gels for application on the conjunctive of the eye

## Requirements to ophthalmic OINTMENTS

- Maximal dispersion of medicinal substances
- Sterility
- Stability
- Uniform distribution on the mucus of the eye with formation of the thinnest film
- The absence of the irritant action and sticking of the eyelid
- Uniform distribution, and the exact Concentration medicinal substances

# OPHTHALMIC OINTMENTS




If the base for the ophthalmic ointment is not indicated in the prescription used:

| | |
|---|---|
| **Vaseline** of «for ophthalmic ointments» type | **9** portions |
| **Anhydrous lanolin** | **1** portion |

# TECHNOLOGY OF OPHTHALMIC OINTMENTS

Introduction of medicinal substances (MS)

| | |
|---|---|
| **MS soluble in water** | **dissolve in the minimal amount of water and mix with the ointment's base** |
| **MS insoluble or poorly soluble in water and in a base** | **triturate in a dry form and then with half of the amount of the liquid suitable with a base or a melt base** |
| **MS soluble in a base** | **dissolve in the liquid suitable with the base or a melt base** |

**Resorcine and zinc sulphate into ophthalmic ointments can be introduced only after dissolving them in water**

***All ophthalmic ointments are prepared in aseptical conditions***

| № | Name | Properties of substances | Peculiarities of introduction into medicinal forms / *Incompatibilities* |
|---|---|---|---|
| 1 | Base for ophthalmic ointments (sterile) | Auxiliary substance | 9 parts of vaseline for ophthalmic ointments and 1 part of anhydrous lanoline.<br>Reducing agents are absent in vaseline for ophthalmic ointments. The base is sterilized by dry heat (180 °C for 2 hours) |
| 2 | Yellow mercury ointment (ophthalmic) | Ointment-suspension | Composition: mercury yellow oxide, sterile vaseline oil, sterile vaseline (for ophthalmic ointments) and anhydrous lanoline in the ratio of 5:1<br>Technology: In aseptic conditions grind mercury yellow oxide with a sterile vaseline oil (according to Deryagin rule), add sterile vaseline (for ophthalmic ointments) and anhydrous lanoline |
| 3 | Ascorbic acid | Soluble in water. | Dissolve in the half amount of the water volume. Isotonate by sodium chloride<br>*Physical and chemical:*<br>*formation of a damp mixture with hexamethylenetetramine, sodium hydrocarbonate* |

| № | Name | Properties of substances | Peculiarities of introduction into medicinal forms / *Incompatibilities* |
|---|---|---|---|
| 4 | Benzalkonium chloride | Organic preservatives | Is used as a preservative in the eye drops technology |
| 5 | Benzyl alcohol | Organic preservatives | Is used as a preservative in the eye drops technology |
| 6 | Collargol | A strong effective, light sensitive substance. Slowly soluble in water | without isotonating and sterilization |
| 7 | Glucose | Soluble in water. | by the general rules.<br>Take into account % of humidity; dissolve in the half amount of the water volume.<br>Isotonate by sodium chloride |
| 8 | Merthiolate | Metal organic preservative | Is used as a preservative in the eye drops technology |
| 9 | Methylcellulose | Prolongation agent | Is used as a prolongation agent in the eye drops technology |
| 10 | Polyvinyl alcohol | Prolongation agent | Is used as a prolongation agent<br>in the eye drops technology |

| № | Name | Properties of substances | Peculiarities of introduction into medicinal forms / *Incompatibilities* |
|---|---|---|---|
| 11 | Pilocarpine hydrochloride | Pilocarpine hydrochloride A poisonous substance (check of doses). Soluble in water. | Ophthalmic drops: By the general rules, dissolve in the half amount of the water volume, isotonate by sodium chloride<br><br>Ophthalmic ointments:<br>As a water solution by the type of emulsion mixing with a sterile base (9:1) |
| 12 | Potassium iodide | Soluble in water | Ophthalmic drops: By the general rules. Introduce potassium iodide in aseptic conditions in the presence with ascorbic acid, after sterilization of the prepared drops<br><br>*Chemical: with ascorbic acid* |
| 13 | Protargol | A colloidal substance (contains 8 % of silver oxide), soluble in water, glycerin | By the general rules.<br>Without sterilization and isotonation |

| № | Name | Properties of substances | Peculiarities of introduction into medicinal forms / *Incompatibilities* |
|---|---|---|---|
| 14 | Resorcin | Soluble in water | **Ophthalmic drops:** Introduce in aseptic conditions after sterilization of the prepared drops **Ophthalmic ointments:** As a water solution by the type of emulsion mixing with a sterile base (9:1) |
| 15 | Riboflavin | A dyer. Soluble in water | As a concentrated solution 0.02 % |
| 16 | Silver nitrate | A poisonous substance (check of doses). Soluble in water. | By the general rules. Isononate by sodium chloride |
| 17 | Zinc sulphate | Soluble in water | **Ophthalmic drops:** By the general rules. Dissolve in the half amount of the water volume; isononate by sodium sulphate **Ophthalmic ointments:** As a water solution by the type of emulsion mixing with a sterile base (9:1) |

# OPHTHALMIC LOTIONS, WASHES, SUSPENSIONS, EMULSIONS AND OTHER MEDICINAL FORMS

**Eye lotions** are sterile aqueous solutions intended for moistening and washing of eyes, as well as for saturating materials applied on the eye. The technology of eye lotions is similar to those of eye drops

**Liquids for treating contact lenses** are sterile wetting, moistening, and disinfectant aqueous solutions for storing, cleaning and facilitating of application of contact lenses or contact glasses of the ophthalmological devices used for research

**Suspensions** and **emulsions** are prepared in conditions of the manufacture and at the chemist's diluting them with water to the required concentration. In the case of overcoming sedimentation instability of suspensions and keeping particles with the size not more than 10 μm in them, the medicines obtained are not felt by a patient and have the same effect as eye drops

**Powders are** used for powdering of the eye fluids. Prepare them in aseptic conditions from the medicinal substances of the thinnest dispersity subjecting the thermostable substances to sterilization

**Eye sprays** are solutions for injections, which are applied on the eye without contact. Nitrogen and nitrogen dioxide are used as a carrier for dosing aerosols. The index of pressure is limited in a balloon in order to be exactly dosed.

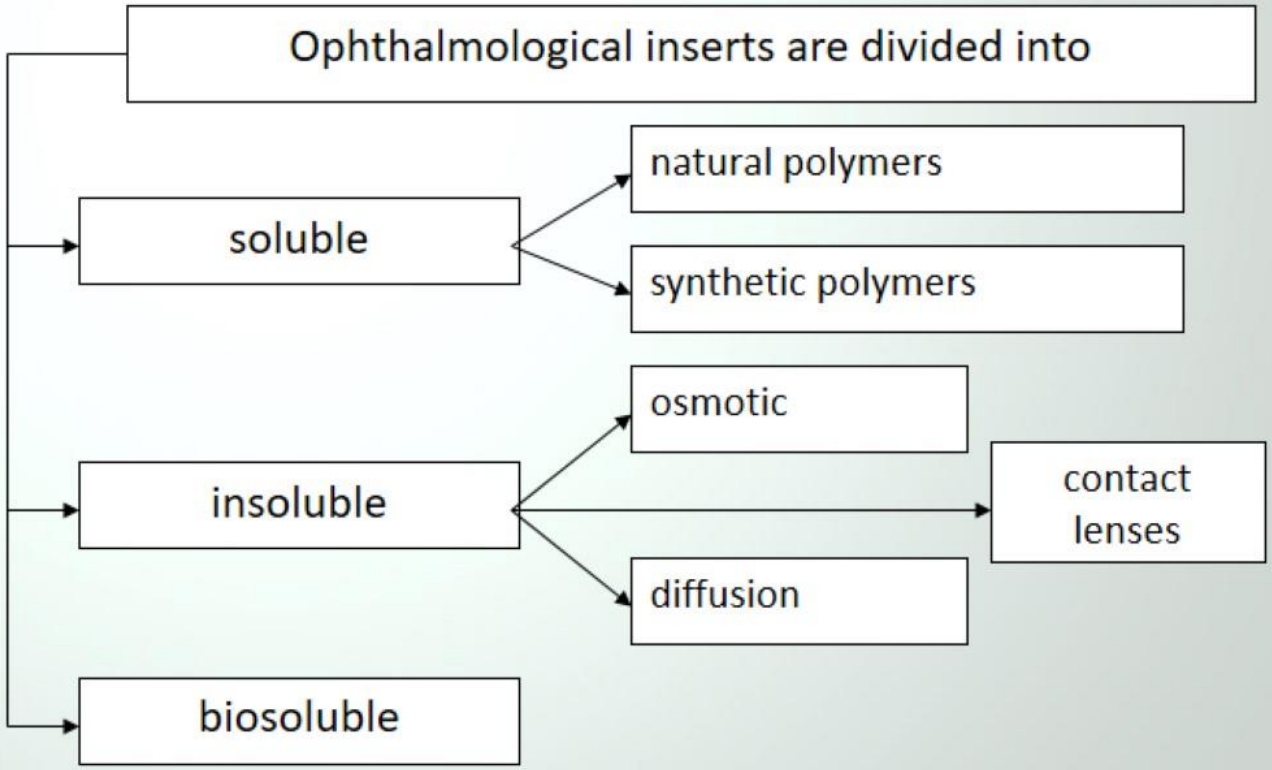
# OPHTHALMIC INSERTS

**Ophthalmic inserts** — are sterile dry or soft medicines with the proper size and shape intended for insertion in the conjunctival sack

**Ophthalmic inserts** usually consist of the matrix, in which the active substance is included, or the active substance is surrounded by the membrane that controls the rate of releasing.

**Advantages of eye inserts:**

- improvement of bioavailability of a medicinal substance due to the increase of the contact time with the mucous membrane;
- providing of the prolonged releasing of a medicine;
- diminishing of the systemic side effects;
- possibility of introducing the exact dose of a medicinal substance into the eye.



# THE QUALITY CONTROL AND STORAGE OF OPHTHALMIC MEDICINAL FORMS

Quality control includes ***all types of the intra-chemist's control***:

- Written;
- Questioning;
- Organoleptic (colour, odour, uniformity) and the absence of particulate matters, transparency;
- Physical (the total amount or the weight, which after preparation should not exceed the norms of permitted deviations, the size of particles in ointments);
- Chemical control (primary and secondary (it is selective);
- Control at the dispensing.

**For dispensing and storages** of eye drops use bottles of a neutral glass (bottles for antibiotics) closed by rubber corks and sealed by aluminium cover.

**Conditions of storage** of ophthalmic medicines depend on properties of the medicinal and auxiliary substances. If there are no special indications, eye drops, lotions and ointments are kept in a cool place for 10 days protected from light.

# Conclusions:

1. Definition and classification of ophthalmic medicinal forms were given.
2. Requirements of ophthalmic medicinal forms were considered.
3. Classification of ophthalmic medicinal forms were given.
4. Definition and requirements of ophthalmic drops were given.
5. Technology of preparing ophthalmic drops were considered.
6. Ophthalmic ointments peculiarities were considered.
7. Stages of the technological process of preparing ophthalmic ointments were considered.

***THANK YOU FOR YOUR ATTENTION!***