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Selection Of The Optimal Anti-Healthy Ointment And Determination Of Biopharmasevic Aspects

Rizaeva Nilufar Mukhutdinovna[1], Dustmurodova Shaxlo Jumanazarovna[2], Aripova Nozima Xakimdjanovna[3], Baratova Malika Baxtiyarovna[4]

shahlodustmurodova@gmail.ru

Annotation: One of the most pressing issues facing the pharmaceutical science of the Republic of Uzbekistan is to meet the needs of the population in medicines with relatively inexpensive and effective treatment and prevention products produced in the country. As a result of research conducted by a number of scientists in research institutes, bioactive substances with various therapeutic effects were isolated from local raw materials. The main goal of the drug policy of our country is to provide the population with effective, high quality, safe, cheap and local raw materials.

Keywords. Lubricant, grease, sodium hydroxide, dermatology, base, Vaseline, technology.

1. INTRODUCTION.

It is known that a person's beauty is the first sign of his health. In dermatology, warts are a viral disease. New modern methods of treating them go back to the practice of surgery.

oday, the share of mild drugs in the overall range of drugs is relatively low. The ones that are produced are often old. Therefore, one of the main directions of scientific research is the creation and expansion of the range of drugs of this group. According to the results of 2007, 4790 drugs were registered in the Republic of Uzbekistan, of which 170 were ointments, 53 were creams and 55 were gels. This figure is only 5.8%.

Ointments (Unguenta) are mild forms of medicine, mainly for local use. Their dispersed media have such rheological properties (sufficient viscosity, plasticity and pseudoplasticity) that as a result, the greases can sufficiently maintain their stability even at a given temperature.

Ointments are included in the XI DF in the form of official dosage forms and are intended for application to the skin, wounds and smooth layers. [2,4]

2. PART OF METHODS

Preparation of Sodium hydroxide grease on various hydrophilic bases

When choosing the composition of this ointment, it is recommended to use it for skin care, treatment and prevention.

At the same time, we chose odorless, colorless hydrophilic bases for the preparation of grease. These principles are:

1. Methyl cellulose (MC)
2. Sodium carboxy methyl cellulose (Na-KMC)
3. Preparation of grease on the basis of bentonite

4. Vaseline - preparation of ointment on the basis of lanolin
5. Preparation of grease with hydrophobic base and Emulgator T2

On the basis of the above hydrophilic and hydrophobic anti-aging ointments on 10 ingredients were prepared.

Greases prepared on hydrophilic and hydrophobic bases

Table 1

Name	Quantity, g									
	I-T	II-T	III-T	IV-T	V-T	VI-T	VII-T	VIII-T	IX-T	X-T
MC	3,0	4,0	-	-	-	-	-	-	-	-
Na-KMC	-	-	6,0	5,0	-	-	-	-	-	-
Bentonit	-	-	-	-	70,0	65,0	-	-	-	-
Sodium hydroxide	4,0	4,0	4,0	4,0	4,0	4,0	4,0	4,0	4,0	4,0
Water	71,0	72,0	80,0	75,0	16,0	16,0	16,0	16,0	16,0	16,0
Vaseline	-	-	-	-	-	-	70.0	60.0	-	-
Glycerin	22,0	20,0	10,0	16,0	10.0	20.0	-	-	-	-
Anhydrous lanonin	-	-	-	-	-	-	10.0	20.0	-	-
Emulgator T2	-	-	-	-	-	-	-	-	10.0	10.0
Vaseline Oil	-	-	-	-	-	-	-	-	20.0	10.0
Paraffin	-	-	-	-	-	-	-	-	50.0	60.

										0
Total weight	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0	1000,0

In the selection of these 10 different compositions, the quality indicators of their appearance, color, uniformity, abrasion, temperature resistance and colloidal stability were determined.

Quality indicators of lubricants prepared on hydrophilic and hydrophobic bases
Table 2

Quality indicator	Contents									
	I-T	II-T	III-T	IV-T	V-T	VI-T	VII-T	VIII-T	IX-T	X-T
Colour	Colorless	Colourless	Colourless, odorless	Colourless, odorless	Brown, black	Grey, black	Yellow	Yellow	White, colourless	White, colourless
Same mixing degree	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed	Same mixed
Rubbing	Easy	Easy	Easy	Easy	Difficult	Difficult	Easy	Easy	Difficult	Dificult
Temperature stability	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers	Did not separate into layers

Colloidal stagnation	Liquid	Normal	Normal	Liquid	Dark	Normal	Normal	Normal	Dark	Normal

№1,2,3,4,5,6,8,9,10 prepared hydrophilic and hydrophobic-based lubricants did not meet the regulatory requirements by changing their quality during storage. Tarkib7-digit content maintained good quality. [3,6,7]

3. RESULTS SECTION

Grease technology

Technology of preparation of the content meeting the requirements on the selected quality indicators.

In a clean room, we prepare all the necessary utensils and tools before preparing the grease. It is known that sodium hydroxide is an alkaline substance, and before working with it, it is necessary to observe technical safety. We put on our protective masks, then put on medical gloves and started our first work. Sodium hydroxide powder was accurately weighed on an analytical balance. Dissolve the sodium hydroxide in the flask with purified water and prepare an alkaline solution. Anhydrous lanolin and Vaseline were weighed on the scales. Carefully add three to four parts to the prepared alkaline solution of anhydrous lanolin (36-42°C), previously extracted and dissolved in a water bath. In a water bath, melt Vaseline (37-50°C) in a porcelain bowl and slowly pour over the lanolin mass, stirring until a distinctive crackling sound is formed and a uniform mass is formed. We prepared the prepared grease in a brown container and left it at room temperature for storage. [5,6,7,8]

4. ASSESSMENT AND MAINTENANCE OF GREASE QUALITY.

1. Evaluation of grease quality.

Grease technology also follows the rules of sanitation and hygiene, and is prepared in accordance with the requirements of the Ministry of Health of the Republic of Uzbekistan San-PiN №0152-04.

All greases are inspected on the basis of approved normative technical documents for qualitative and quantitative analysis. Greases are stored in dry, cool rooms with a humidity of 70% and a temperature of + 50°C.

Assess the appearance of the grease.

Yellow, odorless, dark, viscous, uniform mass.

Determining the color of the grease.

The color of the grease is determined by the unarmed eye. To do this, the test specimens are filled into 2 test tubes with the same thickness of glass walls and the same diameter of the test tube. The 1st solution is filled with grease prepared without sodium hydroxide solution and the 2nd solution is filled with grease prepared with sodium hydroxide solution (5.0 g). Their color is compared on a black and white background. The color of the grease is determined relative to the base color.

Determine the same mix.

To do this, the prepared grease is sampled from different parts and inspected with the naked eye. There should be no insoluble particles, no crumbly mixture. Such grease is considered to be uniformly mixed.

To do this, take 4 samples weighing 0.02 g. Pour 2 samples on a glass plate, cover with a second glass plate and glue the sample until it is 2 cm in diameter. The sample on the glass plates is then carefully observed with the unaided eye at a distance of 30 cm. 3 out of 4 samples did not contain visible particles. Thus, the prepared grease met the requirement for uniform mixing.

Determining the wear.

To do this, take a sample of the grease being tested using the thumb and index finger and rub it on the surface of the thumb of the left hand. The grease should be easy to apply to the skin without external pressure. [1,9]

Determination of temperature resistance.

To do this, check the stability of the grease at low and high temperatures. The grease is placed in the freezer (-16OC) for one day and then in the thermostat (40 ± 20C). In this case, the frozen grease and the grease that has been thawed for a day must be stable, ie not separated into layers.

Determination of colloidal stability.

To do this, the test grease is added to the TsLI-2 centrifuge solution and determined at a rate of 6000 rpm for 5 minutes. In this case, the greases should not separate into layers. Then the grease is considered colloidal stable.

Determination of pH

The pH of the grease was determined in pH meters. To do this, we took 1.0 g of the detected grease, dissolved it in 10.0 g of purified water in a water bath, cooled and measured in pH meters. The pH of the grease was 10.0.

Determination of the dispersion of the drug in the ointment.

0.05 g of grease is applied to a specially treated glassware and held in a water bath until the base melts. It is mixed dropwise with 0.1% water in solution III. Then the top is covered with a cover glass. Using a microscope with an ocular micrometer MOB-1 (15x eyepiece and 8x lens), the size of the particles inside the square is checked.

2. Development of a method of quantitative analysis of anti-wax grease.

Quantitative analysis of anti-wax grease was carried out by a simple "titration" method on sodium hydroxide. 2.06 g of net weight was placed in a 250 ml conical flask, filled with 50.0 ml of purified water and kept in a water bath to dissolve. Once the grease had melted, it was cooled to room temperature. To the solution was added 2-3 drops of indicator phenolphthalein and rubbed with 1.0 m of hydrochloric acid from pink to colorless. 2-3 drops of indicator metiorange were added to the shaken solution and re-titrated with 1.0 m of hydrochloric acid from yellow to red.

The amount of sodium hydroxide in the drug is calculated as a percentage by the following formula.

$$X = \frac{(V1 + V2) * T * K * 100}{a}$$

Here:

V is the volume of solution used to titrate the net, in milliliters;

T is the titration of the titrated solution;

K - coefficients;

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The exact weight of the sample to be tested, grams;

Results of quantitative analysis of sodium hydroxide grease

Table 3

	Exact drawer of the grease	The amount of sodium hydroxide in the grease, %	Metrological characteristics
1	2.06	3.786%	$\overline{X}$,%=3.775% f=4 S^2=0.00275 S=0.0524 $\Delta\overline{X}$ =3.864 $\overline{\varepsilon}$,%=1.728
2	2.10	3.714%	
3	2.03	3.842%	
4	2.09	3.732%	
5	2.05	3.804%	

3. Determination of rheological properties of grease

A Reotest-2 (Germany) instrument was used to determine the viscosity of the grease. To do this, place 20 ml of the sample in the coaxial cylinder cell (S / S1) of the instrument and determine the change in the internal friction of the grease under the influence of external forces. The effect of its density, temperature and concentration on the viscosity of greases was studied. Based on the results of the experiments, a curve of dependence on the speed class of the movement was drawn. (Figure 1)

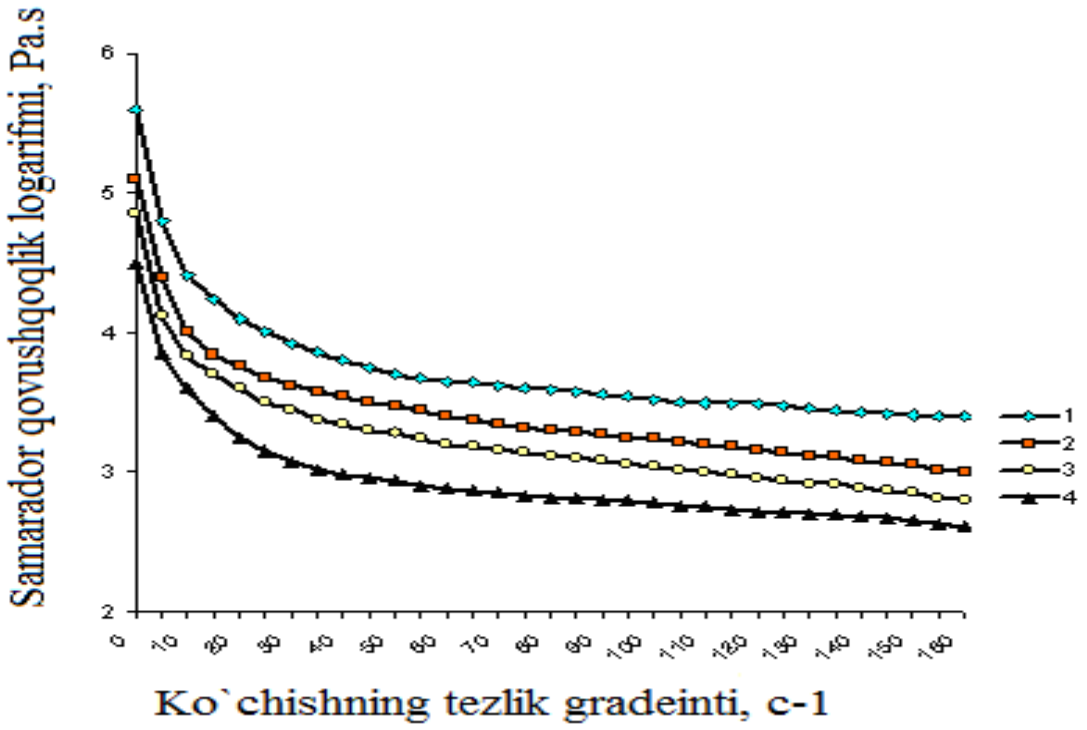

Figure 1. Dependence curve on the graph of the velocity gradient.

Dependence of the velocity gradient (γ) on the effective viscosity logarithm (***lnη***$_{эфф.}$)
At different temperatures
1 - t = 20 ^{o}C; 2 - t = 30 ^{o}C; 3 - t = 40 ^{o}C; 4 - t = 50 ^{o}C.

The effect of temperatures of 20C, 30C, 40C, 50C on the viscosity of the grease was studied. The results of the dynamic viscosity were as follows:

1 - $t = 20\ ^oC$; $\boldsymbol{ln\eta_{эфф.} = 5{,}6\eta_{20} = 270\ Па.с}$

2 - $t = 30\ ^oC$; $\boldsymbol{ln\eta_{эфф.} = 5{,}1\eta_{30} = 164\ Па.с}$

3 - $t = 40\ ^oC$; $\boldsymbol{ln\eta_{эфф.} = 4{,}8\eta_{40} = 127\ Па.с}$

4 - $t = 50\ ^oC$; $\boldsymbol{ln\eta_{эфф.} = 4{,}5\eta_{50} = 90\ Па.cO}$

According to the results of determining the rheological properties of the grease, the grease prepared on the selected basis is resistant to temperature changes during storage and transportation. [5,6]

3. In vitro study of bioavailability of ointments against warts

The therapeutic efficacy of drugs is determined by the processes of their absorption, distribution and excretion in the body, and the study of the effect of the separation of drugs from the drug form and the physicochemical properties of excipients. It is known that the degree of release of bioactive substances in highly effective drugs when introducing new drugs on a production scale determines the pharmacological and technological properties of the proposed drug. Not all pharmaceutical factors that affect the biological activity of the ointment (physicochemical state of the drug, modification, dosage form, technological process) do not affect the drug as important and complex as excipients. In the field of biopharmaceuticals, a great deal of attention is paid to excipients, and it is also considered as a science that studies the effect of excipients on the bioactivity of the drug. this type of drug is not prepared. Excipients used in the preparation of drugs in accordance with the doctrine of biopharmacy are not indifferent. To some extent, they affect the rate of separation and absorption of drugs from the drug.

In hydrophobic lubricants and creams, the right choice of base helps the active solvent to reach the destination faster and achieve long-term results. Today, much attention is paid to the relationship between the main active ingredients and excipients. Excipients must be technologically biologically inert. Products must be chemically and physically stable.

The separation of the active substance from the drug type is the first stage of the process. The type of ointment, the anatomy, physiology, properties and proportions of the active ingredients are of great importance in the separation of the drug substance. There are the following stages in the absorption of drugs, ie their transdermal transfer:

- Diffusion of the dissolved drug into the stratum corneum;
- Panetration (absorption) of the stratum corneum, successive transition to the lower layers of the epidermis, dermis and hypodermis;
- Transfer of the substance into blood vessels.

If the drug is soluble, its excretion is directly proportional to the previous dose.

$$\overline{Q=2\cdot C_0}\sqrt{(Dt)/n}\ ;$$

In hydrophobic lubricants (semi-solid preparations), the drug must dissolve on the basis of the substance before the onset of diffusion. Therefore, the release of the drug is very slow from the base (Higuchi's square root law).

$$\overline{Q=\sqrt{2\cdot C_0\cdot D\cdot C_S\cdot t}}$$

Hence, the amount of excreted drug Q is directly proportional to the square root of the total concentration of the drug C_0, its solubility C_s and its diffusion coefficient D.

The fact that the drug is slightly soluble in the base, the pH value, the high concentration of the drug after dissociation contributes to the release of the drug.

The involvement of excipients in the drug is especially noticeable in ointments. By controlling the shape of the drug type, the bases for greases can be included in the class of excipients.

Therefore, it is important to determine the release of the active substance from the base in vitro. When modeling the release of the active substance from the grease, it is necessary to diffuse the gel and use different membrane methods.

We compared the release of the drug in hydrophilic bases (MS) and hydrophobic bases (Vaseline and anhydrous lanolin). Our goal is to ensure the optimal bioavailability of the main bioactive substances that affect the therapeutic activity of drugs for the treatment of health diseases, as well as theoretical and experimental substantiation. Due to the relationship between the rate of dissolution of the drug and the rate of absorption of the drug, the determination of the rate of dissolution of the drug is one of the main methods for determining the effectiveness of the separation of the active substance from the drug. Biopharmaceutical comparative analysis of drugs, selection of their composition, setting standards for the addition of excipients in the development of drug preparation processes, ensures the production of drugs with high bioavailability. At the same time, various methods are used to determine the bioavailability of lubricants. The main of them is based on the diffusion of active substances. This not only draws conclusions about their effectiveness, but also allows the results of the applied method to be accepted as the norm. The determination of the dynamics of the release of bioactive substances in the grease was tested in vitro.

Greases for the treatment of skin diseases were obtained on the basis of hydrophilic (MS) and hydrophobic bases (Vaseline and anhydrous lanolin) and their bioavailability was determined by direct diffusion of agar. [10]

The essence of the method. This was done in the following order: initially 100 ml of 2% agar gel was prepared. To do this, add 2 g of agar to the container, pour 100 ml of purified water at room temperature and leave to suffocate for 30 minutes. Then boil for 1-2 minutes and make up to 100 ml with water. The cooled agar gel was mixed with phenolphthalein as an indicator and detected by two different detection methods: Petri dish and test tubes.

1. 2% agar gel was poured warmly into test tubes of the same diameter. It is then placed in the refrigerator for 10-15 minutes, then 2.0 g of the mass of grease on different bases is slightly softened to improve the interaction, and 2% of the test tube is placed on the agar gel.

2. 2% agar gel with a thickness of 3-5 mm was poured into a petri dish and after cooling, the same 8 mm groove was formed and the mass of grease from 2 g was slightly softened.

The diffusion rate of the bioactive substances in the sample of the lubricating ointment mass in the Petri dish was determined every 30 minutes by measuring the painted area on a millimeter scale. At the same time, the depth of absorption in the test tubes was measured in millimeters. The results of determining the time-dependent bioavailability of greases prepared on two different bases in a Petri dish and the depth of absorption in millimeter solutions are given in Table 4-5 and the kinetics of release of active substances from grease are shown in Figures 2-3 below [7, 8.10]

Results of the study of the direct diffusion of greases obtained on different bases (distribution)

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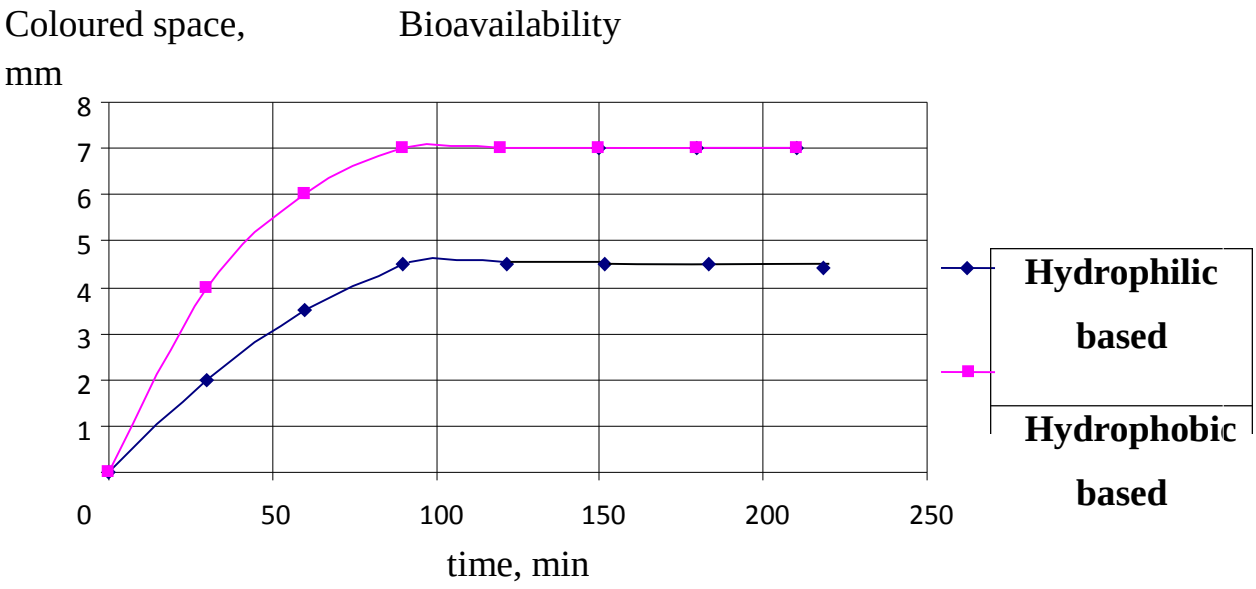
Table 4

Time (minute)	0	30	60	90	120	150	180	210
Hyrdrophobic based grease, mm	0	4	6	7	7	7	7	7
Hyrdrophilic based grease, mm	0	0	2	3,5	4,5	4,5	4,5	4,5

Figure-2. Kinetics of drug release from the composition of healing ointments prepared on hydrophilic and hydrophobic bases.

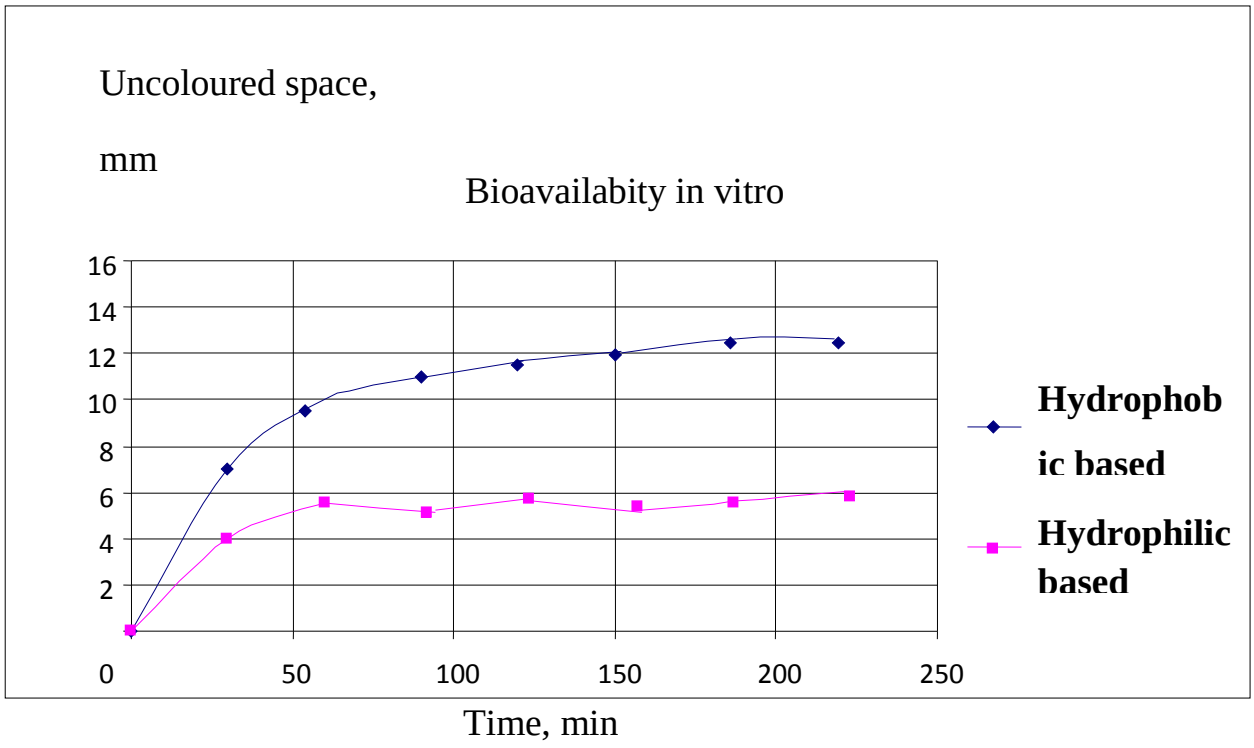


Results of the study of the direct diffusion of greases obtained on different bases (absorption)

Table 5

Time (minute)	30	60	90	120	150	180	210
Hyrdrophobic based grease, mm	2	4	6,5	8	9,5	10	12,5
Hyrdrophilic based grease, mm	1	2	2 ,5	4	4,5	5	5

Figure-3. Kinetics of drug release from the composition of healing ointments prepared on hydrophilic and hydrophobic bases. (absorption**)**



The diffusion coefficient (K) was calculated by the following equation:

$K = U / X$

Where: K is the diffusion coefficient

U- diffusion depth, mm

X- diffusion time, hours

When the results were summarized and analyzed, it was found that the release of the drug substance in hydrophobic-based lubricants is high.

5. CONCLUSION

The quality of lubricants was assessed and storage conditions were studied. Bioavailability of sodium hydroxide-containing ointments for the treatment of warts. The main effect of sodium hydroxide-containing ointments on the cross-distribution in petri dishes by the method of direct diffusion of agar-agar gel, the depth of absorption in millimeter solutions found to be highly excretory.

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