STUDY OF RHEOLOGICAL AND TEXTURAL PROPERTIES OF EMULSION OINTMENT BASES USING MODERN EMULSIFIERS

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Introduction

Dermatological diseases are not only a medical, but also a social problem, which significantly worsens the quality of life of people suffering from them.

Assessment of quality of life is important not only for determining the patient's current condition. It can influence the choice of treatment tactics. Improving the quality of life in many cases is the main goal of treatment. The quality of life of a sick person in modern times medicine is considered as an integral characteristic of its condition, consisting of physical, psychological and social components. Each of the components, in turn, includes a number of components, for example, physical - symptoms of the disease, the ability to perform physical work, the ability to self-care; psychological - anxiety, depression, hostile behavior; social - social support, work, public relations, etc. [1,2].

According to the American Academy of Dermatology, acne affects about 50 million Americans nationally and about 85 percent of people ages 12 to 24 worldwide.

The results of research by scientists of the National Psoriasis Foundation, psoriasis occurs in about 2-3% of the population, and more than half of patients suffer from diffuse psoriasis [3].

According to reports from the World Health Organization, eczema affects about 15–20% of children and 1–3% of adults worldwide. According to the American Academy of Dermatology, more than 5 million cases of skin cancer are diagnosed in the United States every year, of which more than 90% are related to exposure to ultraviolet radiation [4, 5].

These data show that dermatological diseases constitute a significant part of the medical problems in the world and emphasize the importance of timely diagnosis, prevention and treatment of these diseases [6].

Emulsion-based ointments are the most adapted to human skin medicinal form in extemporaneous practice. They have high therapeutic efficiency and satisfactory consumer properties due to the presence of two phases at once, are able to provide improved diffusion of active pharmaceutical ingredients (API), maintain optimal concentration in the area of application, have high adhesive properties, which allows them to be well distributed on the skin; provide close contact with tissues and high bioavailability of API, have an immediate or, if necessary, prolonged effect of the drug [7].

In view of the above, the development of new modern emulsion bases will make it possible to solve a number of urgent issues: to expand the range of effective extemporaneous MLF for use in dermatology, to individualize the approach to the patient and to ensure an increase in the quality of life of patients.

Based on the results of our own preliminary pharmacotechnological research, we selected samples with emulsifiers of the first kind: Olivem 1000 and Emulpharma 1000 [7] for the development of the emulsion base.

These emulsifiers are able to independently form stable emulsions with a light texture, which are well distributed on the surface of the skin, without leaving stains on clothes.

Crucial in choosing an emulsifier is the study of the rheological and textural properties of the ointment base, because it is these indicators that characterize the quality of the emulsion base, and the biopharmaceutical and consumer properties of MLF, the competitor's capacity of the medicinal product, largely depend on them [8, 9].

The purpose of this work was to analyze the texture of samples of emulsion ointment bases developed to replace petroleum jelly bases, which are traditionally used to make ointments in pharmacies. The composition of the bases was selected based on the results of previous studies [7].

Materials and methods

The following emulsifiers were chosen for the study: Olivem 1000 ® (INCI: Cetearyl Olivate, Sorbitan Olivat; Hallstar, Italy) and Emulpharma 1000 ® (INCI: Cetearyl alcohol, Glyceryl stearate, Sorbitan stearate, Cetearyl glucoside; Res Pharma, Italy). As oil, corn oil was chosen for the oil phase.

Steady shear behavior. Rheological studies were carried out on a BROOKFIELD HB DV-II PRO viscometer (USA) in the range of shear rates from $18.6 s^{-1}$ to $93 s^{-1}$ (SC4-21 spindle for a chamber with a volume of 8.3 ml) at a temperature of 25°C.

Textural properties. The tests were carried out using a TA-XT2 texturometer (Stable Micro Systems, UK) BackExtrusion Cell (A / BE) using a 5 g strain gauge. The inner diameter of the cup is 55 mm. The height of the cup and the pressure plate with a diameter of 70x45 mm. The data were entered into the Texture Expert Exceed program (Stable Micro Systems, UK) [10, 11]. During the test, the following parameters were evaluated: firmness, consistency, cohesiveness and index of viscosity. For this, the drugs were loaded into 125 ml containers. 55 mm in diameter. The height of the cup and the pressure plate with a diameter of 70 x 45 mm. In this test, firmness is obtained from the maximum value of the positive curve, consistency - from the area under the positive curve, cohesiveness - from the maximum value of the negative curve, and index of viscosity - from the area under the

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negative curve [3, 12]. The return distance used was 25 mm, the return speed was 10 mm/sec, and the contact force was 30 g. The data obtained from the negative curve were analyzed as absolute values (Fig. 1).

Table 1. Parameters of the testBackExtrusion Cell (A / BE)

Parameter	Data
Test mode and measurement options	**compressive/return forces**
Speed pre-test	**1.0 mm/ sec**
Test speed	**1.0 mm/ sec**
Speed post-test	**1.0 mm/ sec**
Distance	**5 mm**
Time	**25 sec**
Trigger type	**automatic**
Trigger strength	**100 g**
Speed of data collection	**200 pps**

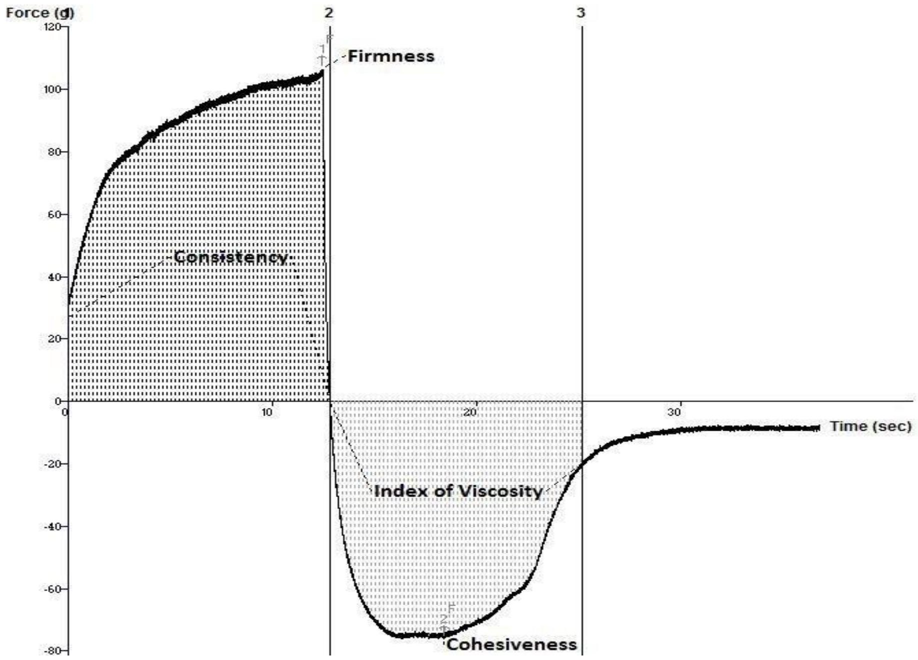

Fig. 1 Typical plot of texture analysis with plot of data and its interpretation

Results and discussion

There are many studies on changing the rheological properties of emulsion ointments and creams depending on the type and percentage of emulsifier.

Our rheological and textural research is devoted to the development of a universal emulsion base for use in extemporaneous practice.

In addition to fluidity and viscosity, an important parameter in the development was the evaluation of cohesive-adhesive properties of emulsion bases when using different emulsifiers from the point of view of physiological aspects of its use.

To determine the optimal formulation, we made model samples using the first-of-its-kind emulsifier Olivem 1000, which includes Cetearyl Olivate, Sorbitan Olivate, which forms a lamellar emulsion (liquid crystals), which provides a long-term moisturizing effect and gradual release of active substances, is quickly absorbed by the skin, without leaving a sticky greasy mark on it. And the emulsifier of the first kind Emulpharma 1000, which includes cetearyl alcohol, glyceryl srearate, sorbitan

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stearate, cetearyl glucoside, is a natural "PEG free" emulsifier that forms stable emulsions. Determination of flow curves and structural viscosity of the studied samples of emulsion bases was carried out in the range of shear rates from 18.6 to 93 s -1. The resulting base samples had a plastic flow type and were characterized by a significant hysteresis loop, that is, thixotropy, which is a feature of all types of emulsions. The rheogram of the studied foundations is presented in Figure 2.

Table 2. Composition of experimental samples of emulsion ointment

The name of the components	Quantitative content, % / number of samples	
	1	**2**
Corn oil	**10.0**	
Olevem 1000 (Cetearyl Olivate / Sorbitan Olivat)	**5.0**	
Emulpharma 1000 (Cetearyl alcohol, Glyceryl stearate, Sorbitan stearate, Cetearyl glucoside)		**6.0**
The water is purified	**up to 100.0**	

To evaluate the rheological parameters of the selected emulsion samples, we constructed rheograms that represent the dependence of the shear stress (τ) on the shear rate (Dr). The analysis was performed to compare two samples.

Rheological analysis was carried out in accordance with the requirements of the European Pharmacopoeia 8.0 (Ph.Eur.) using a rotary coaxial cylindrical viscometer at 25 °C in the range of cylinder rotation speed from 20 to 100 rpm.

The rheograms presented in fig. 3, showed the rheological similarity of the samples.

Data analysis shows that the use of the emulsifier Olivem 1000 5% and Emulpharma 1000 6% makes it possible to obtain a stable, practically unchanged structure of emulsion bases with high viscosity, which can be justified by the creation of surfactants (surfactants) of an ionic layer between the drops, which electrostatically repel each other. As a result, a system is formed that redistributes energy between elastic and viscous components in a viscoelastic medium. The obtained data make it possible to predict convenience during use, namely application and uniformity of distribution on the skin, which may indicate satisfactory consumer properties.

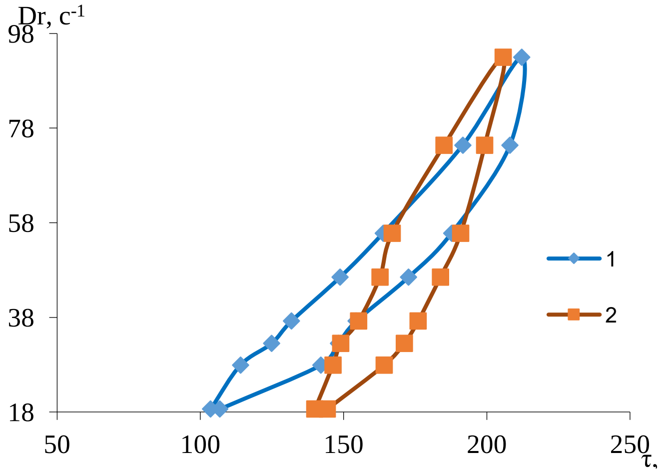

Fig. 2. Representative rheogram of the flow of emulsion samples (sample No. 1 Olivem 1000 5%, sample No. 2 Emulpharma 1000 6%)

Since the textural properties also affect the consumer characteristics of the emulsion ointment, as a result, the effectiveness of the therapy, one of the goals of this study was to study the textural properties of the investigated samples of the emulsion base. Research was conducted using Texture Analyzer.

Emulsion semi-solid dosage form should have a structure that will withstand all technological stages and not change the structure, be evenly applied and distributed over the entire surface of the skin, ensure close and stable contact with skin or mucous membrane tissues, maintain a balance between adhesiveness and cohesiveness [9].

Back extrusion analysis can help determine these properties. The results of the reverse extrusion test are presented at Fig.4 and in table. 3.

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The test was performed at a storage temperature of 25 °C and 32 °C, which correspond to the storage conditions and skin surface temperature.

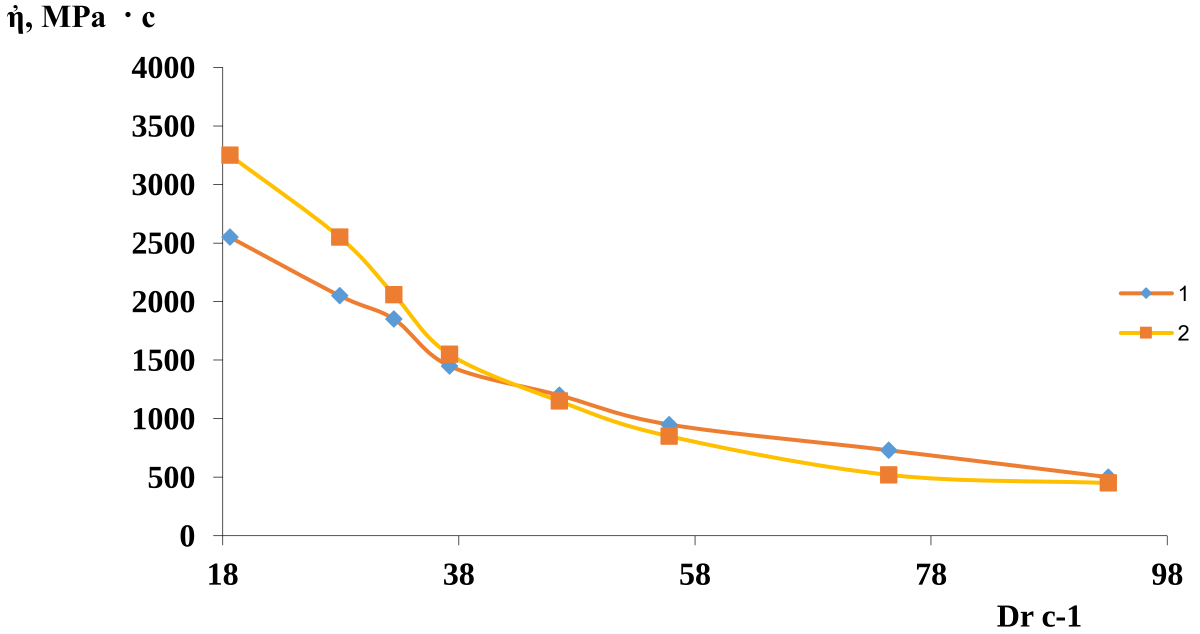
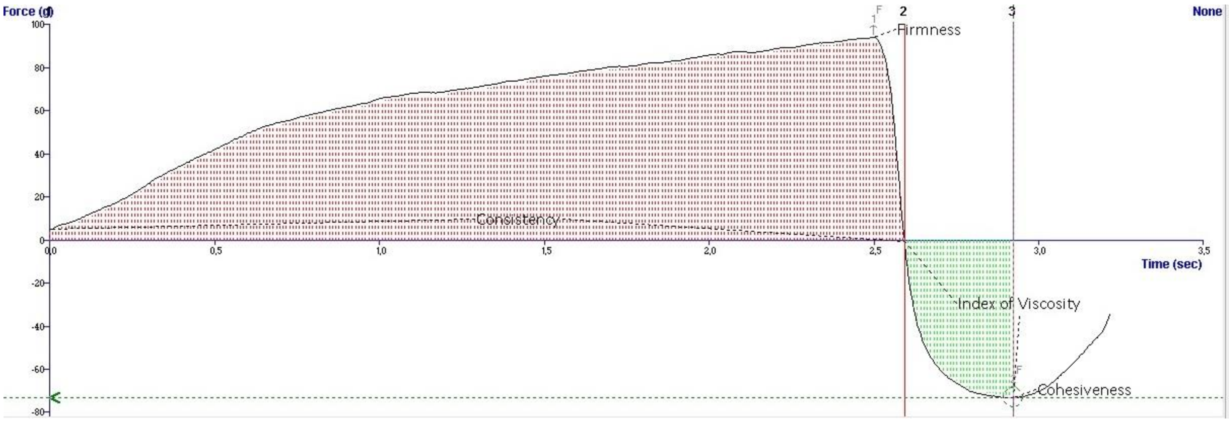


Fig. 3 Dependence of the structural viscosity of the model samples on the shear rate (Dr) at a temperature of 20 ° C

Sample



No. 1 (25 °C)

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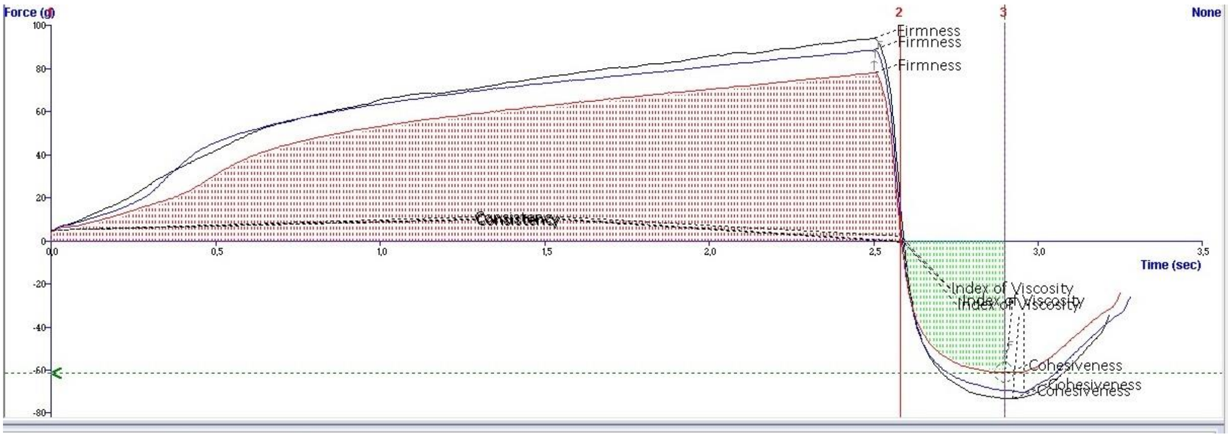
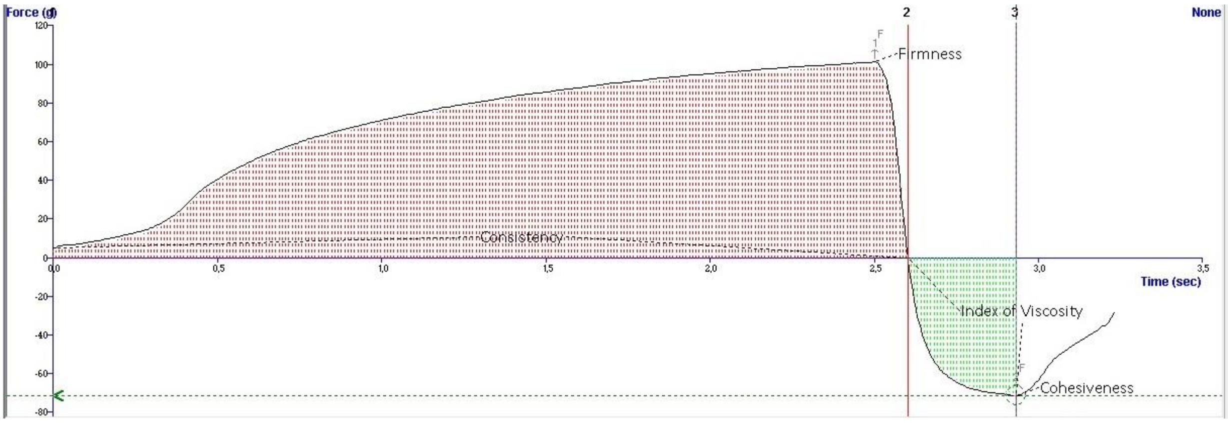
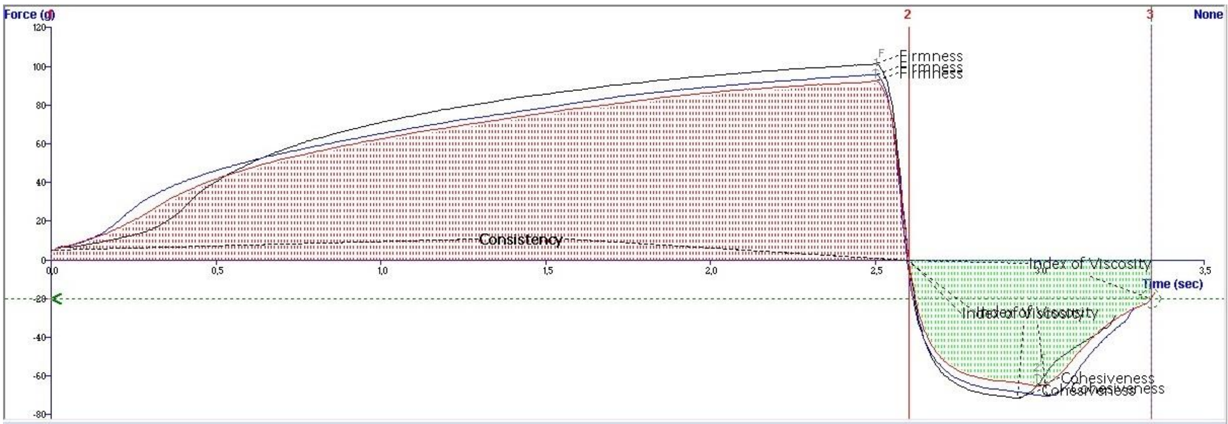


No. 1 (25 °C) (n=3)



No. 2 (25 °C)



No. 2 (25 °C) (n=3)

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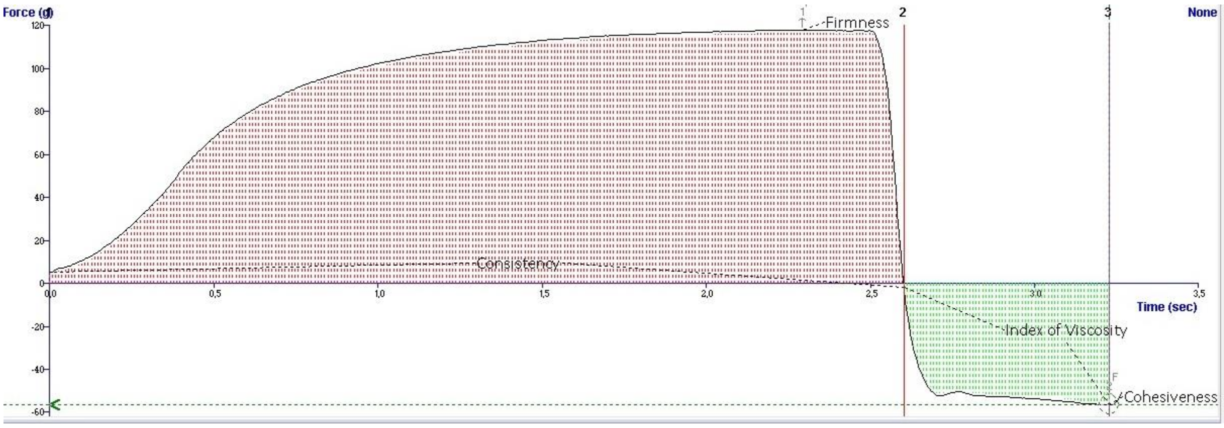
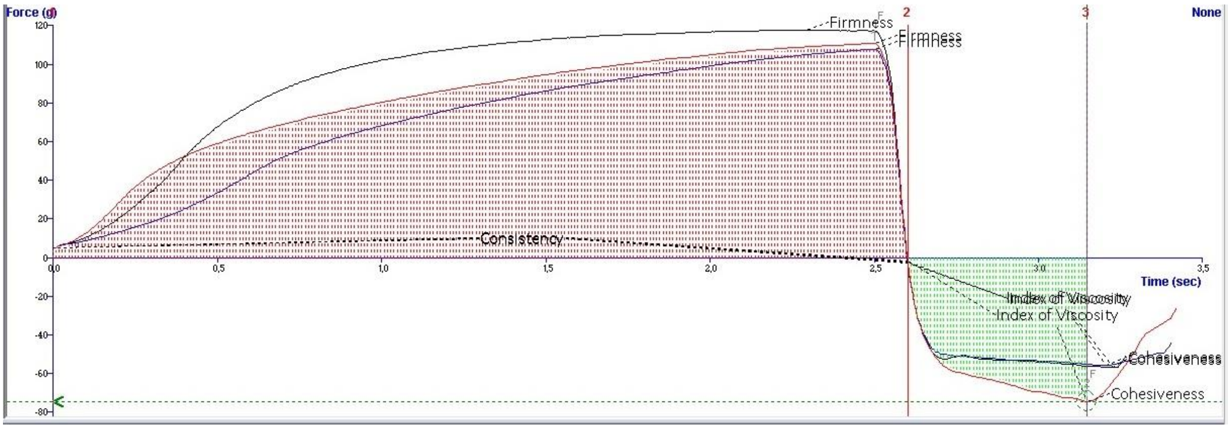
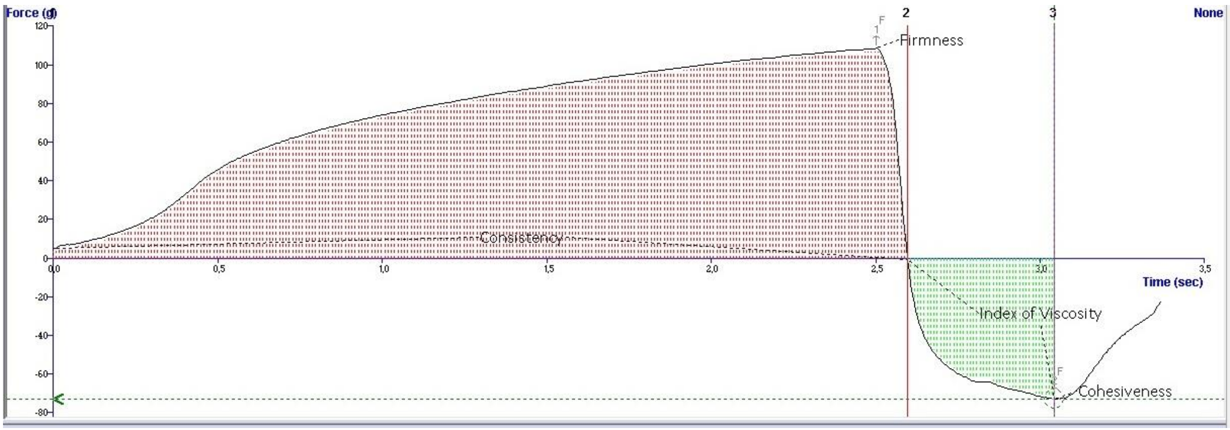


No. 1 (32 °C)



No. 1 (32 °C) (n=3)



No. 2 (32 °C)

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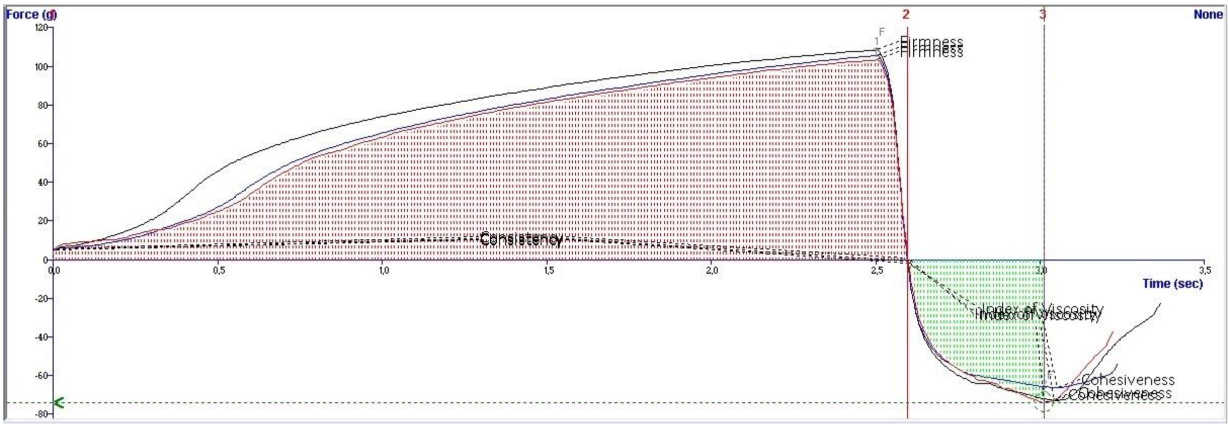

No. 2 (32 °C) (n=3)

Fig. 4. Force / time curves of the samples obtained by the test BackExtrusion Cell (A / BE).

Test results obtained from both of the two formulations (stored at 25 °C and tested at 25 °C and 32 °C) give the following typical mean maximum +ve force, mean +ve area, mean maximum -ve force and mean -ve area values. Analyzing the obtained data, it can be seen that the quantitative indicators differ slightly in terms of the ratio both within one sample when the temperature changes and between sample No. 1 (25 °C) and No. 1 (32 °C) in comparison with sample No. 1 (25 °C) and No. 1 (32 °C). Also, when the samples were measured three times, the value of the standard deviation was greater in sample No. 1 both at 25 and 32 °C. These data demonstrate that the emulsifier Emulpharma 1000 is more stable to mechanical and temperature effects on the emulsion system.

Table 3. Test results Back Extrusion Cell (A/BE)

Sample	Mean Max. +ve Force 'Firmness' (+/- SD) (g)	Mean +ve Area *'Consistency'* (+/- SD) (g/s)	Mean Max. -ve Force 'Cohesiveness' (+/- SD) (g)	Mean -ve Area *'Index of Viscosity'* (+/- SD)(g/s)
No. 1 (25 °C)	81.1 +/- 7.2	136.8 +/- 22.8	-10.4 +/- 5.6	-17.1+/- 3.9
No. 1 (32 °C)	112.5 +/- 5.04	209.7 +/- 28.99	-62.5 +/- 10.4	-31.69 +/- 1.4
No. 2 (25 °C)	96.9 +/- 4.5	172.9 +/- 7.2	-69.02 +/- 3.4	-26.4 +/- 8.2
No. 2 (32 °C)	106.3 +/- 2.6	177 +/- 11.6	-71.1 +/- 4.04	-24.8 +/- 1.5

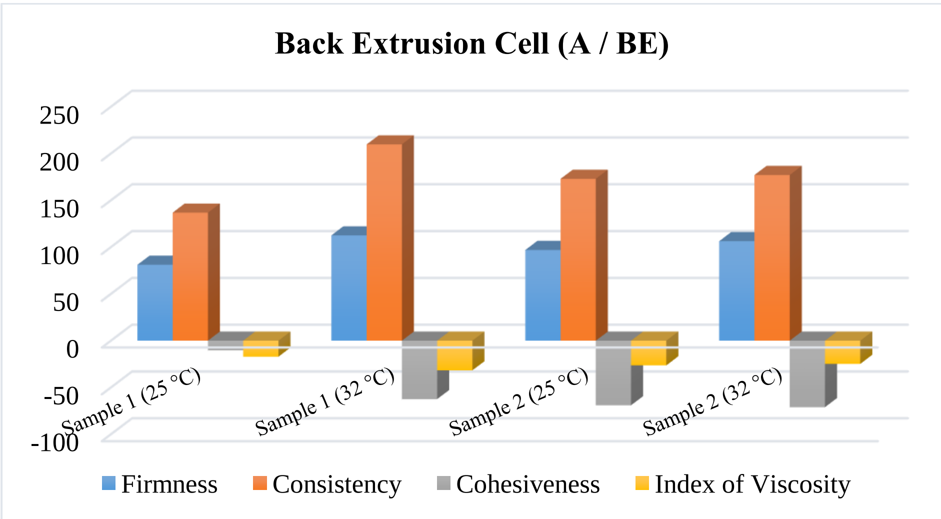

Fig. 5. Texture profile characterization of the formulations

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Conclusions

1. The effectiveness of topical emulsion semi-solid dosage form is related to their rheological and textural properties, which directly affect the outcome of therapy and the consumed properties of the drug.
2. Samples of emulsion bases using Olevem 1000 and Emulpharma 1000 emulsifiers showed visco-elastic, plastic behavior. The texture analysis revealed consistency properties (firmness, consistency, cohesiveness and index of viscosity).
3. The relationship between these parameters and their dependence on temperature changes and the type of emulsifier in the samples was established. Testing the texture of the bases showed a correlation with the rheological parameters.
4. The results of the study of the rheological and textural properties of the samples showed that the behavior of the developed emulsion bases did not change significantly, however, in the comparative analysis of all parameters and their standard deviation values, sample No. 2 using Emulpharma 1000 had more acceptable values.

Study of rheological and texture properties of emulsion ointment bases using modern emulsifiers

Zuikina Ye. V., Buryak M. V., Zuikina S. S.

Introduction. Dermatological diseases are not only a medical, but also a social problem, which significantly worsens the quality of life of people suffering from them. Emulsion-based ointments are the most adapted to human skin medicinal form in extemporaneous practice. They have high therapeutic efficiency and satisfactory consumer properties due to the presence of two phases at once, are able to provide improved diffusion of active pharmaceutical ingredients (API), maintain optimal concentration in the area of application, have high adhesive properties, which allows them to be well distributed on the skin; provide close contact with tissues and high bioavailability of API, have an immediate or, if necessary, prolonged effect of the drug. In view of the above, the development of new modern emulsion bases will make it possible to solve a number of urgent issues: to expand the range of effective extemporaneous MLF for use in dermatology, to individualize the approach to the patient and to ensure an increase in the quality of life of patients. **The purpose of this work** there was a textural analysis of samples of emulsion ointment bases, designed to replace the vaseline base, on which ointments are traditionally made in pharmacies. The composition of the foundations was chosen based on the results of previous research. **Materials and methods.** The following emulsifiers were chosen for the study: Olivem 1000 ® (Cetearyl Olivate / Sorbitan Olivat) (Hallstar) and Emulpharma 1000 (Cetearyl alcohol, Glyceryl stearate, Sorbitan stearate, Cetearyl glucoside). As oil, corn oil was chosen for the oil phase. Steady shear behavior. Rheological studies were performed on a BROOKFIELD HB DV-II PRO viscometer (USA). Textural properties. The tests were carried out using a TA-XT2 texturometer (Stable Micro Systems, UK) BackExtrusion Cell (A / BE). **Results and discussion.** Analyzing the obtained data, it can be seen that the quantitative indicators differ slightly in terms of the ratio both within one sample when the temperature changes and between sample No. 1 (25 °C) and No. 1 (32 °C) in comparison with sample No. 1 (25 °C) and No. 1 (32 °C). Also, when the samples were measured three times, the value of the standard deviation was greater in sample No. 1 both at 25 and 32 °C. These data demonstrate that the emulsifier Emulpharma 1000 is more stable to mechanical and temperature effects on the emulsion system. **Conclusion.** The results of the study of the rheological and textural properties of the samples showed that the behavior of the developed emulsion bases did not change significantly, however, in the comparative analysis of all parameters and their standard deviation values, sample No. 2 using Emulpharma 1000 had more acceptable values.

Keywords: texture, back extrusion, semi-solid dosage forms, emulsion.

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