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STUDY OF RHEOLOGICAL PROPERTIES OF REGENERATING OINTMENT MADE ON THE BASIS OF CHITOSAN

Abstract. *Secondary plant metabolites found in the organs of medicinal plants have therapeutic properties due to the presence of complex chemicals of various compositions. That is why, extensive microbiological studies of hibiscus flowers (Hibiscus Sabdariffa L.), clove buds (Syzygium aromaticum L.) and yarrow plants (Achillea millefolium L.) have been conducted and it has been found that the essential oils in these plants (eugenol, acetyl evgenol, cariophyllen etc.), flavonoid derivatives (rutin, quercetin, kaempferol, etc.), as well as various organic acids and vitamin-mineral compounds, have strong antimicrobial properties. Phytoextracts obtained from these plants in optimal proportions and by efficient technological methods have been proven to have a sufficient antibacterial and antifungal effect. It is considered expedient to prepare regenerating and anti-inflammatory ointments and creams on the basis of phytoextracts using various natural polymers that ensure the transport of drugs. [1, 2, 3].*

Keywords: *rheological properties, chitosan, regenerating ointment, Newtonian and non-Newtonian fluids, viscosity, Anton Paar-Rotational Rheometer:Rheolab QC, viscosity curve*

It is known that soft dosage forms (ointments, creams, gels, etc.) are dispersed systems with a viscous-plastic condition characterized by a non-Newtonian flow. Their viscosity varies non-linearly, depending on the shear rate gradient at a given temperature regime and shear stress. The study of their rheological properties has a great importance in the technology of ointments. Thus, the study of structural and mechanical parameters of ointments is a main indicator of their durability and stability. Exactly these indicators are considered to be effective and objective criteria

for quality control at the stage of technology, production, storage and use of soft dosage forms. Rheological properties play an important role in the easy release of medicine, the therapeutic efficacy of medicine, consumer requirements (tube compression process, ease of use, ease of spreading on the skin, etc.) and production (dispersion and packaging process) [7,8].

Today, combined medicines are among the leading pharmacotherapeutic agents, along with drugs used in the treatment of various infections, purulent-inflammatory wounds that require complex treatment. Based on this, the study of rheological properties is important for the reliability of any soft dosage form [12,13,14,15].

The purpose of the research. Preparation of an ointment based on natural polymer-chitosan and study of its rheological properties from an extract obtained by efficient extraction from natural raw materials.

Materials and methods. A sample of ointment based on phytoextracts with anti-inflammatory and antimicrobial properties was used in the teaching laboratory of the Department of Pharmaceutical Technology and Management of the Azerbaijan Medical University as the object of research. For this purpose, a colloidal solution of silver nanoparticles, liquid extract of clove, yarrow and hibiscus with , regenerative, anti-bacterial and anti-fungal effect, chitosan gel with nourishing and regenerating properties as an ointment base, as well as various plant oils (peach almond and linen) , emulsifiers (TVIN - 80, soy lecithin, etc.), stabilizers (citric salt solution, ascorbic acid solution) were used. In the laboratory, chitosan was extracted and inflated in 5% lemon salt solution. Peach oil was dispersed in an emulsifier in a colloidal silver solution and added to chitosan gel. After the plant extracts were weighed and added to the gel mass, the ointment sample was homogenized in a Stegler DG-360 homogenizer [4]. It was considered important to determine the static shear stress and viscosity of the ointment in accordance with the standard rules. For this purpose, the study of the rheological properties of the ointment was carried out in the research laboratory of the " Neftqazelmitədqiqatlayihə" Institute of SOCAR.

Equipment: The rheological properties of the ointment (viscosity, shear stress, shear rate gradient, etc.) were studied in the Anton-Paar Rotational Rheometer -

Rheolab QC (Germany made) device and the relevant indicators were recorded and the relevant results were obtained. The RheolabQC rotational rheometer can measure dynamic viscosity over a wide range from low-viscosity samples to semi-solid samples. The sample to be studied can be studied with the RheolabQC device, whether it is of ideal viscosity (Newtonian fluids) or sliding stress-generating (non-Newtonian fluids) type [5,6].

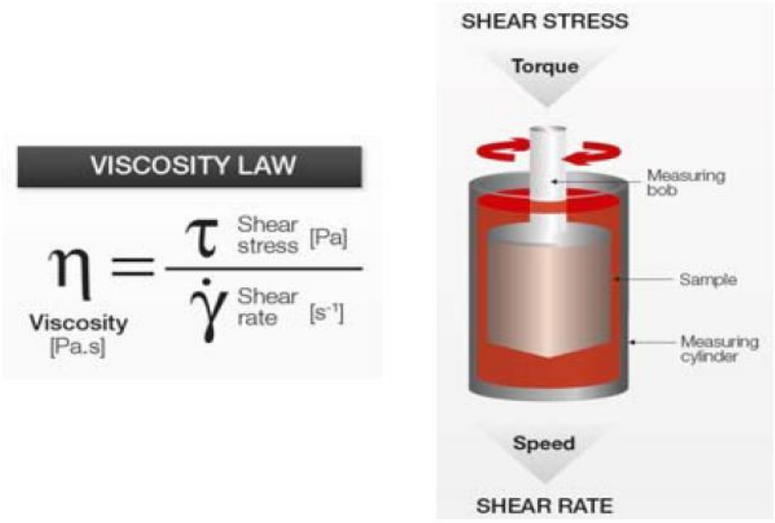


Fig. 1. **Viscosity law and model of the principle of operation of the device RheolabQC**



Fig. 2. **Measuring vessel and cylinder (CC39)**

The flow and viscosity graphs obtained from the rheometer tests are described as shown in the figure below.

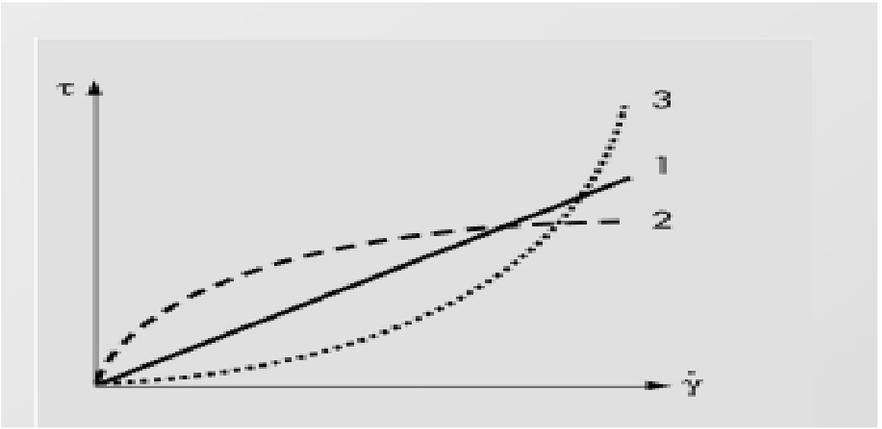


Fig. 3. **Flow curves**

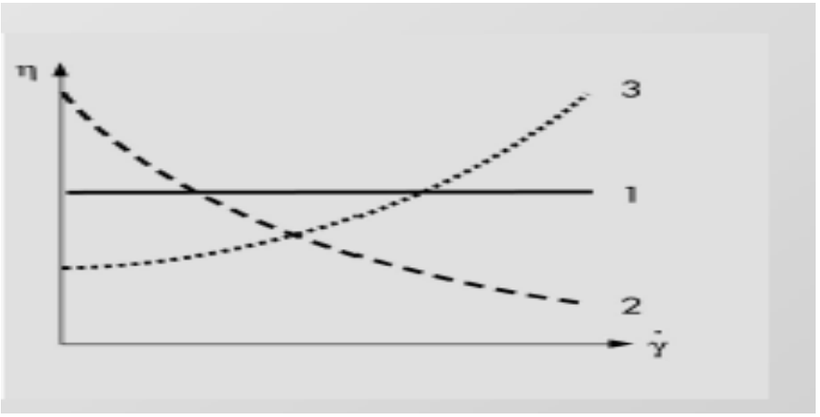


Fig. 4. **Viscosity curves**

1) Fluids with ideal viscosity (Newtonian)

2) Fluids whose viscosity decreases with increasing shear stress (pseudoplastic)

3) Fluids that thicken viscosity as the shear stress increases (dilatant)

Analysis conditions: The sample of ointment is added to the cylinder of the device in Figure 2 in such a way that it does not exceed the measuring line. The volume of the measuring vessel is 56 ml. One of the important points to pay attention to in the researches to be carried out in the rotational rheometer is to maintain the stability of the quantity and viscosity of the substances in the measuring vessel. The rheological properties of the ointment sample in three temperature regimes were studied in Antor Paar (Germany) Rotational viscometer and the curves were constructed. The studies were conducted at 20 ^{0}C, 40 ^{0}C, 60 ^{0}C in 10 different modes, and the results are presented appropriatively in tables and figures [9,10,11].

Results and discussion. Initially, the ointment sample was examined at 20 °C at 10 different time intervals. According to preliminary data, the viscosity of the ointment decreases with increasing velocity gradient in the studied sample. The results of the study are presented in detail in Table 1.

Table № 1

Description of the results obtained in the experiment at 20 ^{0}C

	I	II	III	IV	V	VI	VII	VIII	IX	X
η (Pas•s)	429.5	412.8	395.4	378.1	361.70	340.60	323.40	308.7	296.3	284.9
t (sec.)	30	60	90	120	150	180	210	240	270	300
τ (Pa)	53.65	69.32	85.25	100.03	116.53	131.69	145.85	159.16	171.85	183.55
Ɣ (s^{-1})	64.44	128.87	193.31	257.75	322.19	386.62	451.06	515.50	579.94	644.37

The ointment sample then was examined similarly at 40 °C at 10 different time intervals. These indicators also prove that the viscosity of the sample decreases by the time. The process is a reversible process. The results are presented appropriatively in Table 2.

Table № 2

Description of the results obtained in the experiment at 40 ^{0}C

	I	II	III	IV	V	VI	VII	VIII	IX	X
η (Pas•s)	341.49	303.4	278.8	260.8	246.6	234.8	224.9	216.8	209.9	203.5
t (sec.)	30	60	90	120	150	180	210	240	270	300
τ (Pa)	22.03	39.11	53.90	67.22	79.45	90.77	101.42	111.74	121.71	131.14
Ɣ (s^{-1})	64.44	128.87	193.31	257.75	322.19	386.62	451.06	515.5	579.94	644.37

In the end, the ointment sample was examined in the same manner at a temperature of 60 0C for 10 different time intervals. According to other indicators, this time the rheological behavior of the sample changes depending on the time of deformation. That is, the shear rate and viscosity are inversely proportional to time. The results of this study are shown in Table 3.

Table № 3

Description of the results obtained in the experiment at 60 ^{0}C

	I	II	III	IV	V	VI	VII	VIII	IX	X
η (Pas•s)	197.5	180.8	169.2	160.7	154.80	149.80	145.40	141.40	137.9	134.5
t (sec.)	30	60	90	120	150	180	210	240	270	300
τ (Pa)	12.72	23.31	32.70	41.41	49.86	57.9	65.59	72.87	79.98	86.68
Ɣ (s^{-1})	64.44	128.87	193.31	257.75	322.19	386.62	451.06	515.50	579.94	644.37

Based on the obtained results, curves were constructed accordingly. The curve of dependence of the static shear stress from the shear rate in the sample of the studied ointment is shown in Figure 5.

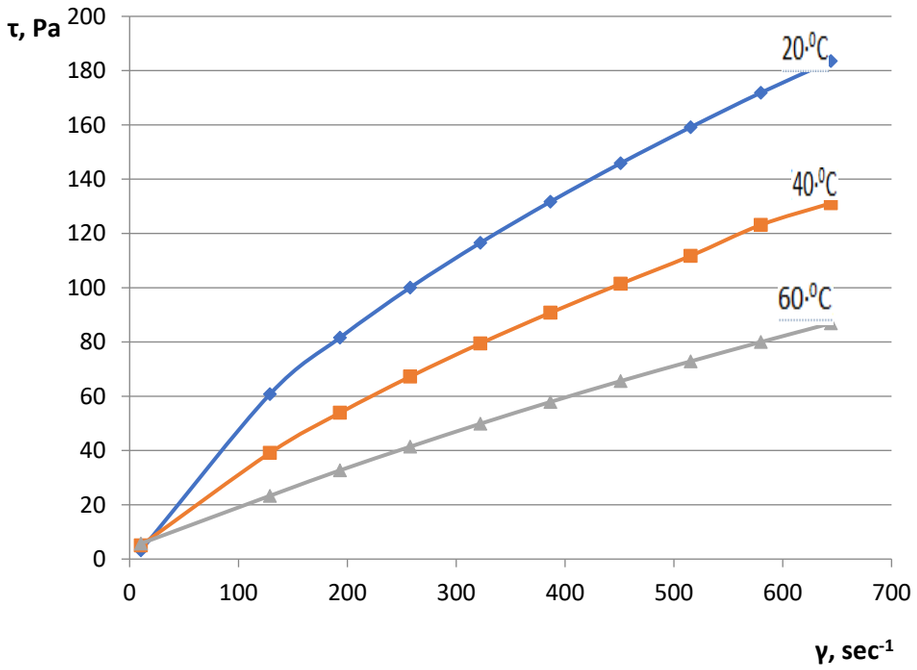


Fig. 5. **Dependence of static shear stress from the shear rate**

As can be seen from the curves, the sample of the ointment is non-Newtonian. It is a time-independent fluid on rheological characteristics. It is a pseudoplastic.. The motion of such fluids is expressed by the Shvedov-Bingham equation:

$$\tau = \tau_0 + \mu \gamma$$

Here: γ-shear rate gadient; μ –viscosity; τ_0- is the starting or static shear stress.

The viscosity of the ointment sample was also studied at 20 ^{0}C, 40 ^{0}C, 60 ^{0}C at 10 different time intervals and it was found that the value of viscosity decreases significantly as the shear rate gradient and its duration of action increase. The results are summarized in Figure 6 according to the temperature regimes.

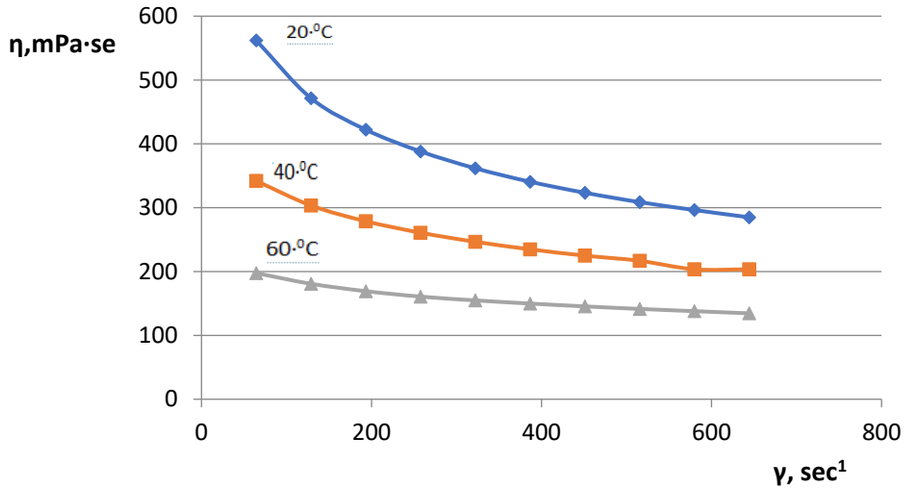


Fig. 6. **Dependence of viscosity from the shear rate gradient**

Conclusion.

The rheological properties of the ointment prepared from the extract obtained by efficient extraction on the basis of natural raw materials were studied at different temperature regimes. The structural-mechanical activity of the ointment was determined by the Anton-Paar Rheolab QC rotary rheometer. It turned out that the studied ointment has a non-Newtonian characteristic and a pseudoplastic flow. The ointment also showed a homogeneous rheological flow. Based on research, it can be said that the sample of the ointment fully meets the standards from a rheological point of view. Thus, the soft consistency of the ointment facilitates its extrusion ability (easy removal from the tube) and its application to the skin surface. The viscosity of the ointment can be considered satisfactory.

Reference:

1. 1.Məmmədov B.S. “Regenerasiya prosesini stimullaşdıran fitokompozisiyanın optimal tərkibinin seçilməsi.” “Sağlamlıq” jurnalı №2/2021, Səh. 175-180
2. Məmmədov B.S., Mehralıyeva S.C. “Regenerativ fitoekstraktların alınması və onların

mikrobioloji xüsusiyyətlərinin öyrənilməsi.” “Azərbaycan təbabətinin müasir nailiyyətləri” jurnalı №2/2020 Səh. 77-83

3. B.S.Mammadov, S.C.Mehraliyeva “Acquisition of regenerative phytoextracts and their study of microbiological properties” PS-001 “Uluslararası Bioteknoloji Kongresi”, İstanbul, 5-7 Mart 2020.
4. B.Mammadov, S.Mehraliyeva, T.Suleymanova “Microbiological study of ointments based on silver nanoparticle and phyto extracts” Uluslararası Türkiye Biyo-teknoloji Kongres 5 - 7 Mart 2020, səh.2-3. Osmanlı Arşivi Külliyesi Kongre Merkezi İstanbul
5. G. Geçim “Newtonian ve Newtonian Olmayan Akışkanların Viskozitesinin Belirlenmesi (Rotasyonel Reometre)” Bursa Teknik Üniversitesi DBMMF Kimya Mühendisliği Bölümü, KBM0308 Kimya Mühendisliği Laboratuvarı I
6. T.Ivko, V.Hrytsenko, L.Kienko etc. “Investigation of the Rheological Properties of Ointment Bases as a Justification of the Ointment Composition for Herpes Treatment” Published online 2021 Oct 28. doi: 10.4274/tjps.galenos.2021.93457
7. O.A. Kolpakova, N.V. Kuchrenko, H.P. Kukhtenko “Research Of Rheological Properties Of Ointment With Water- Soluble Protein-Polysaccharide Complex Of Oyster Mushroom” J. Pharm. Sci. & Res. Vol. 11(5), 2019, 1880-1883
8. B.Ahmad , F.Shireen , A. Rauf “Phyto-fabrication, purification, characterisation, optimisation, and biological competence of nano-silver”. 2021 Feb;15(1):1-18. doi: 10.1049/nbt2.12007. Epub 2021 Feb 2.
9. O.A.Zdoryk, K.O.Khokhlova, V.A.Georgiyants, L.I.Vyshnevska “Investigation of physical and chemical stability of ointment with herbals” Int J Pharm Compd. May-Jun 2014;18(3):248-52.
10. B.Szulc-Musioł, B.Dolińska, J.Kołodziejska , F.Ryszka “Influence of plasma on the physical properties of ointments with quercetin” 2017 Dec 20;67(4):569-578. doi: 10.1515/acph-2017-0038.
11. L.Pu, P.Xu, M.Xu etc. “Effect of Fiber on Rheological Properties and Flow Behavior of Polymer Completion Fluids” 2021 Jul 1;6(27):1713617148. doi:10.1021/acsomega. 0c05346.eCollection 2021 Jul 13.
12. R.Hsissou, A.Bekhta, O.Dagdag etc. “Rheological properties of composite polymers and hybrid nanocomposites” 2020Jun13;6(6):e04187. doi:10.1016/j.heliyon.2020.e04187.e Collection 2020 Jun.
13. http://www/rheologyschool.com/advice/rheology-tips/36-rheology-of-creams-ointments-and- lotions
14. http://wiki.anton-paar.com/en/basics-of-rheology/rheology-in-use/
15. https://www.rheosense.com/applications/viscosity/newtonian-non-newtonian