Study Of The Rheological Properties Of Soft Drug Forms Based On Dry Extracts Of Curcuma Longa L., And Ferula Asafetida L.

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ABSTRACT
Objectives:** **There have been taken rheological indices of the ointment and gel containing dry extracts obtained from Curcuma Longa L. and Ferula asafetida L.
Materials and Methods: According to rheological indices are one of the main quality normative of the ointment and gel, there have been studied their elasticity, viscosity and plasticity properties. There have been conducted experiments on the instrument Rheotest-2 (Germany) by using cell system "cylinder-cylinder" S/S_1 (cell constant z=5,6) at the temperature 25 ^{o} C, 40 ^{o} C, 55 ^{o} C.
Results: According to the results of the researches, there have been determined that viscous stream activity energy of the ointment is 26,6 kJ / mol, viscous stream activity energy of the gel is 23,3 kJ / mol, and it is coincided with viscous stream activity energy level of the ointments and gels.
Conclusion: There has been decided to consider that these contents are perspective according to the rheological properties of the suggested ointments and gels.

Keywords: Curcuma Longa L., Ferula asafetida L., ointment, gel, rheological research, effective viscosity, activation energy of viscose, mechanical stability.

1. INTRODUCTION

There has been considered, that it is important not only increasing concentration for achieving a high therapeutic effect, but it is important the optimal content and correct combinating medicinal substances.
The dry extract of the medicinal plant Curcuma (*Curcuma Longa L.*) has anti-inflammatory and anesthetic effects and it is used for treating such widespread diseases like arthritis, osteoarthritis and others[1,8]. According to these properties it is considered as a perspective raw material. The main active substances of the medicinal plant Curcuma (*Curcuma Longa L.*)

are curcumin, demetoxicurcumin, bismetoxicurcumin, and they are used for inhibiting effect of the inflammable neutrophils, and they are also used for decreasing inflammation in the joints[2,4,7,10].

There have been prepared powders for oral taking and decoctions from roots and fruits of the medicinal plant Ferula (*Ferula asafetida L.*)[5]. Decoctions, obtained from roots, leaves and fruits are used for bandaging to the skin[9]. Its resin is used for treating asthma, convulsions and as sedative in the scientific medicine[6]. It is also used for removing helminthes in the folk medicine[11].

The main quality indices of the semisolid medicinal forms for local application are elasticity, effective viscosity, plasticity, activation energy of viscose, mechanical stability and these indices determine their consistency and the level of their application to the skin.

According to given above information there has been studied the rheological properties of the ointment and gel obtained from roots and rhizomes of *Curcuma Longa L.* and *Ferula asafetida L.* by the modern circulation method developed on the base of dry extracts technology[3].

2. MATERIALS AND METHODS

There have been conducted experiments on the instrument Rheotest-2 (Germany) by using cell system “cylinder-cylinder” S/S_1 (cell constant z=5,6) at the temperature 25 ^oC, 40 ^oC, 55 ^oC. Determination of the viscosity of non-Newtonian fluids under simulated conditions determines the conditions of use and storage of lubricants. Since the proposed grease is a non-Newtonian fluid, its main indicator hysteresis effect was studied.

The determined effective viscosity values of the grease as a result of the studies are given in Table 1.

Table 1

t = 25 ^oC

№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff},*, Pa.c	$\ln\eta_{eff}$., Pa.c	$\ln\eta_{eff}$.*, Pa.c
1a	8	7	44,8	39,2	3	14,93	13,07	2,68	2,67
2a	10	9	56,0	50,4	5,4	10,37	9,33	2,28	2,24
3a	12	11	67,2	61,6	9	7,47	6,84	2,15	1,92
4a	16	15	89,6	84,0	16,2	5,53	5,19	1,71	1,73
5a	21	20	117,6	112,0	27	4,36	4,15	1,47	1,42
6a	28	26	156,8	145,6	48,6	3,23	2,99	1,17	1,09
7a	38	36	212,8	201,6	81	2,63	2,49	0,97	0,91
8a	52	49	291,2	274,4	145,8	1,99	1,88	0,69	0,63
9a	68	63	380,8	352,8	243	1,57	1,45	0,45	0,37
10a	90	89,	503,1	497,7	437,4	1,15	1,14	0,14	0,13

t = 40 ^oC

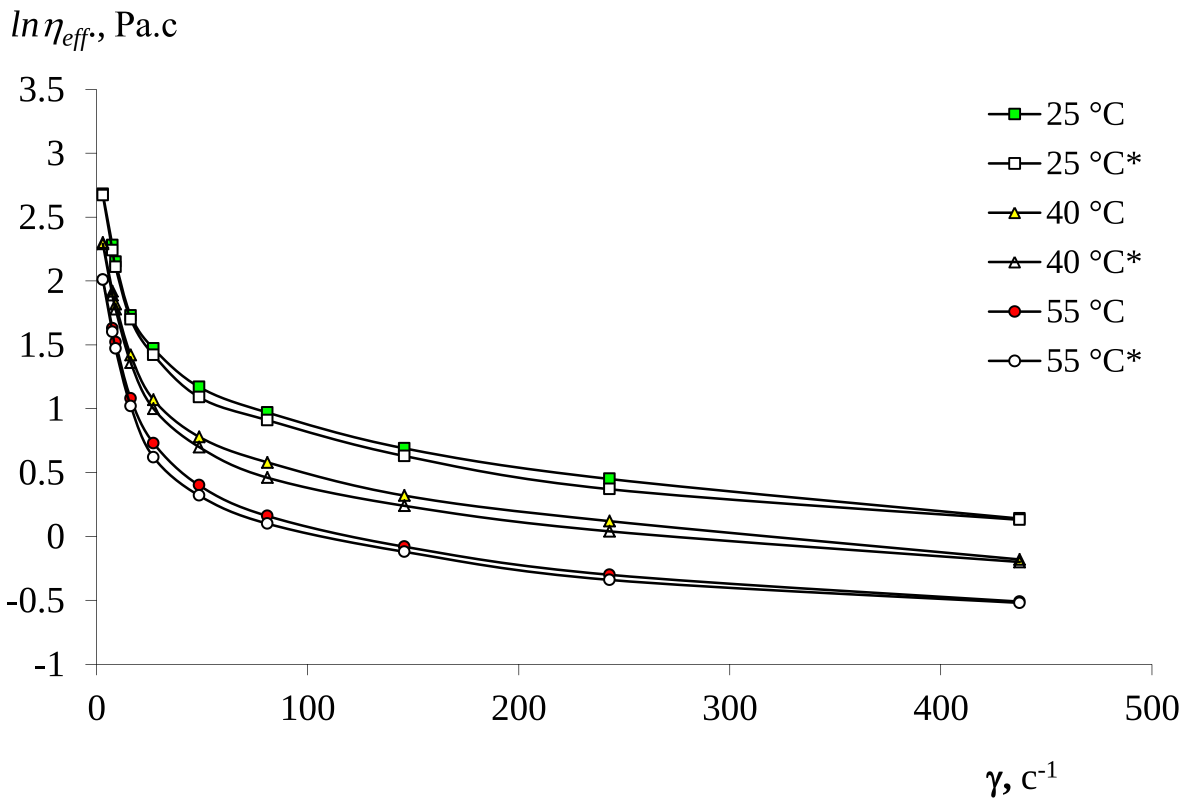
№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff},*, Pa.c	$\ln\eta_{eff}$., Pa.c	$\ln\eta_{eff}$.*, Pa.c
1a	5	7	28	39,2	3	9,33	13,06	2,32	2,29
2a	8	6	44,8	33,6	5,4	8,29	6,22	2,92	1,89
3a	10	7	56,0	39,2	9	6,22	4,36	1.82	1,78

4a	12	9	67,2	50,4	16,2	4,15	3,11	1,42	1,36
5a	14	18	78,4	100,8	27	2,90	3,73	1,07	1,02
6a	19	23	106,4	128,8	48,6	2,19	2,65	0,78	0,71
7a	26	23	145,6	128,8	81	1,79	1,59	0,58	0,46
8a	37	33	207,2	184,8	145,8	1,42	1,27	0,32	0,24
9a	59	45	330,4	252	243	1,36	1,04	0,12	0,04
10a	69	64	386,4	358,4	437,4	0,88	0,82	-0,16	-0,20

$t = 55\ ^{o}$C

№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff},* Pa.c	$\ln\eta_{eff}$., Pa.c	$\ln\eta_{eff.}$*, Pa.c
1a	4	4	22,4	22,4	3	7,47	7,47	2,01	2,01
2a	5	4	28,0	22,4	5,4	5,19	4,15	1,65	1,61
3a	6	5	33,6	28,0	9	3,73	3,11	1,52	1,47
4a	8	7	44,8	39,2	16,2	2,77	2,42	1,08	0,02
5a	10	9	56	50,4	27	2,07	1,87	0,73	0,62
6a	12	12	67,2	67,2	48,6	1,38	1,38	0,39	0,32
7a	17	16	95,2	89,6	81	1,18	1,11	0,16	0,10
8a	24	24	134,4	134,4	145,8	0,92	0,92	-0,08	-0,12
9a	32	32	179,2	178,2	243	0,74	0,74	-0,30	-0,34
10a	47	47	263,2	263,2	437,4	0,60	0,60	-0,51	-0,52

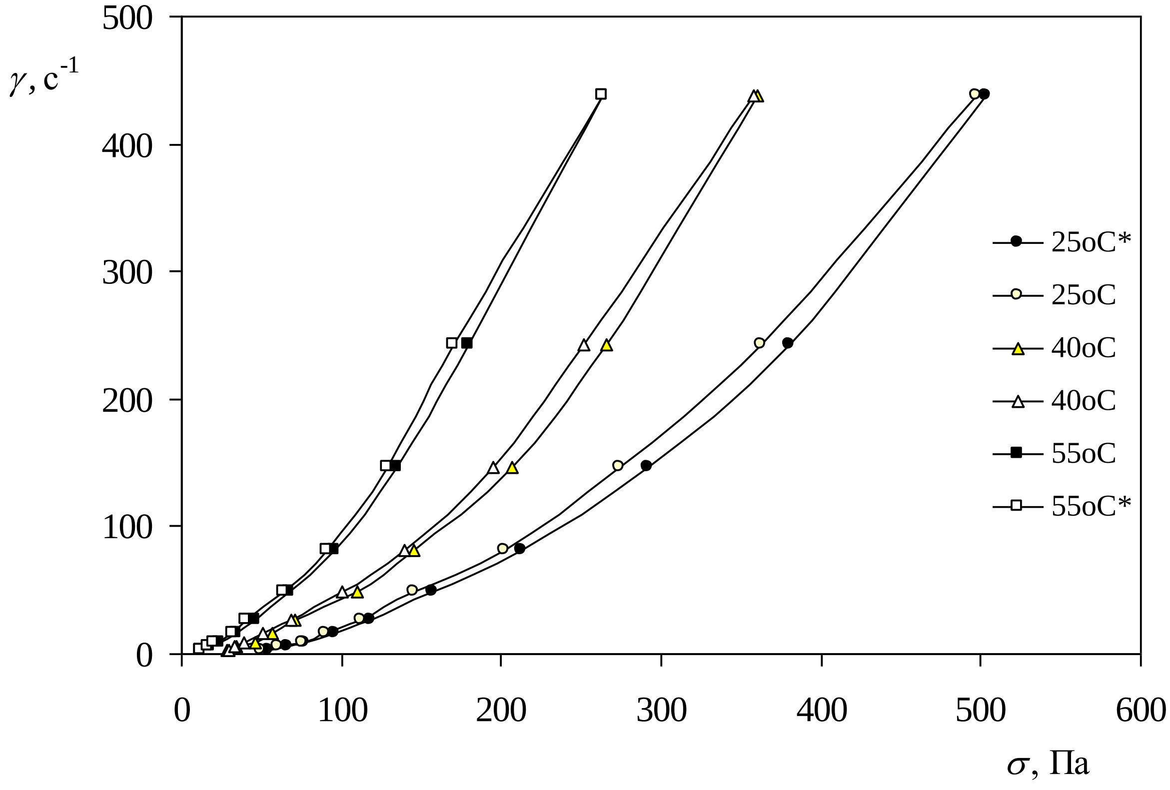
On the base of obtained results there have been made rheogrammes of the effective viscosity *($\ln\eta_{eff.}$)* according to the velocity gradient (γ) at the different temperatures 25 ^{o}C, 40 ^{o}C, 55 ^{o}C, given in the picture 2.



Picture2. Logarithm dependence of the effective viscosity ($ln\square_{eff.}$) **on the velocity gradient (*γ*) of the displacement stream for the ointment at the different temperatures:**
Here 25 °C, 40 °C, 55 °C at the direct measuring (at increasing *γ*),
25 °C*, 40 °C*, 55 °C* at the reverse measuring (at decreasing *γ*).

It is indicated, in all cases of increasing influence of the displacement field, that is with the increasing velocity gradient there has been observed non-rectilinear decreasing $ln\eta_{eff}$, moreover, there has been occurred perceptible rapid decreasing to achieve $\gamma \to 60$ c^{-1}, then moderate slow decreasing $ln\eta_{eff}$ to $\gamma \to 500$ c^{-1}. In this case there has been observed essential influence of the temperature to the viscosity (that is to the fluidity) of the gel and with the increasing temperature the rheogramme shifts to the area of the small meanings $ln\eta_{eff.}$ and large meanings *γ*.

There has been revealed that curved dependences that is rheogrammes perceptibly differ according to the effective viscosity indices $ln\eta_{eff.}$ at the direct measuring (at increasing meaning *γ*) and reverse measuring (at decreasing meaning *γ*) its meanings in the displacement field. It is particularly vivid shown in the interval $\gamma = 40 – 400$ c^{-1} in order to slight hysteresis effect. It is testified to structuring, perceptible deformative-regulated structure-forming gel at the influence of the displacement field in the chosen temperature area. For analyzing presence of the hysteresis effect there have been made rheogrammes in the form of the velocity gradient dependence (γ) from the displacement tension (τ) for gel at the different temperatures (picture 2).



Picture 2. Velocity gradient dependence (*γ*□) from the displacement tension (□) for the gel.

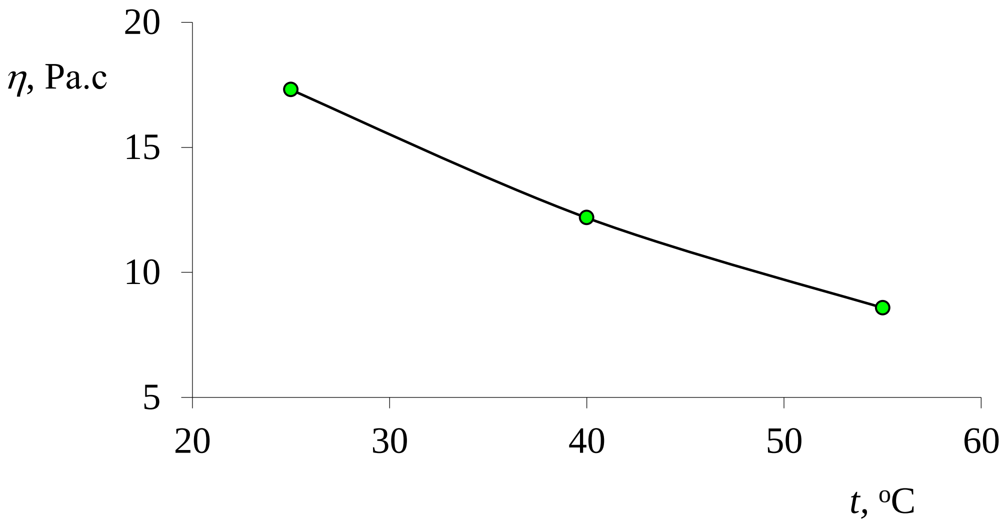
It is also indicated the vivid manifestation of the hysteresis effect at the temperatures 25 °C, 40 °C, 55°C, which confirms the structural changes in the gel in the field of the gradient

velocity 40 – 400 c^{-1}. It apparently occurs perceptible rapid destroying structure of the gel in the field of the gradient velocity and temperature.
In the chart of the picture 2 there have been determined quantities of the limit displacement tension ($□_{limit}$) and a limit flowing tension ($□_k$) and there have been calculated meanings of the mechanical stability MS= $□_k / □_{np}$ at the different temperatures (t, ^oC).

t, ^oC	$□_{limit}$, Pa	$□_k$, Pa	*MS*
25	52	100	1,92
40	28,6	50	1,75
55	12,4	20	1,61

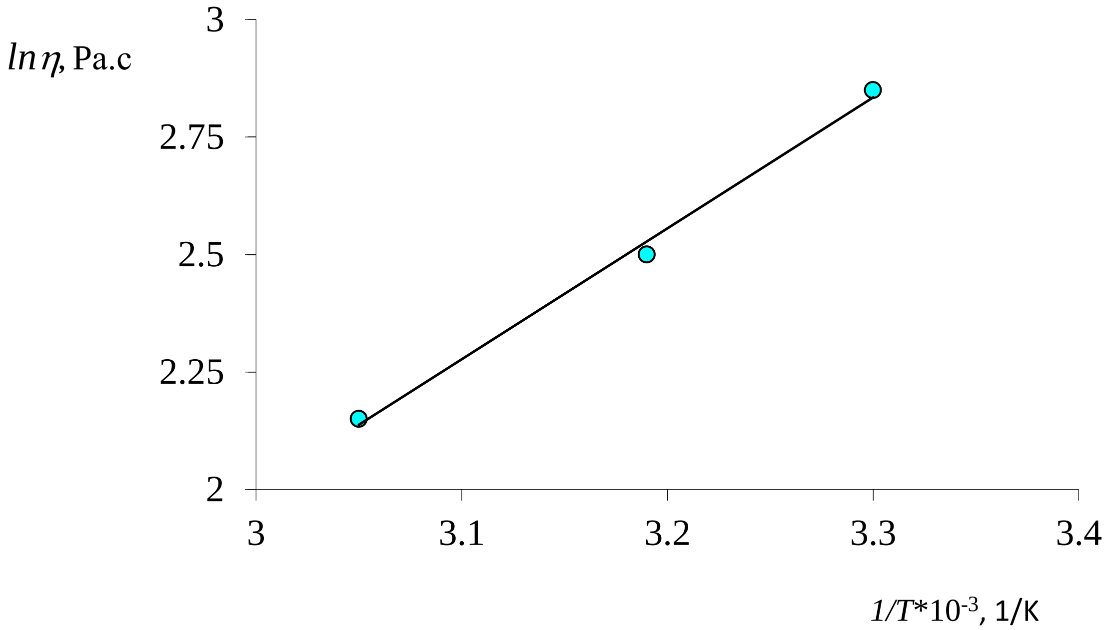
There have been determined meanings of the dynamic viscosity (□) in the picture 1 by conducting extrapolation $\gamma \rightarrow 0$ on condition, that $ln\eta_{eff.} \rightarrow ln□$.

$ln□$ = 2,85 Pa.c. □ = 17,30 Pa.c. at 25 ^{o}C, T = 298 K 1/T = 3,3*10^{-3} K
$ln□$ = 2,50 Pa.c. □ = 12,18 Pa.c. at 40 ^{o}C, T = 313 K 1/T = 3,19*10^{-3} K
$ln□$ = 2,15 Pa.c. □ = 8,58 Pa.c. at 55 ^{o}C, T = 328 K 1/T = 3,05*10^{-3} K



Picture 3. Dependence of the dynamic viscosity (*η*) from the temperature (*t*) for the gel.

There has been made the dependence $ln□$, Pa.c from the reversible temperature according to the formula of Frenkel-Airing $ln\eta = lnA + E_a/RT$ (picture 4). Here lnA –coefficient, E_a – activation energy of viscose flowing; R = 8,31 – universal gas constant.



Picture 4. Dependence of the logarithm dynamic viscosity (*ln*□) from the reversible temperature (*1/T*) for the gel.

The next step in our research was to identify the structural and mechanical parameters of curcuma ointment. There have been conducted experiments on the instrument Rheotest-2 (Germany) by using cell system “cylinder-cylinder” S/S1 (cell constant z=5,6) at the temperature 25°C, 40°C, 55 °C.

t = 25 °C

№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff} ,* Pa.c	lnη_{eff} ., Pa.c	lnη $_{eff}$.*, Pa.c
1a	10	10	56	56	3	18,67	18,67	2,92	2,92
2a	12	11	67,0	61,4	5,4	12,44	11,33	2,52	2,43
3a	14	13	78,4	72,6	9	8,71	8,10	2,16	2,09
4a	18	16	100,6	89,6	16,2	6,22	5,53	1,82	1,71
5a	23	21	128,6	117,6	27	4,77	4,35	1,56	1,47
6a	30	27	168	151,2	48,6	3,46	3,11	1,24	1,13
7a	43	39	240,8	218,6	81	2,97	2,69	1,09	0,99
8a	57	52	319,2	291,4	145,8	2,19	1,99	0,78	0,69
9a	75	70	420	392	243	1,73	1,61	0,55	0,47
10a	92	92	515,1	515	437,4	1,18	1,18	0,16	0,16

t = 40 °C

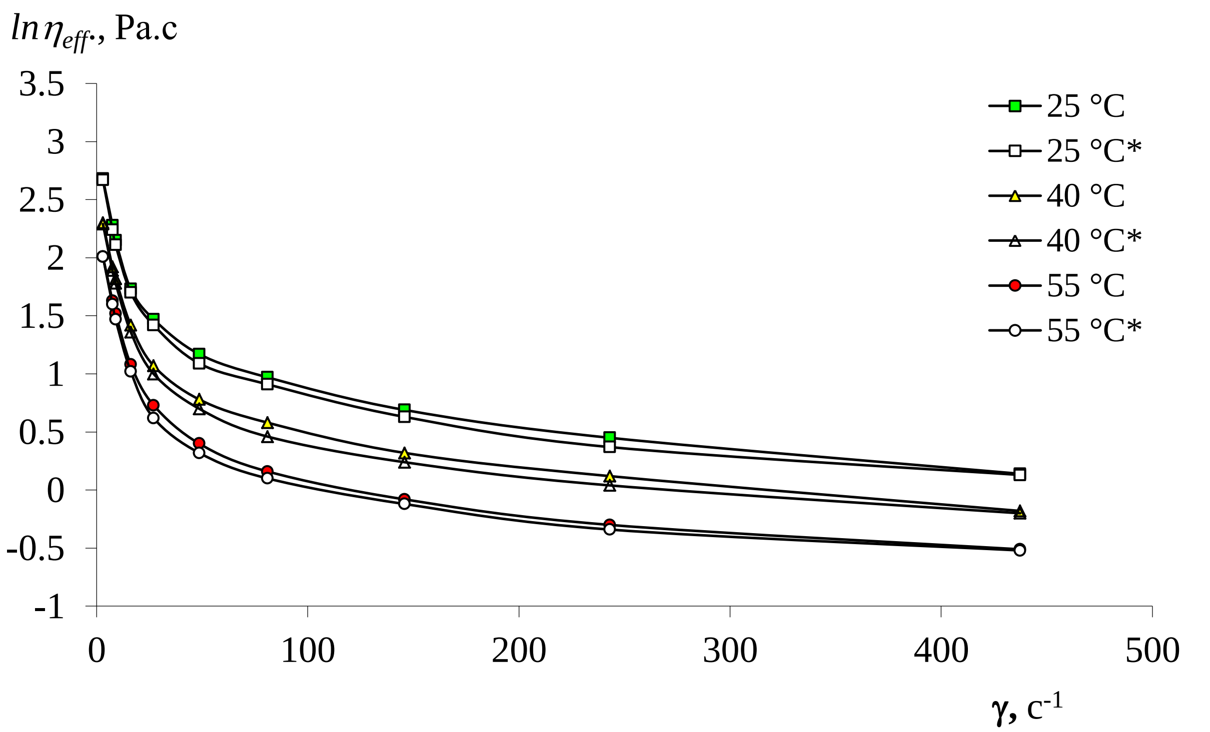
№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff} ,* Pa.c	lnη_{eff} ., Pa.c	lnη $_{eff}$.*, Pa.c
1a	8	8	44,8	39,2	3	14,93	14,93	2,70	2,70
2a	10	9	56,0	50,6	5,4	10,39	9,33	2,34	2,23
3a	12	10	67,2	56	9	7,47	6,22	2.02	1,82
4a	15	13	84,2	72,4	16,2	5,18	4,49	1,65	1,51

5a	19	16	106,4	89,8	27	3,94	3,33	1,37	1,19
6a	23	20	128,4	112,0	48,6	2,65	2,30	0,97	0,83
7a	26	23	145,6	128,8	81	1,79	1,59	0,58	0,46
8a	37	34	207,2	190,8	145,8	1,42	1,31	0,35	0,27
9a	60	56	336,4	313	243	1,38	1,28	0,32	0,24
10a	72	71	403,4	397,4	437,4	0,92	0,90	-0,08	-0,096

t = 55 °C

№	α	α*	τ = α*z, Pa	τ* = α*z, Pa	γ, c^{-1}	η_{eff}, Pa.c	η_{eff}.*, Pa.c	lnη_{eff}., Pa.c	lnη_{eff}.*, Pa.c
1a	6	5,5	33,4	33,2	3	11,3	11,2	2,41	2,40
2a	7	6	39,2	33,6	5,4	7,26	6,25	1,98	1,83
3a	10	8	56	44,8	9	6,22	4,98	1,82	1,60
4a	12	11	67,2	61,6	16,2	4,15	3,80	1,42	1,34
5a	13	12	72	67,4	27	2,69	2,49	0,99	0,91
6a	16	14	89,6	78,2	48,6	1,84	1,64	0,61	0,48
7a	20	18	112,2	100,8	81	1,38	1,28	0,32	0,22
8a	25	23	140,4	128,4	145,8	0,96	0,88	-0,04	-0,12
9a	33	30	184,2	168,2	243	0,76	0,69	-0,37	-0,37
10a	50	49	280,2	275,2	437,4	0,62	0,64	-0,47	-0,46

On the base of obtained results there have been made rheogrammes of the effective viscosity (*ln*□*eff.*)according to the velocity gradient (*γ*) at the different temperatures 25°C, 40°C, 55 °C, given in the picture 5.

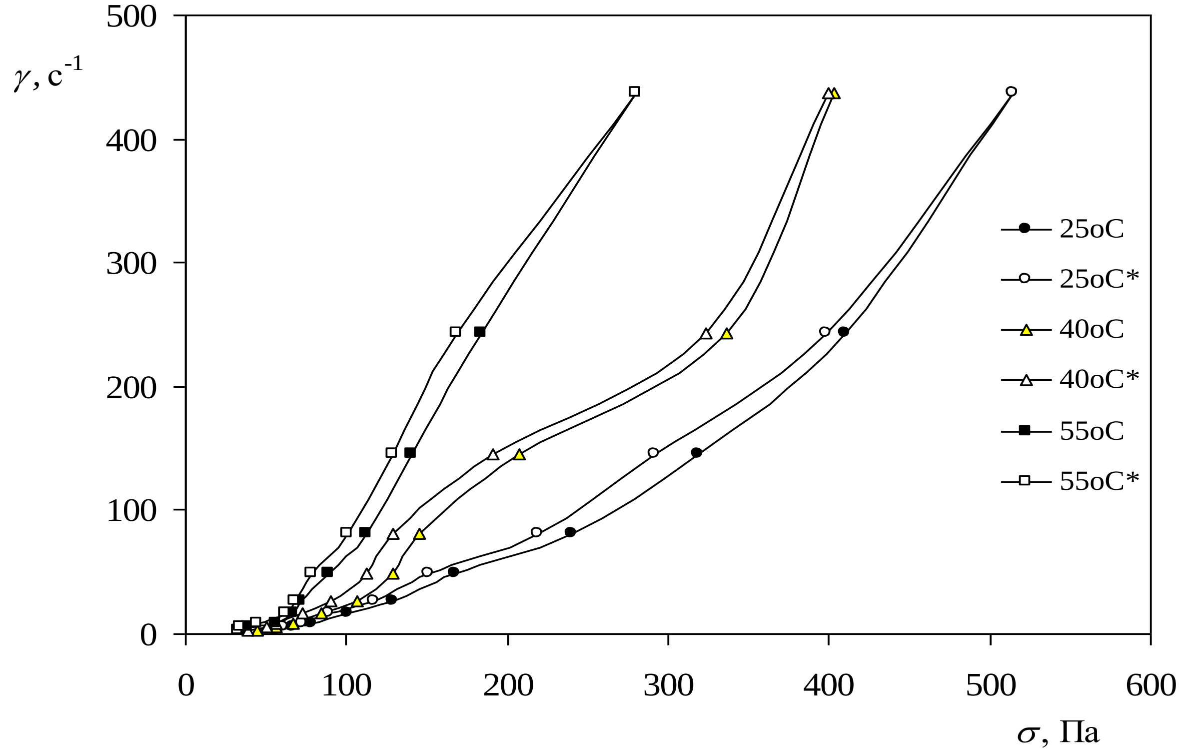


Picture 5. Logarithm dependence of the effective viscosity (*ln*□*eff.*) on the velocity gradient (*γ*) of the displacement stream for the ointment at the different temperatures:

Here 25 °C, 40 °C, 55 °C at the direct measuring (at increasing *γ*), 25 ^{o}C*, 40 ^{o}C*, 55 ^{o}C* at the reverse measuring (at decreasing γ).

It is indicated, in all cases of increasing influence of the displacement field, that is with the increasing velocity gradient there has been observed non-rectilinear decreasing $ln\square_{eff}$., moreover, there has been occurred perceptible rapid decreasing to achieve $\gamma \rightarrow 40$ c^{-1}, then moderate slow decreasing $ln\square_{eff}$ to $\gamma \rightarrow 500$ c^{-1}. In this case there has been observed essential influence of the temperature to the viscosity (that is to the fluidity) of the ointment and with the increasing temperature the rheogramme shifts to the area of the small meanings $ln\square_{eff}$ and large meanings γ.

There has been revealed that curved dependences that is rheogrammes perceptibly differ according to the effective viscosity indices $ln\square_{eff}$ at the direct measuring (at increasing meaning γ) and reverse measuring (at decreasing meaning γ) its meanings in the displacement field. It is particularly vivid shown in the interval $\gamma = 50 - 500$ c^{-1} in order to slight hysteresis effect. It is testified to structuring, perceptible deformative-regulated structure-forming ointment at the influence of the displacement field in the chosen temperature area. For analyzing presence of the hysteresis effect there have been made rheogrammes in the form of the velocity gradient dependence (γ) from the displacement tension (τ) for ointment at the different temperatures (picture 6).



Picture 6. Velocity gradient dependence (□□) from the displacement tension (□) for the ointment.

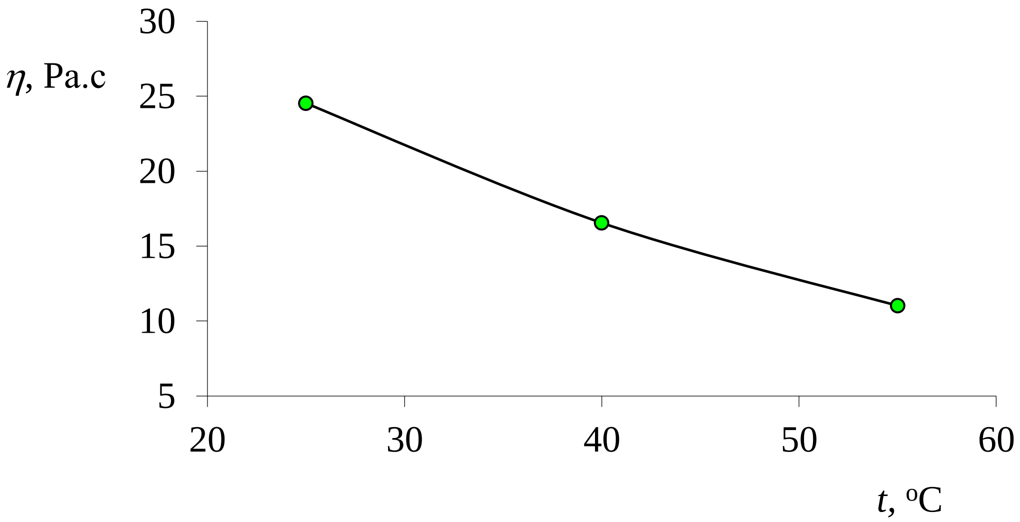
It is also indicated the vivid manifestation of the hysteresis effect at the temperatures 25 ^{o}C, 40 ^{o}C, 55^{o}C, which confirms the structural changes in the ointment in the field of the gradient velocity 50 – 300 c^{-1}. It apparently occurs perceptible rapid destroying structure of the gel in the field of the gradient velocity and temperature.

In the chart of the picture 6 there have been determined quantities of the limit displacement tension (τ_{limit}) and a limit flowing tension (τ_k) and there have been calculated meanings of the mechanical stability M*S* = τ_k / τ_{np} at the different temperatures (t, ^oC).

t, ^oC	□$_{limit}$, Pa	□$_k$, Pa	*MS*
25	56	115	2,05
40	45	85	1,88
55	33	55	1,67

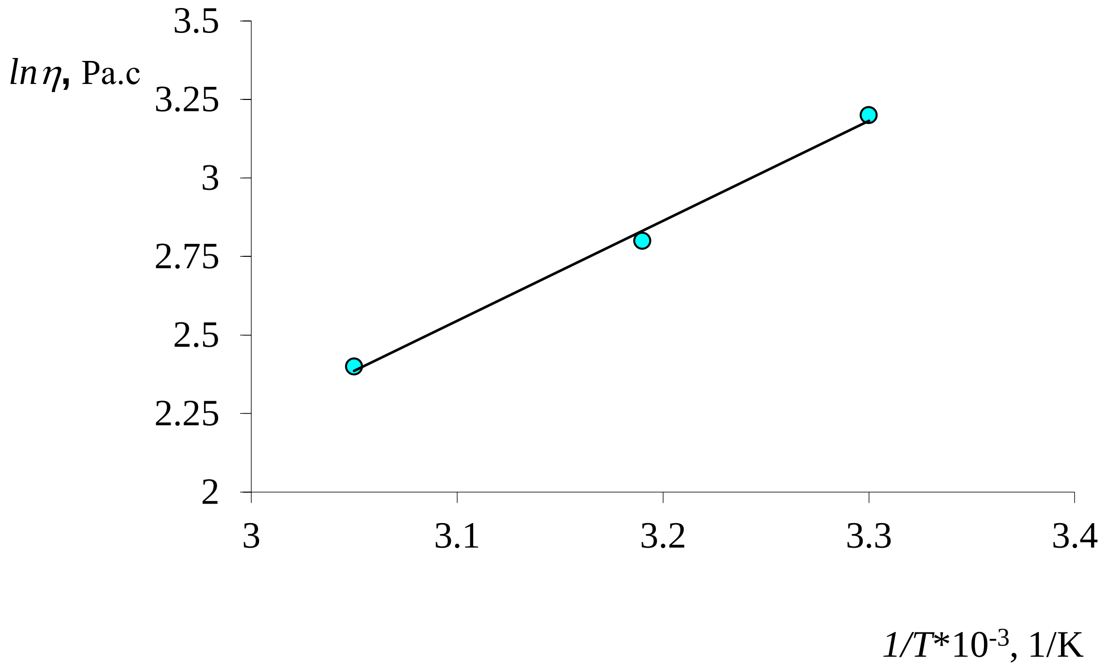
There have been determined meanings of the dynamic viscosity (η) in the picture 5 by conducting extrapolation $\gamma \to 0$ on condition, that $ln\eta_{eff.} \to ln\,\eta$.

$ln\,\eta$ = 3,20 Pa.c. η = 24,53 Pa.c. at 25 ^{o}C, T = 298 К 1/T = 3,3*10^{-3} К
$ln\,\eta$ = 2,80 Pa.c. η = 16,45 Pa.c. at 40 ^{o}C, T = 313 К 1/T = 3,19*10^{-3} К
$ln\,\eta$ = 2,40 Pa.c. η = 11,02 Pa.c. at 55 ^{o}C, T = 328 К 1/T = 3,05*10^{-3} К



Picture 7. Dependence of the dynamic viscosity (η□) from the temperature (*t*) for the ointment.

There has been made the dependence $ln\eta$, Pa.c from the reversible temperature according to the formula of Frenkel-Airing $ln\eta = lnA + E_a/RT$ (picture 8). Here lnA –coefficient, E_a – activation energy of viscose flowing; R = 8,31 – universal gas constant.



Picture 8. Dependence of the logarithm dynamic viscosity (*lnЛ*) from the reversible temperature (*1/T*) for the ointment.

Results: As a result of the research, the viscous flow activity energy of the grease and gel was calculated:
From the slope of the curve dependence (pic.4) $ln\eta$ - $1/T$ there has been found $a = E_a/R$

$a = E_a/R$ = (2,85 – 2,15)/(3,30 – 3,05)*10^{-3} = 2,8*10^{3}
and there has been calculated the meaning of the activation energy of viscose flowing E_a equal

$E_a = aR$ = 2,8*8,31*10^{3} = 23268 J / mol = 23.3 kJ / mol
From the slope of the curve dependence (pic.8) $ln\eta$ - $1/T$ there has been found $a = E_a/R$

$a = E_a/R$ = (3,20 – 2,40)/(3,30 – 3,05)*10^{-3} = 3,2*10^{3}
and there has been calculated the meaning of the activation energy of viscose flowing E_a equal

*Ea = aR = 3,2*8,31*103 = 26592* J / mol = 26,6 kJ / mol
According to the results of the researches, there have been determined that viscous stream activity energy of the ointment is 26,6 kJ / mol, viscous stream activity energy of the gel is 23,3 kJ / mol, and it is coincided with viscous stream activity energy level of the ointments and gels.

3. CONCLUSION:

There has been decided to consider that these contents are perspective according to the rheological properties of the suggested ointments and gels.

Acknowledgements: We thank the “Med Standard” Limited Liability Company for their financial support.

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