Development Of Gel Technology For Anti-Inflammatory Dental Practice.

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Abstract: This article discusses the idea of conducting research to study the quality and quantity of the gel, which is based on the tincture of mavrak leaves, effective, harmless, easy to use, shelf life. There are also conclusions about the research on the selection of the composition and technology of Mavrak gel. There are several advantages of preparing gel on the basis of mavrak tincture on the basis of sodium carboxymethylcellulose (Na-KMC).

Key words: Parodont, salavia leaves, mavrak gel, viscosity, thixotropy, dynamic viscosity, fitopreparation.

1. INTRODUCTION

Using fitopreparations in treating illnesses, especially incessant ones is one of the main topic of todays' medicine. Pharmocological impact spectrum of the medicinal plants related to the biological active substances. Soft impact of the fitopreparation to the body is using widely in pediatrics. Creating standardizing types and modermn drug types, testing these drugs from clinic check-out and publicizing them by the help of natural recources of Uzbekistan, developing local pharmacy industry, publicizing drugs which are created by Uzbekistan scientists and based on the modern technologies, delivering these drugs to the internal and external market of the pharmacy helps for rising pharmaceutical potential.

It is known from historical evidences, clinical views of dental illnesses were revealed by French doctor Foshar[1746]. Abu Ali ibn Sino told about dental illness and for treating it we must act to the mouth blowhole hygiene and improve general condition of the body in his well-known book '' medicine principles[tib qonunlari]''. In central Asia illnesses are multiplying because of ecological deterioration. Creating new and effective medicine types is one of the main problems of pharmacy and medicine. Healing mucus of the mouth blowhole and dentall illnesses and preventing is the main problem of stomatology. For healing parodont   stomach-intestine illnesses, cardio-vascular, kidney,diabetes. reumatism,liver illnesses are checked through laboratory and treated. Scientists found that incessant illnesses take place main role for emanating parodont, therefore vegetative nerve system, flu, blood diseases, hypovitaminisis are healed together with parodont.

We must explore quality and expiry date, affective, safe, harmful usage of Gel wich is prepared based on salavia leaves infusion.

For reaching these points, these things which are below must be tackled;

-get informed with medicine types which are prepared with the help of natural plants which is used for mouth blowhole diseases;

- selecting structure of the gel medicine which is prepared from salavia leaves, constructing technology, using bases which is allowed in medicine;

- learning pharmocological property of prepared gel;

-during preservation date pointing explory date and learning stomatological steadiness.

However, the disadvantage of sodium carboxymethylcellulose (Na-KMC) is that it is resistant to microorganisms and deteriorates rapidly. Therefore, long-term storage of gels prepared on such a basis is a complex matter. [6,7,8,9]

Table 1

Na-KMC-based mavrak tincture dental gel ingredients

Name	Quantity, g			
	I-content	**II-content**	**III-content**	**IV-content**
Tincture of mavrak leaves	80 ml	80 ml	80 ml	80 ml
Na-KMC	4	6	8	3
Glycerin	10	10	10	10
Purified water	4ml	6ml	2ml	7ml

The gels were prepared according to the ingredients listed in Table 1 and their quality was evaluated according to the methods described in Chapter 3.1. The results of the experiments obtained are presented in Table 2.

Table 2

Study of the quality characteristics of Na-KMC-based mavrak tincture dental gel

Quality indicators	I-content	II-content	III-content	IV-content
Colour	Dark brown	Dark brown	Dark brown	Dark brown
The same mix	Same mix	Same mix	Same mix	Same mix
Rubbing	More difficult	easy	More difficult	More difficult
Temperature stability	Didn't seperate	Didn't seperate	Didn't seperate	Didn't seperate
Colloidal stability	Liquid	Normally	More liquid	solid

According to the experimental results given in Table 2, the color of the gels I, II, III and IV was satisfactory with the same mix. However, due to the colloidal stability, it was difficult to apply the first component, and only the third and fourth components were difficult

to rub. The structure of the foundations in structures III and IV could not withstand the heat and changed and disintegrated into layers. Content II was selected for further research.
Preservatives are added to make the gels stable during storage. It is recommended to add the following preservatives to the gel:
-0.2% boric acid;
-0.2% salicylic acid;
-0.2% sorbic acid;
-0.9% benzyl alcohol;
-0.2% nipagin and nipazole in a 1: 3 ratio;
-96% ethyl alcohol;
-0.2% nipagin;
The above nipagin was used to stabilize the gels.

The above gels contain preservatives and can be stored at room temperature. The follow-up lasted for 1 month, 3 months, 6 months, 12 months, during which time the best saved gel was selected. The quality of the gel was determined every 30 days for 12 months. These preservatives increase the stability of the gels and prevent the growth of mold fungi. Researches have been conducted on the choice of preservative for the stabilization of gels.

Stabilization of Na-KMC-based mavrak tincture dental gel

Preservatives have been added to stabilize this mavrak gel (ingredient II). The stability of the gel was determined by evaluating a number of quality parameters during storage. The results of the experiments obtained are presented in Table 3.

Table 3
The effect of nipagin on the stability of dental gel tincture based on Na-KMC

Period of preserve		Primary index	1 month	3 month	6 month	12 month
Colour	Nipagin	Dark brown	Dark brown	Dark brown	Dark brown	Dark brown
	Ascorbic acid	Dark brown	light brown	light brown	light brown	light brown
The same mix	Nipagin	The same mass	The same mass	The same mass	The same mass	The same mass
	Ascorbic acid	The same mass	The same mass	The same mass	The same mass	The same mass
Separation into layers	Nipagin	Didn't seperate	Didn't seperate	Didn't seperate	Didn't seperate	Didn't seperate
	Ascorbic acid	Didn't seperate	Didn't seperate	Didn't seperate	seperated	-

The experiments in Table 3 showed that the stability of the gel was satisfactory for 12 months.

Development of dental gel technology.

This chapter describes the composition and technology of the gel selected on a scientific basis. The composition of this gel is as follows:

Table 4

The composition of mavrak gel based on Na-KMC

Mavrak tincture	84 ml
Na-KMC	6,0 g
Glycerin	10,0 g
Nipagin	0,1 g

Technology. Initially, 10 g of product is placed in a container of infusion apparatus, 120 ml of boiling water at room temperature is poured over it and covered with a lid, heated in infusion apparatus for 15 minutes and cooled to room temperature for 45 minutes. The drip is extracted from the infusion apparatus. When cooled, the stabilizer is dissolved in a tincture of nipagin mavrak leaves and Na-KMC is added to the tincture. After boiling, add glycerin for 1 hour and mix until a gel-like mass is formed. A gel is formed.

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 lubricants are inspected on the basis of approved normative technical documents for qualitative and quantitative analysis. Greases are stored in dry, cool rooms, humidity 70% and temperature up to + 50C .

Appearance evaluation. Dark brown, fragrant leaves with a soft consistency.

Determining the color of the gel.

The color of the gel 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. Tuber 1 is filled with gel prepared without mavrak and tube 2 is filled with gel prepared with mavrak (5.0 g). Their color is compared on a black and white background. The color of the gel is determined relative to the color of the base.

Determine the same mix.

The gel is sampled from different parts and examined with the naked eye. The insoluble particle should not be a sticky mixture. Such a gel is considered to be uniformly mixed.

For this purpose, 4 samples weighing 0.02 g were taken from the gel. Place 2 specimens on a glass plate, cover with a second glass plate, and seal the specimen until it is 2 cm in diameter. The sample on the glass plates was then carefully observed with the unaided eye at a distance of 30 cm. 3 out of 4 samples did not have visible particles. This means that the prepared gel meets the requirements for uniform mixing.

Detection of rubbing.

To do this, take a sample of the gel being tested with the thumb and forefinger and rub it on the surface of the thumb of the left hand. The gel should be easily applied to the skin without external pressure.

Determine temperature stability.

To determine the thermal stability of the gels, samples of gels with a diameter of 14 mm and a height of 120 (100) mm are filled to 2/3 of the volume, leaving no air bubbles. The test tubes are sealed and placed in a thermostat at 40-420 C for 24 hours. Samples placed in the

thermostat are mixed with a glass rod after 1 hour to prevent air bubbles in the test tubes. Overlap ping should not be observed in gel samples during the observation period.

Determination of colloidal stability.

To determine the colloidal stability of the gels, a sample of 3-5 g (up to 2/3 volume, 0.2 g accuracy) is taken and placed in a centrifuge glass. Samples from centrifuge cups are placed in a water bath or thermostat at 42-45⁰ C for 20 minutes. The outer part of the beakers is then wiped and placed in a CUM-1 centrifuge for 1500 rpm. rotated for 5 minutes at speed.

Determination of pH indicator.

The pH of the gel was determined by potentiometry. 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 gel had a pH of 5.5.

Creating a method of quantitative analysis of Mavrak gel.

The amount of biologically active substances - additives in the dental gel, obtained on the basis of medicinal mavrak tincture, was carried out spectrophotometrically at the expense of tannin. A gel sample of about 1.0 g (clear box) is placed in a 50 ml volumetric flask, filled with 70% ethyl alcohol, brought to the volume mark and mixed. 2.5 ml of the resulting solution was then transferred to a 2.5 ml volumetric flask and made up to the mark with 70% ethyl alcohol. The optical density of the resulting solution is measured on a SF-101 spectrophotometer in a 10 mm cuvette at a wavelength of 275 nm relative to the comparative solution - 70% ethyl alcohol. In parallel, a standard sample solution of tannin (RSO) is also measured.

Preparation of a solution of a standard sample of tannin: take about 0.0025 g (net weight) of a standard sample of tannin dried to a constant mass at a temperature of 100-105⁰C, put it in a 50 ml volumetric flask, and twice add 25 ml of 70% ethyl alcohol. stir until the tannin is dissolved. Take 2.5 ml of the resulting solution, transfer to a 25 ml volumetric flask, add 70% ethyl alcohol, make up to volume and mix.

The sum of additives is calculated in tannins (X,%) according to the following equation:

$$X = \frac{D_x \times M_{cm} \times 100 \times 50 \times 25 \times 2,5 \times 100}{D_{cm} \times M_x \times 5 \times 2,5 \times 50 \times 100} \quad (3)$$

Here

M_{cm} - is the net gravitational mass obtained to prepare a standard sample solution of tannin, g;

M_x -is the mass of the gel sample, g;

D_{cm} -is the optical density of the standard sample solution of tannin;

D_x - is the optical density of the sample solution.

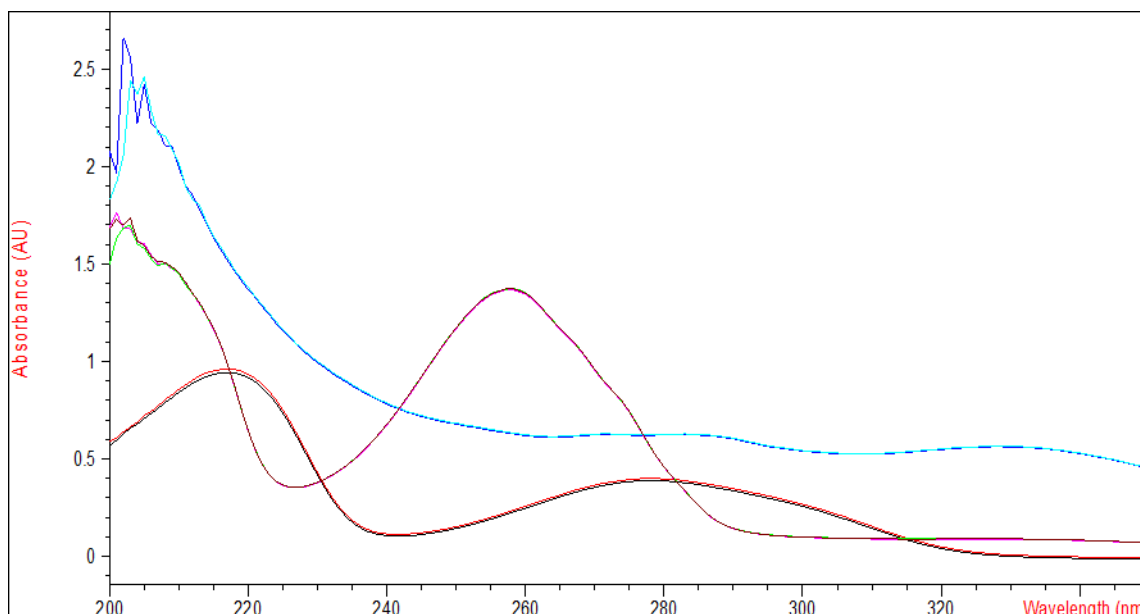The experimental results are shown in Table 5 and Figure 1.

Figure 1. Results of spectrophotometric determination of the amount of additives (due to tannin) in the medicinal mavrak dental gel.

Table 5

Quantitative analysis results of Mavrak gel

№	The exact drawer of the gel ,g	The amount of additives in the gel (in terms of tannins)%	Metrological characteristics
1	1,0502	17,416	X=17,221 f=4
2	1,0495	17,315	S²=0.0422;
3	1,0503	17,011	S =0.2055;
4	1,0498	16,988	Sx=0.0919;
5	1,0505	17,375	$\Delta \overline{X}$ =3.864
			$\overline{\varepsilon}$,%=1.728

Study of rheological properties of dental gel, determination of mechanical properties of the structure.

One of the modern requirements for the quality of lubricants is that they have constant structural and mechanical properties, as these parameters determine the therapeutic and consumption properties of lubricants. These quality indicators include the structural and mechanical properties of the gel during its shelf life, the results of quantitative analysis, its rate of exfoliation, and its application to the skin.

In view of the above, in recent years the study of rheological properties in the technology of soft drugs has become mandatory. Rheological properties are the indicators of effective viscosity, shear stress, mechanical stability, thixotropy, dynamic viscosity. The rheological properties of the gel under study were studied in Reotest 2 (Germany). Take a clear naveska, put it in a measuring cup and thermostat at a certain temperature for 30 minutes.

The Republic of Uzbekistan is located in the continental climate and is characterized by sharp changes in the weather, so we can study the temperature range to 25 ° C, 30 ° C, 35 ° C,

40 ° C, 50 ° C. Thermostated samples were taken in ascending order for every 10 readings starting from the minimum rotation in the measuring tube in the cylinder, and each reading was recorded. The order of decreasing (decreasing) rate of disintegration of the gel at maximum speed was recorded for 10 min. The experimental results obtained are the shear tension and effective viscosity, and a rheogram was constructed (gel flexibility).

The effective viscosity (τ) is calculated using the following formula (1):

$$\tau = Z \cdot \alpha \quad , (1)$$

Here τ - is the shear stress, Pa;

Z -is the cylinder constant, equal to 5.6 Pa;

α - is the indication of the measuring instrument.

The effective viscosity is determined using the following formula (2):

$$\eta = \frac{\tau}{\gamma} , \quad (2)$$

Here η - is the effective viscosity, Pa · c;

τ - shear stress, Pa;

γ- is the displacement velocity gradient, c^{-1}.

Shear strength and effective viscosity are related to velocity shear at 25 ° C, 30 ° C, 35 ° C, 40 ° C, and 50 ° C.

Table 6

a) in 25 ^{o}C

Tool indicator		Sliding tension $\tau = \alpha*Z$, Па	Gradient speed, γ, c-1	Effective viscosity $\eta эфф. = \tau / \gamma$, Па.с	effective viscosity logarithm $\ln\eta эфф.$, Па.с
№	α				
1a	10	80,6	1,5	53,73333	3,984034
2a	15	120,9	2,7	44,77778	3,801712
3a	20	161,2	4,5	35,82222	3,578568
4a	23	185,38	8,1	22,88642	3,130544
5a	29	233,74	13,5	17,31407	2,85152
6a	36	290,16	24,3	11,94074	2,479956
7a	45	362,7	40,5	8,955556	2,192274
8a	59	475,54	72,9	6,523182	1,875362
9a	71	572,26	121,1	4,725516	1,552977
10a	92	741,52	218,7	3,390581	1,221001

7-jadval

b) in 30 ^{o}C .

Tool indicator		Sliding tension $\tau = \alpha*Z$, Па	Gradiyent speed, γ, c-1	Effective viscosity $\eta эфф. = \tau / \gamma$, Па.с	effective viscosity logarithm $\ln\eta эфф.$, Па.с
№	α				
1a	10,5	84,63	1,5	56,42	4,032824
2a	13	104,78	2,7	38,80741	3,658611
3a	14,8	119,288	4,5	26,50844	3,277463

4a	19	153,14	8,1	18,90617	2,939488
5a	23,5	189,41	13,5	14,03037	2,641224
6a	30	241,8	24,3	9,950617	2,297635
7a	37,5	302,25	40,5	7,462963	2,009953
8a	50	403	72,9	5,528121	1,709848
9a	65	523,9	121,1	4,326177	1,464684
10a	86	693,16	218,7	3,169456	1,15356

8-jadval

v) in 35 ^{o}C .

Tool indicator		Sliding tension $\tau = \alpha*Z$, Па	Gradient speed, γ, с-1	Effective viscosity $\eta_{эфф.} = \tau / \gamma$, Па.с	effective viscosity logarithm $ln\eta_{эфф.}$, Па.с
№	α				
1a	11	88,66	1,5	59,10667	4,079344
2a	12,5	100,75	2,7	37,31481	3,61939
3a	13,5	108,81	4,5	24,18	3,185526
4a	16,5	132,99	8,1	16,41852	2,79841
5a	20	161,2	13,5	11,94074	2,479956
6a	26	209,56	24,3	8,623868	2,154534
7a	33	265,98	40,5	6,567407	1,882119
8a	41,5	334,49	72,9	4,58834	1,523518
9a	59	475,54	121,1	3,926837	1,367834
10a	79	636,74	218,7	2,911477	1,06866

9-jadval

g) in 40 ^{o}C .

Tool indicator		Sliding tension $\tau = \alpha*Z$, Па	Gradient speed, γ, с-1	Effective viscosity $\eta_{эфф.} = \tau / \gamma$, Па.с	effective viscosity logarithm $ln\eta_{эфф.}$, Па.с
№	α				
1a	9	72,54	1,5	48,36	3,878673
2a	10,8	87,048	2,7	32,24	3,473208
3a	11,8	95,108	4,5	21,13511	3,050936
4a	15	120,9	8,1	14,92593	2,7031
5a	18	145,08	13,5	10,74667	2,374596
6a	23	185,38	24,3	7,628807	2,031931
7a	30	241,8	40,5	5,97037	1,786809
8a	39,5	318,37	72,9	4,367215	1,474126
9a	52	419,12	121,1	3,460941	1,241541
10a	71	572,26	218,7	2,616644	0,961893

10-jadval

d) 50 ^{o}C da.

Tool indicator	Sliding tension	Gradient speed,	Effective viscosity	effective viscosity logarithm

№	α	τ = α*Z, Па	γ, c-1	ηэфф. = τ / γ, Па.с	lnηэфф., Па.с
1a	7,8	62,868	1,5	41,912	3,735572
2a	8,5	68,51	2,7	25,37407	3,233728
3a	10	80,6	4,5	17,91111	2,885421
4a	12	96,72	8,1	11,94074	2,479956
5a	15	120,9	13,5	8,955556	2,192274
6a	19,5	157,17	24,3	6,467901	1,866852
7a	24	193,44	40,5	4,776296	1,563665
8a	32	257,92	72,9	3,537997	1,263561
9a	42	338,52	121,1	2,795376	1,027967
10a	58,5	471,51	218,7	2,155967	0,768239
11a	77	620,62	364,5	1,702661	0,532192

The results show that an increase in the shear stress of the gel under test results in a decrease in viscosity under the influence of deformation forces. The dependence of the change in the effective viscosity logarithm (lgη$_{эфф}$) on the gradient of the displacement velocity (γ), as well as the dependence of the shear stress on the index (τ) are different from the rheograms of the gel under study 5 and Figure 6.
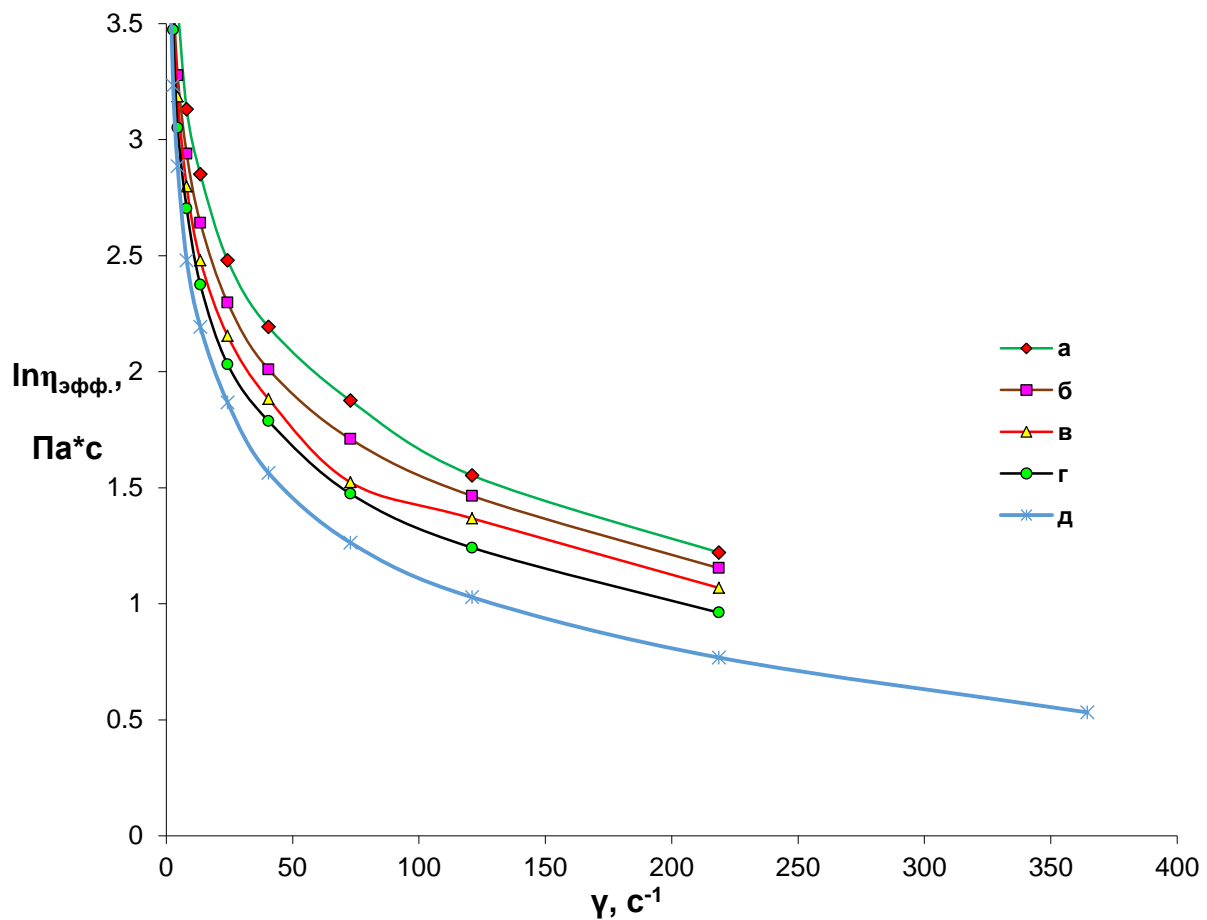
Figure 2. The logarithm of the effective viscosity depends on the shear stress

ln□ = 4,3352   T = 298 K   1/T = 3,355*10^3

ln□ = 4,18487   T = 303 K $1/T = 3,3*10^3$
ln□ = 4,1462   T = 308 K $1/T = 3,246*10^3$
ln□ = 3,9833   T = 313 K $1/T = 3,1948*10^3$
ln□ = 3,77   T = 323 K $1/T = 3,096*10^3$
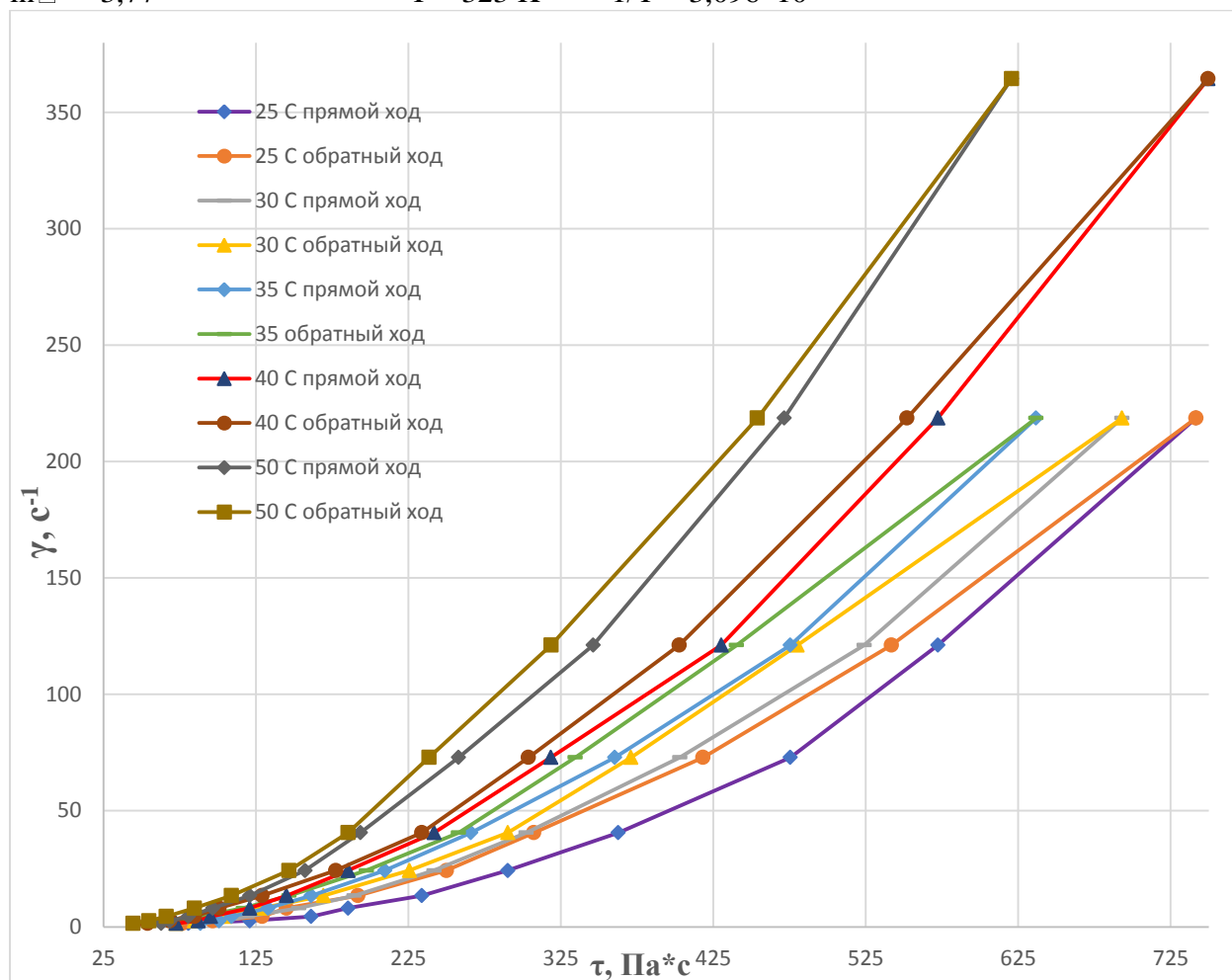
Figure 3. The dependence of the velocity gradient (γ) of the gel on the shear stress (τ) Pharmacological activity of the gel.

One of the most pressing problems of modern dentistry today is inflammatory diseases of the oral cavity: periodontitis, stomatitis, gingivitis. In order to solve this problem, the acute toxicity and specific activity of dental gel were studied.

The flora of Uzbekistan is rich in medicinal plants, which are a reserve of medicines. One of the most pressing issues for pharmacologists today is the comprehensive study of drug forms based on biologically active substances isolated from these plants.

Mavrak is one of the most widely used medicinal plants since ancient times. The Mavrak (Latin: Salvia officinalis) plant and the various preparations made from it are widely used in folk medicine for anti-inflammatory, wound-healing, laxative, diuretic, antitussive, antifungal skin diseases.

In view of the above, the acute toxicity of the gel was studied in laboratory mice. For this purpose, mice weighing 22-26 grams were selected. One day before the experiment, 1x1 cm of skin was removed from the mice. On cleansed skin, 0.1-0.3 g of gel was rubbed twice to the mouse mass, and the next day another 0.3 g of gel was rubbed. The control was performed in a laboratory condition for 14 days. When observed under the influence of the gel, pathological signs were determined by body weight and nerve somatic parameters of

mice: general condition of the mouse, the effect on motor activity, the presence or absence of seizures, coordination of movement, light reaction, respiratory status, condition of hair and skin lining, macroscopic structure of skin lining was not pathological, no change in skeletal muscle tone was observed. The sensitivity of the senses to pain, sound, and light has not changed. No deaths were reported during this follow-up, and no adverse skin reactions were observed at the doses studied.

Table 11

Results of the study of pharmacological activity

Acute toxicity		
Preparation	Dosa mg/kg	Number of dead
Made on the basis of mavrak leaves 6% li gel	5	0/6
Made on the basis of mavrak leaves 6% li gel	10	0/6

The effects of local tickling have been studied in separate experiments. The experiments were performed on 12 mice weighing 22-24 grams and rats weighing 158-195 grams. 0.1 g of ointment was applied to the lumbar region of previously dehaired animals. In the following days, 0.25 g, 0.5 g and 0.5 g of the studied ointment were rerubbed for another 6 days. Prior to the start of the daily experiments, no gel-related tick-borne reactions were observed on the gel-treated skin of the experimental animals: redness of the skin, blistering, and bleeding.

Another separate study examined the effects of superficial wound healing. Superficial wounds were exposed by cutting with a scalpel at a depth of 0.25-0.3 mm in the size of 2x1 cm at the waist of 10 pre-cleaned feather mass 130–160 g rats. The animals were then divided into 2 groups of 5.

Group 1 was a control group in which superficial wounds were treated with appropriate gel application. The treatment lasted 7 days by rubbing 2 times daily (morning and evening). The observation was carried out under vivarian conditions.

It should be noted that in rats in control group 1, a significantly more aggressive condition was noted at 5 days of the experiment, i.e., symptoms of high inflammation at the top of the cut wounds persisted for 4–5 days of the experiment. These cases were not recorded in rats in experimental group 2 from day 1–2 of the experiment. In rats treated with gel prepared on the basis of mavrak leaves, from the 3rd day of the experiment, signs of wound healing were observed on the upper part of the wounds, crusts, alloys on the wound.

The wounds of the rats in the experimental group treated with gel based on mavrak leaves were almost completely healed in 6-7 days. Under the same conditions, the wound healing of the rats in the control group took 12–13 days.

According to the results of the experiment, the gel based on the leaves of mavrak was less toxic, and the gel did not have any adverse effects on the condition of the animals during the whole experiment. Their feathers was clean, their weight was almost unchanged, and there were no symptoms of local itching or inflammation on the gel-treated skin. Rectal temperature was also close to normal.

No pathological changes in the peripheral blood of animals (hemoglobin, erythrocytes and leukocytes) were observed. The animals' weight and body temperature remained within the physiological norm throughout the experiment.

The effectiveness of the anti-inflammatory gel was studied in 15 rats. Rats of both sexes weighed an average of 150–175 g, and a 2% formalin solution was rubbed to the subplantar (lower part of the heel) 0.1 ml per hind leg. The studied mavrak tincture was studied 1 hour before dental gel, as well as „Kamistad'' gel and flagogen in the control group. The rate of the inflammatory response was measured relative to the size of the wound after 4 h (oncometric method).

Tumor of the hind legs was assessed as a percentage with the condition prior to flagogen delivery. The pharmacological activity of the gel was evaluated for their tumor-reducing properties and compared with animals in the control group.

The control group (treated with Vaseline), the second group (treated with mavrak tincture with dental gel) and the third group (treated with kamistad gel) were used at a dose of 0.2 g. The rats were then tied to their tails and placed in separate cages to prevent them from licking drugs from their hind legs. The results were studied after 4 hours.

To study the effect of Mavrak tincture dental gel on formalin-induced inflammation (M ± m; n = 6)

Table 20

№	Drugs to be studied	Number of animals	Dosa, mg	Average volume of drug delivered, ml		Wound changes relative to the study group		Inflammatory effects in%
				Normally in ml	42 hours after taking formalin In ml	Abs. ml larda	% larda	
1.	Control group (Vaseline)	5	0,2	0,76	1,52	0,76±0,08	100	-
2.	The group treated with the examined mavrak tincture dental gel,	5	0,2	0,74	1,23	0,49±0,073	66,2	33,8
3.	The group treated with comparative "Kamistad" gel	5	0,2	0,75	1,26	0,51±0,052	69	32,0

As can be seen from the table, the gel under study has a clear anti-inflammatory effect. In rats, the mean increase compared to the control volume on the hind leg scale was reduced to 33.8% and 32%, respectively.

2. CONCLUSION.

For the first time, the composition of mavrak gel was selected on a scientific basis and the technology was created. The base, excipients and preservative in the selected

composition have been proven to ensure the quality and stability of the gel. The most satisfactory composition of the gel was selected in terms of quality indicators: appearance, color, abrasion, colloid and temperature resistance. A method of quantitative analysis of the selected gel was developed. Accordingly, it was proposed to determine the amount of mavrak leaves by spectrophotometric method.

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