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Technology and Composition of Saperavi-Based Cosmetic Emulgel

Tamar Kirvalidze,[1,ID] Lasha Bakuridze,[2] Dali Berashvili,[2] Gulnara Mikaia,[2] Ia Tsurtsumia,[2] Tamaz Murtazashvili,[1] Aliosha Bakuridze[2,ID]

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ABSTRACT

Background: In recent years, wine has gained increasing recognition as a functional food product that is essential for the treatment and prevention of various kinds of diseases. Saperavi grape variety, which has a high concentration of phenolic compounds, is particularly noteworthy from the perspective of its application in cosmetology practices.

Objectives: In this research, we have determined the recipe and developed the technology of the cosmetic emulgel that contains wine and oil of the Georgian grape variety "Saperavi."

Methods: Modern pharmaco-technological, biopharmaceutical, physicochemical, and structural and mechanical methods were used in the research. The pH of the aqueous fluid extraction of the researched emulgels was determined by the potentiometric titration method. The osmotic activity of emulgels was determined by the gravimetric method. The colloidal stability of emulgels was determined on a laboratory centrifuge. The rheological characteristics of the composition were studied on a Viscometer RVDV-1 T.

Results: Based on biopharmaceutical studies, the recipe of Saperavi emulgel was developed with the following composition: saperavi wine 20.0 g, carbopol 940 - 1.5 g, propylene glycol - 5.0 g, glycerin - 5.0 g, Saperavi grapeseed oil - 5.0 g, Tween 80 - 1.0 g, sodium hydroxide - 0.8 g, sorbic acid - 0.45 g, potassium sorbate - 0.15 g, purified water up to 100.0 g. Using Saperavi emulgel on the clean facial skin of volunteers for 21 days led to a sharp reduction in oiliness, cleansing of pores, reduction in the number of keratinocytes, and noticeable whitening of pigment spots.

Conclusions: Overall, the Saperavi wine cosmetic emulgel formula and technology have been developed through this study. Additionally, the developed emulgel demonstrated some therapeutic benefits on volunteers' skin.

Keywords: Cosmetic emulgel; Saperavi grapeseed oil; Saperavi wine.

INTRODUCTION

According to the latest scientific literature, wine is widely considered a functional food product that significantly treats and prevents various diseases. From the point of view of its use in cosmetology practice, it is particularly noteworthy to use Saperavi (a grape variety), which contains a large number of phenolic compounds (phenol carboxylic acids, flavonoids, anthocyanins), vitamins, micro- and macro-elements, amino acids, etc. Grapevine processing by-products: grape juice, vine leaf extract, grapevine seed phenolic compounds, and essential oil are used successfully in producing medical, preventive, and cosmetic products.[1-10,12,13] The formulation and technology of cosmetic products incorporating wine are topics not extensively covered in the literature.

Soft pharmaceutical forms commonly used in cosmetology, such as ointments, creams, and lotions, may have disadvantages, such as stickiness, which causes discomfort to the patient when administered. Additionally, they are less stable and have a low spreadability coefficient. These elements have boosted the usage of gel in both cosmetics and pharmaceuticals. The gel is a colloidal, 99% liquid mass held in place by fibers of a highly molecular cellular structure and surface tension. The gel's key drawback is its inability to distribute and integrate hydrophobic preparations to the target spot. Emulsion gels, which include hydrophobic chemicals in their oily portions, can remedy this issue. Emulge is the term used to describe a mixture of gel and emulsion.[14]

Emulgels have the beneficial properties of both emulsions (two-phase system) and gels (high stability). The emulgel's medicinal component passes through the corneal layer of the skin. The surfactants (amphoteric surface-active chemicals) and the fatty acids of the oil phase of the emulgel improve its absorption and accumulation of medicinal substances into the skin.[11]

The current study aimed to define the composition of the cosmetic emulgel, composed of wine and oil from a Georgian grape variety - Saperavi, and develop the production technology.

METHODS

Modern pharmaco-technological, biopharmaceutical, physicochemical, structural, and mechanical methodologies were employed in this research. The uniformity of emulgel

was defined according to the relevant monograph of the International European Pharmacopoeia. According to the current edition of International European Pharmacopeia, the pH of the aqueous fluid extraction of the researched emulgels was determined by the potentiometric titration method on the universal ionomer EV-74. The osmotic activity of emulgels was determined by the gravimetric method. The osmotic activity was determined in a dialyzer (semipermeable membrane-cellophane with a diameter of 65 mm and pore size of 0.025 mm). The colloidal stability of emulgels was determined on a laboratory centrifuge: type 310 (METRONEX, Poland) with the reference method number 29188.3-91 - "Cosmetic products; Method for determination of emulsion stability." Thermal stability was conducted under conditions of extreme temperature changes - according to reference method 18-21-81-cosmetic creams. The dispersion characteristics of the research objects were determined by the microscopy method.

We have studied the rheological characteristics of the composition on a Viscometer RVDV-1 T (equipped with a circulating water bath and a temperature gauge), using an N4 spindle (25±1°C) at different rotation frequencies.

During the current study, we have defined the structural viscosity at a temperature of 20±0.2°C. We used a portion of the sample (weighing 25 g), placed it in a cylinder (cylinder system S/S1), and recorded the value of the viscometer at each indicator of the deformation rate with a time interval of 30 seconds. At the maximum value of the rotation speed of the system, we delayed the sample for 10 min until the complete breakdown of the structure. Then, to restore the structure, we delayed the samples for 10 minutes and again recorded the value of the viscometer against the background of the decrease in the rotation speed of the cylinder at each indicator of the speed deformation. Based on our results, we created a shear speed (sec-1) and shear stress (MPa) graph.

Mechanical stability was calculated based on rheological data with the formula MC= t1/t2, where t1 is the shear stress during the increasing (upward) shear rate, and t2 is the shear stress decreasing (downward) during the shear rate.

The spreadability was determined using the wooden block and glass plate method. For this, we placed 20 g of emulgel on a wooden board, covered it with two glass slides, timed, and then separated the slides. We expressed the spreadability using the following formula: S=M*L/T, where S is the distribution (g/cm/s), M is the weight of the sample, L is the space of the glass slide, and T is the time in seconds that takes the separation of the glass slides.

The release of biologically active substances (flavonoids) from the investigated emulgels was studied using Franz diffusion cells, followed by spectrophotometry.

In order to determine the therapeutic effect of the composition of three emulgels, an experiment was conducted on female volunteers of different ages (52, 55, and 63 years old). Emulgel was applied to the volunteers' faces and skin daily in the morning. The period of experiment of the therapeutic effect was 21 days. A unique facial skin diagnostic device determined the skin surface oiliness, pore size, the number of keratinocytes, and the presence/absence of pigment spots. Pictures of the skin were taken with the skin diagnostic device before using the emulgel and after the treatment course.

The statistical processing of the experiment results was carried out according to the method described in State Pharmacopeia XI. Each experiment was performed independently 3-times before statistical analysis. Results were expressed as mean ± SEM.

RESULTS

At the first stage of the research, nine variants of the emulgel composition containing Saperavi wine and oil were prepared. The ratio of excipients that made up the emulgel was selected based on the analysis of literature data. The compositions are given in Table 1.

TABLE 1. Composition of the experimental research formulations of Saperavi emulgel

Ingredients	Formulation numbers and amount of the components, g								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
	Emulsion								
Saperavi wine	15	15	15	15	15	15	15	15	15
Saperavi oil	3	4	5	6	4	5	6	4	5
Propylene glycol	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Glycerol	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Tween 80	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Sorbic acid	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45
Potassium sorbate	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Purified water	Up to 50								
Gel									
Carbopol	0.5	1.0	1.5	-	-	-	-	-	-
Xanthan gum				0.5	1.0	1.5			
HPMC	-	-	-	-	-	-	0.5	1.0	1.5
Sodium hydroxide 1N	0.8	0.8	0.8						
Purified water	Up to 50								
Emulsion gel	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1

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Emulgels from the formulation mentioned above were prepared in two stages. At the first stage, gels were prepared to take into account the physicochemical properties of gel-forming substances, namely, by delaying dispersed carbopol and xanthan gum in distilled water, adding hydroxypropylmethylcellulose to distilled water with a temperature of 80°C and further delaying for 12 hours at room temperature. Mixing was performed in each case using a moderate-speed mechanical stirrer (1000 rpm).

Carbopol 934 was used for the formulation of the compositions F1, F2, and F3; xanthan gum was used for F4, F5, and F6, and hydroxypropylmethylcellulose - for F7, F8, and F9. In the second stage, emulsions were prepared: the oily phase of the emulsion was presented by the Saperavi oil, in which Tween-80 and Sorbic acid were dissolved. The aqueous phase was presented with Saperavi wine and water, which were measured according to the recipe. Both the oil and water phases were heated up to 70 - 80°C. The water phase was added to the oil phase under constant stirring conditions until the mass was cooled, and in the final stage, glycerin and propylene glycol were also added under stirring conditions. The formulated emulsion was gently mixed with the gel in a 1:1 ratio to obtain an emulgel.

Before starting the analysis, we visually analyzed the experimental samples of emulgels. They had homogeneous gel-like systems of light purple. All the samples were stable and homogeneous, and no separation between lipophilic and hydrophilic phases was observed in them.

Prepared emulgels were evaluated according to organoleptic indicators: pH, colloid stability (during centrifugation), and thermostability. Table 2 represents the results of the analysis.

The data in Table 2 shows that the first, second, fourth, fifth, seventh, and eighth compositions are not thermostable. Accordingly, Further studies continued on the third, sixth, and ninth compositions. One of the essential properties of gels is the presence or absence of an osmotic effect. The osmotic effect is essential in maintaining the skin's moisture and enhancing its effectiveness.

The osmotic activity was determined by the dialysis method using a semipermeable membrane. The amount of the absorbed water was determined gravimetrically and expressed as a percentage of the initial mass. The results are shown in Table 3.

Table 3 shows that F3 composition is distinguished by its humectant activity; the amount of water absorbed by it is 28.5%, which indicates its low osmotic activity. F6 and F9 compositions have high and almost equal osmotic activity.

To select the optimal gel recipe for comparative evaluation, we studied the degree of release of flavonoids by measuring quercetin release with the Franz diffusion cells system, followed by spectrophotometry. The obtained results are given in Table 4.

TABLE 2. Results of determination of organoleptic and physicochemical indicators of the experimental compositions of Saperavi emulgel

Quality index	Formulation numbers								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Oily feel	0	0	0	0	0	0	0	0	0
Spreadability	+++	+++	+++	+++	+++	+++	+++	+++	+++
Ease of absorption	+++	+++	+++	+++	+++	+++	+++	+++	+++
Homogeneity	+++	+++	+++	+++	+++	+++	+++	+++	+++
Stickiness	+++	+++	+++	+++	+++	+++	+++	+++	+++
Water dilution	+++	+++	+++	+++	+++	+++	+++	+++	+++
Odor	+++	+++	+++	+++	+++	+++	+++	+++	+++
Color	P	P	P	P	P	P	P	P	P
pH	5.8 ± .045	5.9 ± .034	6.0 ± .057	6.1 ± .031	5.9 ± .065	6.4 ± .058	6.2 ± .042	6.0 ± .038	5.9 ± .054
Colloid stability	C	C	C	C	C	C	C	C	C
Thermal stability	DC	DC	DC	DC	DC	DC	DC	DC	DC

Abbreviations: C: conforms; DC: does not conform; P: purple.

TABLE 3. Statistically processed results of determination of the osmotic activity of Saperavi emulgel

Composition of emulgels	Absorbed solution (%)	Absorption time, hour (hr)
Control (sodium chloride 10% solution)	18.5± 2.48	8
F3 composition	28.5±4.28	8
F6 composition	146.5±3.78	8
F9 composition	166.3±3.78	8

According to the results given in Table 4, It is noticeable that the kind of polymer impacted how flavonoids were released from emulgels. It can be categorized as F9<F6<F3. Flavonoids are maximally released from the F3 gel composition (75.79%) during exposure. From F6 and F9 compositions, practically equal amounts of active substance are released, 67.82% and 63.55%, respectively.

Based on the conducted biopharmaceutical studies, the F3 composition of the gel stands out with the best indicators at almost all stages of the experiment.

We investigated the rheological characteristics of emulgel in order to predict its technological and consumer properties. Flow rheograms were created based on the data (Fig.1).

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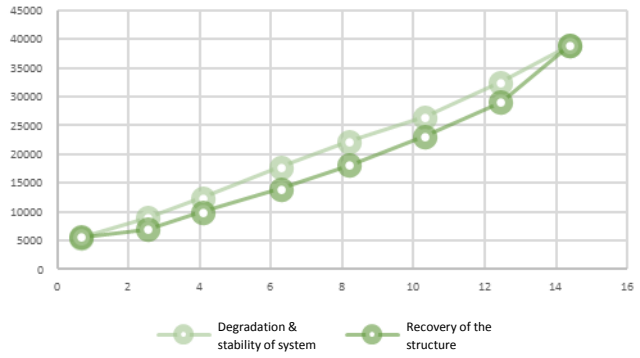
TABLE 4. Statistically processed results of determining the degree of release of flavonoids from Saperavi emulgel (%)

Time (h)	Composition (formulation) N and dynamics of flavonoid release (%)		
	F3	F6	F9
1	12.24±0.31	9.18±0.23	8.43±0.27
2	17.32±0.23	11.64±0.30	10.70±0.25
3	21.76±0.16	12.21±0.24	13.45±0.34
4	26.54±0.34	16.66±0.48	17.86±0.29
5	31.66±0.32	23.23±0.24	20.52±0.46
6	36.71±0.24	29.56±0.68	23.65±0.24
7	41.68±0.23	35.19±0.28	30.87±0.54
8	47.34±0.29	42.48±0.81	36.40±0.64
9	55.65±0.47	49.34±0.52	42.17±0.23
10	62.69±0.37	55.64±0.39	48.88±0.89
11	68.37±0.48	61.55±0.72	55.67±0.42
12	75.79±0.41	67.82±0.65	63.55±0.64

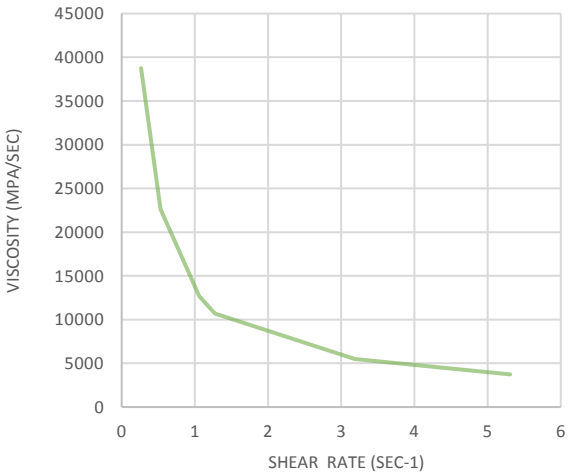
FIGURE 1. Rheogram of F3 composition emulgel



The graph of the relationship ratio of "shear rate and shear stress" of the experimental composition is given in Figure 1. The diagram (rheogram) results are non-linear by nature. They are presented in the form of a hysteresis loop. The upward curve shows the degradation and stability of the system concerning load. Emulgel retains residual deformation even after the structure is broken down; the downward curve corresponds to the recovery of the structure with the reduction of load (impact). The hysteresis loop shows that the research object has thixotropic properties, indicating an optimal soft consistency, good distribution capacity, and extrusive properties (ability to release from the tube).

One of the distinguishing characteristics of emulgels is viscosity. The results of the study of the relationship between the "shear rate and viscosity" of the composition are given in Figure 2. The graph shows that there is an inverse relationship between the mentioned values; with the gradual increase in speed, the viscosity decreases, which is related to the breakdown of the emulgel structure and, at the same time, it determines its optimal distribution capacity.

FIGURE 2. The relationship of "shear rate versus viscosity" of the F3 composition



Using the rheological data, we calculated the mechanical stability of the emulgel as well as the dynamic liquefaction coefficient to determine the extrusion properties (Tab.5).

TABLE 5. Coefficients of mechanical stability and dynamic liquefaction of Saperavi emulgel

Name of the drug	Mechanical stability	Dynamic liquefaction coefficient (KD1, %)
Saperavi	1.71	67.26

The indicator of mechanical stability (Tab.5) testifies to a minor breakdown of the framework of the system structure, which indicates the restoration of the structure by the system. This also proves that the system withstands mechanical impact during the homogenization process.

The high index of the dynamic liquefaction coefficient (Tab.5) testifies to the suitable distributive property of the provided emulgel. It characterizes them as forms capable of sufficient liquefaction in the mixing mode, the property of easy filling of the tube, and the high-quality dispersion of the active pharmaceutical ingredient (API) that is added to the base.

Thus, based on the results of the rheological research, the developed Saperavi emulgel appears to have a dispersion system with elastoplasticity properties.

We performed the emulsion system's dispersion analysis by determining the diameter of the particles in the dispersion phase with a light microscope under the conditions of 100X magnification (Tab.6).

According to the results of the determination of oil phase particle sizes of Saperavi emulgel, the studied emulgel is polydisperse. In the studied emulgel, the oil phase particles of the second and third groups, 3 to 10 µm in size, were predominantly observed, 66% of which were 4.59±0.7 µm in size. A large amount of large oil phase particles was

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observed - 23% (7.12±0.6μm). This is consistent with the literature data, in which the emulsion system of a similar type is rarely mono and finely dispersed.

TABLE 6. Results of the determined oil phase particle sizes of Saperavi emulgel (P<0.05, n=1000)

Fraction Group Size	Sizes (μm)	Saperavi emulgel	
		The average diameters of oil phase particles (μm)	Content, %
I	Up to 3	3.24±0.6	4
II	3-5	4.59±0.7	66
III	5-10	7.12±0.6	23
IV	Above 10	14.8±1.2	7

The quality of the drug, its therapeutic effectiveness, and consumer properties are influenced by the preparation technology. From the mentioned point of view, the stages of diluting, thawing, and mixing are essential during emulsification, during which the aggregate state of medicinal and auxiliary substances changes, and the areas of contact surfaces between them also change. Based on conducted pharmaco-technological and physico-chemical studies, technology has been developed, and a technological scheme of Saperavi emulgel has been drawn up with a specific sequence of technological stages.

According to the outcomes of the experiment done on female volunteers to assess the therapeutic effect, the usage of Saperavi emulgel on the clean facial skin of volunteers for 21 days led to a sharp reduction in oiliness, cleansing of pores, reduction in the number of keratinocytes, and noticeable whitening of pigment spots.

DISCUSSION

Based on biopharmaceutical studies, the recipe of Saperavi emulgel was developed with the following composition: Saperavi wine 20.0 g, carbopol 940 - 1.5 g, propylene glycol - 5.0 g, glycerin - 5.0 g, Saperavi grapeseed oil - 5.0 g, Tween 80 - 1.0 g, sodium hydroxide - 0.8 g, sorbic acid - 0.45 g, potassium sorbate - 0.15 g, purified water up to 100.0 g.

Based on the dynamics of the release of active substances, which have been studied concerning gel-forming substances, it is established that different types of gelling agents affect the release of active substances from emulgels differently.[15-21] Flavonoids are maximally released from the emulgel, prepared based on 1.5% carbopol. During the study of the rheological characteristics of the experimental emulgel, it was discovered that there was an inversely proportional relationship between the viscosity efficiency and the shear speed values at different stages in all the analysis intervals. Also, the rheological characteristics of the emulgel are within the parameters of the technological optimum effectiveness of soft dosage forms. According to the excellent quality indicators: homogeneity, pH of the aqueous extract, colloidal and thermal stability, and viscosity, the experimental emulgel meets the requirements of the State Pharmacopoeia for soft drug forms.

CONCLUSIONS

The developed Saperavi emulgel also demonstrated some therapeutic benefits on women volunteers' skin.

AUTHOR AFFILIATION

1 Department of Pharmaceutical and Toxicological Chemistry, Faculty of Pharmacy, Tbilisi State Medical University, Tbilisi, Georgia;
2 Department of Pharmaceutical Technology, Faculty of Pharmacy, Tbilisi State Medical University, Tbilisi, Georgia.

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