DEVELOPMENT OF THE EMULGEL FOR THE ANDROGENIC ALOPECIA TREATMENT

Inna Yarema
Department of Organization and Economics in Pharmacy and Drug Technology[1]
yarema.inna88@gmail.com

Mariana Fedorovska
Department of Organization and Economics in Pharmacy and Drug Technology[1]

Natalia Polovko
Department of Drug Technology
National University of Pharmacy
53 Pushkinska str., Kharkiv, Ukraine, 61002

[1]*Ivano-Frankivsk National Medical University*
2 Halytska str., Ivano-Frankivsk, Ukraine, 76018

Abstract

Androgenic alopecia (AGA) is the most common alopecia that is heritable, androgen-dependent and occurs in both sexes with defined patterns such as Male pattern hair loss in men and Female pattern hair loss in women. AGA affects at least 50 % of men by the age of 50 years, and up to 70 % of all males in later life.

The aim. The research was aimed to substantiate the optimal concentration of excipients and active pharmaceutical ingredients (APIs) of the emulgel intended for the topical treatment of androgenic alopecia.

Materials and methods. In this study the samples of the emulgel bases containing different carbomer Ultrez10 concentrationsin the range of 0.3–0.6 % and its neutralizers (0.1 % of potassium sorbate and 0 % or 0.2 % of triethanolamine) were used. Colloidal and thermal stability, pH, rheological properties (structural viscosity, mechanical stability, degree of thixotropy) of these samples were determined. The emulgel samples with different percentages of the Serenoa repens dry extract and the Sophora japonica tincture were used in the biopharmaceutical studies. The samples of the emulgel with the antioxidant butylhydroxytoluene different concentrations (0 %, 0.01 %, 0.02 %, 0.03 %) were used to determine acid value during 1 year of the emulgel storage.

Results and discussion. It was experimentally substantiated the optimal ratio of the emulgel ingredients that provide good APIs release and necessary consumer properties of the semi-solid remedy like application compliance, safety and storage stability.

Conclusions. Physicochemical, rheological and biopharmaceutical properties of emulgel bases have been studied. It was found that the base No. 2 (in which the concentrations of Carbomer Ultraz 10, potassium sorbate and triethanolamine are 0.3 %, 0.1 %, 0.2 % respectively) possessed the optimal properties. Considering the results of the complete range of experimental research it was developed the final formulation of the emulgel intended for AGA treatment which included the concentration of the APIs, neutralizers, preservatives, antioxidant and fragrance.

Keywords: androgenic alopecia, emulgel, Serenoa repens dry extract, Sophora japonica tincture, excipients, physicochemical and biopharmaceutical studying.

DOI: 10.21303/2504-5679.2020.001427

1. Introduction

Skin diseases and pathological conditions significantly affect human psycho-emotional health and quality of life [1, 2]. Therefore, effective prevention and treatment of dermatological diseases is a significant task of contemporary medicine. Excessive hair loss or alopecia is one of the most common dermatological pathologies. Alopecia is a multi-etiologic disease that is divided into different types such as androgenic alopecia (AGA), telogen effluvium, anagen effluvium, alopecia areata, scarring alopecia, etc. [3, 4].

AGA is the most common alopecia that is heritable, androgen-dependent and occurs in both sexes with defined patterns such as Male pattern hair loss (MPHL) in men and Female pattern hair

loss (FPHL)in women. AGA affects at least 50 % of men by the age of 50 years, and up to 70 % of all males in later life. Epidemiological situation of FPHL is fewer in number but AGA incidence among women also tends to increase with age. AGA becomes a medical problem when the hair loss is excessive, premature and stressful to the patients, especially for women and young men [5].

In AGA, continuous miniaturization of sensitive hair follicles takes place that results in the conversion of thin terminal hairs into fine vellus hairs. A key role in the AGA development is played by the interrelationship between male sex hormones testosterone (TS) and dihydrotestosterone (DHT), androgen receptors (AR) in the genetically predisposed hair follicle of the temporal and vertex regions and 5-α-reductase (5AR) type-2 enzyme (it converts intra-follicular TS to the more potent DHT). Following binding to the AR, DHT leads to miniaturization and in general a reduction of hair growth rate [6]. Modern scientific research confirms the involvement of new mechanisms in AGA development, such as oxidative stress, micro-inflammation, prostaglandin misbalance [5, 7].

For AGA prevention and treatment different types of active pharmaceutical ingredients (APIs) are used such as synthetic capillary vasodilators (minoxidil, aminexil), 5-α-reductase inhibitors (finasteride, dutasteride, β-sitosterol, lauric acids), androgen receptor blockers (spironolactone, cyproterone acetate, fluoride, phytosterols), cutaneous irritants (20 % Capsicum annum L. tincture, Turpentine essential oil, Spongilla lacustris L. powder), natural and synthetic vasoconstrictors and vasoprotectors (aescin, quercetin, routine, troxerutin, xanthinol nicotinate, pentoxifylline), antioxidants of plant origin (flavonoids, hydroxycinnamic acids, phytosterols, carotenoids, etc.) [3, 4, 8–10].

Finasteride (FS),a specific inhibitor of the 5AR-type II enzyme, is the only United States Federal Drug Administration (FDA) approved oral API for AGA treatment in men. Minoxidil (MNX) is the other FDA approved topical API for AGA treatment, both in men and women. MNX apparently acts by increasing follicular vascularity as a potassium channel opener. It increases the blood supply to the scalp allowing more oxygen, blood and nutrients that is why prolonging anagen and shortening telogen and also convertingpartially miniaturized hair follicles to terminal hair [7, 11]. However, these APIs are characterized with side effects and contraindications. In particular, FS weakens the erectile function and contraindicated in fertile women due to fetus feminization; MNX negatively affects the cardiovascular system, exacerbates hair loss after the treatment cessation [12].

Taking into account the above-mentioned, it is important to develop an effective and safe topical medicine with plant APIs, which would affect the main links of the AGA pathological process. Serenoa repens dry extract (SRDE) and Sophora japonica tincture (SJT) were chosen as APIsof the developing semi-solid remedy. SRDE contains a group of free and conjugated with fatty acids or sugars phytosterols (β-sitosterol, campesterol, stigmasterol), fatty acids (lauric, linoleic, linolenic, etc.). These biological active substances (BAS) reveal the anti-androgenic effect through 5-α-reductase inhibition and blocking androgen receptors, possess antioxidant and anti-inflammatory properties [13]. SJT contains a high concentration of flavonoids, which act as antioxidants and vasoprotectors [14].

Emulgel was chosen as a semi-solid dosage form of the developing medicine. Emulgels are emulsion gels which are hydrogels containing randomly distributed oil microdroplets. They have many advantages in comparison with emulsionsor gels like as:

– incorporation of hydrophobic and hydrophilic APIs;
– better stability with less concentration of emulsifiers;
– better rheological properties;
– controlled release;
– improve patient compliance and suitability when medication applied on the scalp;
– ability to easily withdraw the medicineafter its application [15].

According to the results of experimental studies, the optimal ratio of emulsifiers (polysorbate-20, cetyl alcohol) and a gelling polymer (carbomer Ultrez 10) of the emulgel base was chosen [16]. An increase in structural viscosity was observed when a preservative potassium sorbate was added into the base [17]. Potassium sorbate is a salt formed by a strong base and a weak acid,

so in an aqueous solution the substance undergoes hydrolysis and the solution becomes alkaline. Accordingly, potassium sorbate additionally acts as a neutralizer of the carbomer in the developed base [16]. Considering these observations, the next stage of our research was to find the rational concentrations of the carbomer and its neutralizers (potassium sorbate and triethanolamine) which affect the emulgel rheological properties.

Experimental studies on laboratory animals usually are carried out to substantiate the API concentration of semi-solid medicines when its pharmacological activity is not related to the antimicrobial effect. However, such experiments require a large number of animals, they are time-consuming, expensive and contradictory to modern ethical standards. Therefore, the use of alternative experimental methods (biopharmaceutical, biological "in vitro") is a promising research direction of the API concentration selection [16].

The emulgel contains components which are easily oxidized during storage, namely SRDE and pumpkin seed oil (the ingredient of the oil phase). Therefore, to extend theshelf life of the medicine it is necessary to use antioxidants (AO). To reduce the excipient and API oxidation, direct (butylhydroxytoluene, butylhydroxyanisole, tocopherols, ascorbic acid, etc.) and indirect (sodium EDTA, multi-basic acids) AO are used. To achieve the emulgel oxidation stability, butylhydroxytoluene (BHT) was chosen as AO. BHT is a synthetic analogue of tocopherol. BHT is thermostable in contrast to the latter. Compared to butylhydroxyanisole (which characterized with unpleasant phenolic odour) BHT is odourless and additionally possesses the antimicrobial properties [18]. Considering the above-mentioned, at the final experimental stage of the emulgel composition developing it is important to select the BHT optimal concentration.

The aim of the research. This research was aimed to substantiate the optimal concentration of the excipients and the APIs of the emulgel intended for the topical AGA treatment.

2. Materials and methods

1. Samples of the emulgel base with the different concentrations of the excipients (carbopol Ultrez 10, potassium sorbate, triethanolamine) were used for the physico-chemical and rheological studying:

– 1 – 0.3 %carbomerUltrez 10, 0.1 % potassium sorbate, 0 % triethanolamine;
– 2 – 0.3 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0.2 % triethanolamine;
– 3 – 0.4 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0 % triethanolamine;
– 4 – 0.4 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0.2 % triethanolamine;
– 5 – 0.5 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0 % triethanolamine;
– 6 – 0.5 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0.2 % triethanolamine;
– 7 – 0.6 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0 % triethanolamine;
– 8 – 0.6 % carbomer Ultrez 10, 0.1 % potassium sorbate, 0.2 % triethanolamine.

2. Samples of the emulgel with the different APIs concentrations used for the biopharmaceutical studying:

– 6 samples of the emulgel containing the SRDE in the range of 1–6 % with 1 % increments;
– 5 samples of the emulgel containing the SJT different concentrations, namely 3 %, 5 %, 7 %, 10 %, 12 %.

3. Samples of the emulgel containing the BHT different concentrations, namely0 %, 0.01 %, 0.02 %, 0.03 %.

Basic principles of the State Pharmacopoeia of Ukraine (SPhU) 2.0 and the State Standard of Ukraine (SSU) No. 4765:2007 "Cosmetic creams. General technical conditions" 2008 were considered during the development of the emulgel with SRDE and SJT.

Experimental test samples of the emulgel base and emulgel were obtained with alternate adding of both phases to the emulsifiers with the application of 2000 r/min homogenisation speed during 30 min [16].

Colloidal and thermal stability, pH, rheological properties (structural viscosity, mechanical stability, degree of thixotropy) of the different emulgel base samples were evaluated. Biopharmaceutical studying (BAS releasing in agar gel) was carried out in order to substantiate the APIs concentrations. The acid value was evaluated in order to choose the BHT concentration.

2. 1. Colloidal and thermal stability

Colloidal stability (centrifugation test or mechanical stress) was determined with laboratory centrifuge ("Mechanika precyzyjna", Poland). The test tubes were filled with 2/3 volume (approximately 9 g) of the test samples and weighed with 0.01 g accuracy. The samples then were centrifuged for 5 min at a speed of 5000 rpm (the relative centrifugal force was approximately 5,000 g). At the end of each cycle, the samples were checked to see whether there was any change [19–21].

Thermal stability was determined with the emulgel base samples, each of which was placed in glass tubes in an amount of 8–10 ml. The filled tubes were thermostated (TC-80 MG thermostat) at 42.5±2.5 °C for 7 days. The samples were then transferred to the refrigerator at 6±2 °C for 7 days. Thereafter, the test tubes were kept at room temperature for 3 days. The result was evaluated visually. If the aqueous phase formation was not observed in the glass tube the sample was considered as stable [19, 21].

2. 2. pH

pH measuring was performed potentiometrically in a 10 % emulgel base aqueous mixture with the pH-meter EB-74 at 20 ºC (SPhU 2.0, 2.2.3) [22].

2. 3. Rheological studying

Rheological studying of the experimental samples (structural viscosity, mechanical stability, the degree of thixotropy) was carried out with the Brookfield viscometer (Viscotech Hispania, SL), with SC4-21 spindle for chamber volume of 8.3 ml at a temperature of 20 ºC (SPhU 2.0, 2.2.10) [22]. A sample of 8.3 ml was placed in the chamber and the spindle was lowered into it, which was switched into the rotation. The structural viscosity η (MPa·s), shear stress τ (Pa), shear rate Dr (s^{-1}) were measured by increasing the spindle speed from 20 to 100 rpm, reaching constant values at maximum rotation and subsequent reduction in rotational speed.The value of the experimental bases mechanical stability (MS) was determined as the ratio of the shear stress before the destruction (τ_1) to the shear stress after the destruction (τ_2) [23]:

$$MS=\tau_1/\tau_2.$$

2. 4. Biopharmaceutical studying

To carry out the biopharmaceutical studying the 2 % agar gel was prepared. Different analytical reagents for SRDE and SJT identification were used. Sudan III alcohol-glycerol solution in 25 % amount, which reacts with fatty acids of SRDE, and 10 % of Iron (III) chloride solution in 5 % amount, which reacts with the SJT phenolic compounds, were added to the agar gel solutions respectively. Prepared agar solutions were filled in Petri dishes in the amount of 30 ml. In Petri dishes, six holes of an 8 mm diameter were made. Agar holes were filled with the samples (0.5 g) and incubated in a thermostat at 37 °C for 24 hours. The BAS diffused in agar gel and formed with the reagents coloured zones (dark green with Iron (III) chloride and bright orange with Sudan III). The zone diameter was measured every hour during 6 hours, and the last measurement was carried out after 24 hours. If necessary (in the ellipse formation) the greater and lesser diameters were measured [24, 25].

2. 5. Acid value (AV)

The acid value is the number of mg of potassium hydroxide required to neutralize the free acid in 1 g of the substance (the sample). Recommended procedure: about 10 g of the sample was accurately weighed into a 250 ml flask, and 50 ml of a mixture of equal volumes of ethanol (~750 g/l) and ether was added, which was neutralized with potassium hydroxide (0.1 mol/l) after adding 1 mL of phenolphthalein/ethanol. The mixture was titrated with potassium hydroxide (0.1 mol/l), constantly shaking the flask until a pink colour was obtained, which persisted for 15 seconds. The volume of titrant (ml) required was recorded. AV was calculated using the following formula:

$$AV=5.611V/m,$$

where 5.611 – the mass of potassium hydroxide (mg) that is equivalent to 1 ml of 0.1 M potassium hydroxide solution; V – the volume of 0.1 M potassium hydroxide solution (titrant) used, ml; m – emulgel sample mass, g (SPhU 2.0, 2.5.1) [22].

3. Results

Measurement results of pH, rheological properties, the colloidal and thermal stability of the emulgel base samples are summarised in **Table 1**.

Table 1

Physicochemical and rheological characteristics of the emulgel base samples, n=5

Sample No.	pH	Structural viscosity (η, MPa·s, 20 rpm, Dr 18,6 s^{-1}, 20°C)	Mechanical stability	Colloidal stability	Thermal stability
1	4.93±0.11	1560±14	1.09	Stable	Stable
2	5.01±0.13	3560±20	1.10	Stable	Stable
3	4.90±0.10	3908±30	1.11	Stable	Stable
4	5.10±0.13	5500±13	1.29	Stable	Stable
5	4.82±0.13	5120±14	1.09	Stable	Stable
6	5.12±0.13	7600±10	1.15	Stable	Stable
7	4.77±0.16	5376±26	1.08	Stable	Stable
8	5.10±0.16	7801±20	1.25	Stable	Stable

Rheograms of the ratio "shear rate – shear stress" of the samples of the emulgel base are presented in **Fig. 1**.

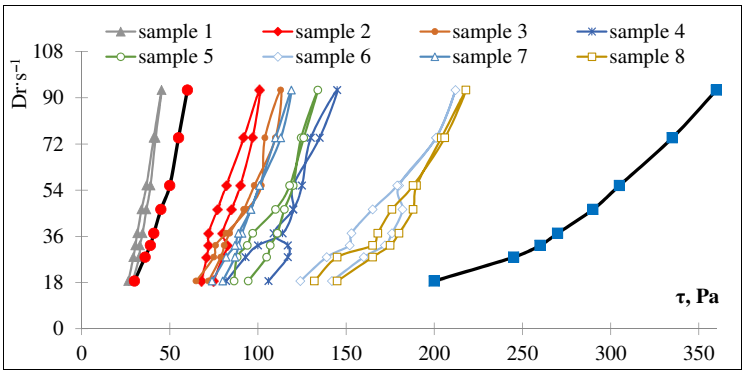

Fig. 1. Rheograms of "shear rate – shear stress" correlation of the emulgel base samples

To substantiate the APIs concentrations in the emulgel formulation, the biopharmaceutical studies were carried out with the method of the BAS diffusion into the agar gel. **Fig. 2** shows the diagrams of the Serenoa repens dry extract BAS penetration in the agar gel depending on the API concentration in the emulgel.

To select SJT concentration in the emulgel formulation, a different amount of this API was mixed with SRDS (3 %), the mixture was added into the base and the samples were used in biopharmaceutical research. Diagrams of the Sophora japonica tincture BAS penetration in the agar gel depending on the API concentration in the emulgel are shown in **Fig. 3**.

AV is an important quality indicator because it can easily increase during the storage of the semi-solid dosage form, which is caused by the hydrolysis and oxidation processes of plant lipoids. In the emulgel formulation the BHT antioxidant effect was evaluated considering AV fluctuation during 1 year of the emulgel storage (**Table 2**).

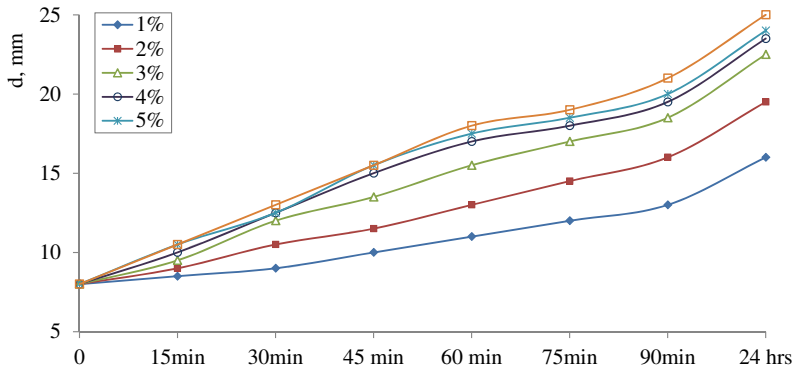

Fig. 2. Diagrams of the Serenoa repens dry extract BAS penetration in the agar gel depending on the API concentration in the emulgel

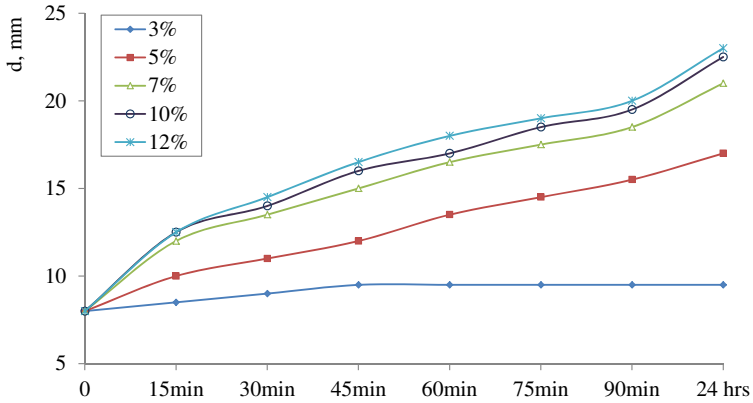

Fig. 3. Diagrams of the Sophora japonica tincture BAS penetration in the agar gel depending on the API concentration in the emulgel

Table 2

Study of the BHT influence on the AV during the emulgel storage, n=5

Sample No	BHT concentration in emulgel, %	Acid value, mg KOH/g
1	**2**	**3**
Freshly prepared samples		
1	0	1.78±0.04
2	0.01	1.78±0.06
3	0.02	1.79±0.05
4	0.03	1.79±0.03
Samples after 3 months of storage		
1	0	2.12±0.04
2	0.01	1.88±0.03
3	0.02	1.81±0.02
4	0.03	1.81±0.05
Samples after 6 months of storage		
1	0	2.42±0.04
2	0.01	1.94±0.03
3	0.02	1.85±0.03
4	0.03	1.84±0.02

Continuation of Table 2

1	2	3
Samples after 9 months of storage		
1	0	2.87±0.03
2	0.01	2.03±0.05
3	0.02	1.90±0.03
4	0.03	1.88±0.04
Samples after 12 months of storage		
1	0	3.25±0.04
2	0.01	2.11±0.03
3	0.02	1.92±0.03
4	0.03	1.91±0.04

To increase the emulgel consuming properties, 0.2 % lavender essential oil was used in the formulation. The selected fragrance, in addition to a pleasant floral scent, possess the antiseptic properties and is used in anti-dandruff remedies.

Thus, considering the complex experimental physicochemical, rheological, biopharmaceuticaland other studies the final composition of the emulgel intended for AGA treatment was developed (**Table 3**). The emulgel is a homogeneous, viscous mass of the yellow-green creamy consistency with the distinctive scent of the lavender essential oil.

Table 3
Formulation of the emulgel intended for the AGA treatment

Ingredients	Quantity, g
Serenoa repens dry extract	3.0
Sophora japonica tincture	7.0
Pumpkin seed oil	5.0
Polysorbate-20	3.0
Cetyl alcohol	3.0
Carbomer Ultrez 10	0.3
Triethanolamine	0.2
Potassium sorbate	0.1
Salicylic acid	0.1
Butylhydroxytoluene	0.02
Lavender essential oil	0.2
Purified water	up to 100.0

The list and ratio of the emulgel ingredients are selected in such a way as to provide good APIs release and necessary consumer properties of the semi-solid remedy like odour, application compliance, safety and storage stability.

4. Discussion

As can be seen from the results of the rheological study, there is a direct correlation between increasing the structural viscosity and the carbomer concentration. Samples No. 1, 3, 5 and 7 with-

out 0.2 % of triethanolamine possess the lower structural viscosity than samples No. 2, 4, 6 and 8 which have the combination of both carbomer neutralizers.

The human skin surface is slightly acidic with pH in the range between 4 and 6. Such skin pH maintains homeostasis of the epidermal barrier and viability of resident microflora. All experimental samples have pH within physiological range. However, the pH increasing of the emulgel samples depends on the triethanolamine presence in the formulation.

The appropriate MS value (optimum value equals 1,0) indicates the emulgel ability to withstand mechanical stress during processing, such as compounding or manufacturing, and storage. The experimental samples have different MS values, mainly No. 1, 2, 3, 5 and 7 have MS close to optimum; No. 4, 7 and 9, samples with the higher carbomer concentration and structural viscosity, have MS values from 1.15 to 1.29.

Colloidal and thermal stability of the experimental samples is not influenced by the concentration or presence of the excipients in the emulgel bases since all samples are stable.

Semi-solid dosage forms (gels, creams, emulgels, etc.) in which structural viscosity is in the range of 2000-10000 MPa·s at 20 rpm possess optimal rheological parameters. The emulgel intended for application on the scalp have to be easily removedand its texture should not be heavy. That is why the optimum viscosity values of the developing remedyare considered in the range of 2000–5000 MPa·s. The emulgel should exhibit pseudoplasticity. It should be dispensable from a container but at the same time should be spread over the scalp with light pressure [23, 26].

Study of the "shear rate – shear stress" correlation (**Fig. 1**) showed that all samples are characterized with the pseudoplastic flow and possess thixotropic properties because ofthe present hysteresis loops of the ascending and descending curves. The larger the hysteresis loop square, the easier a semi-solid medicine is applied on the skin and extruded from a container. As can be seen in **Fig. 1**, only in two samples (No. 1 and 2) the descending and ascending curves do not intersect and the hysteresis loops have a continuous area. However, the hysteresis loop that characterizes the base No 1 is situated beyond the rheological optimum.

Thus, taking into account all the studied parameters, the sample No. 2 has improved physicochemical and rheological properties, namely, the structural viscosity at 20 rpm is 3560±20 MPa·s (the optimum range is 2000–5000 MPa·s), MS – 1.1 (optimum = 1.0), the base has pseudoplastic flow and a high level of thixotropy, the ascending and descending curves do not intersect and form a large area of hysteresis; pH value 5.01±0.13 is within the skin physiological range.

Biopharmaceutical studies in the selection of SRDE concentrations represents that with the API concentration growth from 1 % to 3 % the speed of its BAS diffusion intensively increases, namely, for the sample with 1 % of the API the color zone changes from 8 mm (the initial diameter of all holes) to 16 mm, for 2 % API - to 19.5 mm, for 3 % API – to 22.5 mm respectively (**Fig. 2**). Further the API concentration increase from 4 % to 6 % does not significantly change the level of the BAS release since the colour zone diameters at the end of the experiment are 23.5 mm, 24 mm and 25 mm respectively. Considering the BAS release, it was chosen 3 % of the SRDE concentration. The higher API percentage (with slightly better release rates) can significantly affect the rheological properties of the emulgel and would rise production expenses.

According to the results of determining the SJT concentration it was found that with API concentration growth from 3 % to 7 % the speed of phenolic BAS diffusion intensively increases, namely, for the sample with 3 % of the API the colour zone changes from 8 mm to 9.5 mm, for 5 % API – to 17 mm, for 7 % API – to 21 mm respectively (**Fig. 3**). Further concentration increase does not significantly change the level of the BAS release since the colour zone diameters of the experiment samples with 10 % and 12 % of the SJT are 22.5 mm and 23 mm respectively. Considering obtained results, it was selected 7 % of the SJT. In addition to the proper release, the selected amount of this API is sufficient for the SRDE dispersion and the mixture introduction into the emulgel base.

Study of the emulgel stability samples during storage showed that in samples without antioxidant actively increased AV. The BHT including into the formulation slowed the oxidation processes because AV was slightly increasing during storage period. However, the AV difference in the emulgel samples with BHT concentration of 0.02 % and 0.03 % was insignificant compared with 0.01 % percentage of AO. Therefore, considering the emulgel stability in the process of storage,

its safety when cutaneously applied and the excipient economical use, it was chosen 0.02 % of the BHT concentration.

Study limitations. The difficulty of carrying out the advanced *in vitro* biopharmaceutical study in order to establish the penetrating ability of emulgel bases considering the BAS quantitative content in dialysate.

Prospects for further research. Further research is aimed at establishing the conditions and shelf life of the developed emulgel.

5. Conclusions

Physicochemical and rheological studies have proved that the base No 2 (in which the concentrations of carbomer Ultrez 10, potassium sorbate and triethanolamine are 0.3 %, 0.1 %, 0.2 % respectively) has optimal consuming properties: its structural viscosity is 3560±20 MPa·s, MS is 1.1. It possesses pseudoplastic flow and a high level of thixotropy, its pH value is within the skin physiological range.

1. Considering the biopharmaceutical research data concerning BAS release into agar gel, the rational concentrations of APIs were substantiated, namely, 3 % of Serenoa repens dry extract and 7 % of Sophora japonica tincture.

2. Taking into account the changes in the acid value during 1 year of the emulgel storage, it was selected 0.02 % of the antioxidant BHT. This AO percentage is optimal for ensuring the emulgel stability and safety with topical application.

3. The final formulation of the emulgel intended for AGA cutaneous treatment was developed, which has appropriate organoleptic, physicochemical and consuming properties.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

[1] Sanclemente, G., Burgos, C., Nova, J., Hernández, F., González, C., Reyes, M. I. et. al. (2017). The impact of skin diseases on quality of life: A multicenter study. Actas Dermo-Sifiliográficas, 108 (3), 244–252. doi: http://doi.org/10.1016/j.ad.2016.11.008

[2] Schmitt, J. V., Ribeiro, C. F., Souza, F. H. de M. de, Siqueira, E. B. D., Bebber, F. R. L. (2012). Hair loss perception and symptoms of depression in female outpatients attending a general dermatology clinic. Anais Brasileiros de Dermatologia, 87 (3), 412–417. doi: http://doi.org/10.1590/s0365-05962012000300010

[3] França, K., Rodrigues, T. S., Ledon, J., Savas, J., Chacon, A. (2013). Comprehensive Overview and Treatment Update on Hair Loss. Journal of Cosmetics, Dermatological Sciences and Applications, 3 (3), 1–8. doi: http://doi.org/10.4236/jcdsa.2013.33a1001

[4] Gordon, K. A., Tosti, A. (2011). Alopecia: evaluation and treatment. Clinical, Cosmetic and Investigational Dermatology, 4, 101–106. doi: http://doi.org/10.2147/ccid.s10182

[5] Ramos, P. M., Miot, H. A. (2015). Female Pattern Hair Loss: a clinical and pathophysiological review. Anais Brasileiros de Dermatologia, 90 (4), 529–543. doi: http://doi.org/10.1590/abd1806-4841.20153370

[6] Patel, S., Sharma, V., Chauhan, N., Thakur, M., Dixit, V. K. (2015). Hair Growth: Focus on Herbal Therapeutic Agent. Current Drug Discovery Technologies, 12 (1), 21–42. doi: http://doi.org/10.2174/1570163812666150610115055

[7] Sonthalia, S., Daulatabad, D., Tosti, A. (2016). Hair restoration in androgenetic alopecia: looking beyond minoxidil, finasteride and hair transplantation. Journal of Cosmetology and Trichology, 2. doi: http://doi.org/10.4172/2471-9323.1000105

[8] Dawid-Pać, R., Urbańska, M., Dębosz, I., Nowak, G. (2014). Plants as potential active components in treatment of androgenetic alopecia. Herba Polonica, 60 (1), 49–56. doi: http://doi.org/10.2478/hepo-2014-0005

[9] Rossi, A., Mari, E., Scarnò, M., Garelli, V., Maxia, C., Scali, E. et. al. (2012). Comparitive Effectiveness and Finasteride Vs Serenoa Repens in Male Androgenetic Alopecia: A Two-Year Study. International Journal of Immunopathology and Pharmacology, 25 (4), 1167–1173. doi: http://doi.org/10.1177/039463201202500435

[10] Semwal, D., Kotiyal, R., Chauhan, A., Mishra, A., Adhikari, L., Semalty, A., Semalty, A. (2015). Alopecia and the herbal drugs: an overview of the current status / Advances in Biomedicine and Pharmacy, 2 (6), 246–254. doi: http://doi.org/10.19046/abp.v02i06.01

[11] Suchonwanit, P., Thammarucha, S., Leerunyakul, K. (2019). Minoxidil and its use in hair disorders: a review. Drug Design, Developent and Therapy, 13, 2777–2786. doi: http://doi.org/10.2147/dddt.s214907

[12] Motofei, I. G., Rowland, D. L., Baconi, D. L., Tampa, M., Sârbu, M.-I., Păunică, S. et. al. (2018). Androgenetic alopecia; drug safety and therapeutic strategies. Expert Opinion on Drug Safety, 17 (4), 407–412. doi: http://doi.org/10.1080/14740338.2018.1430765

[13] Wessagowit, V., Tangjaturonrusamee, C., Kootiratrakarn, T., Bunnag, T., Pimonrat, T., Muangdang, N., Pichai, P. (2015). Treatment of male androgenetic alopecia with topical products containingSerenoa repensextract. Australasian Journal of Dermatology, 57 (3), e76–e82. doi: http://doi.org/10.1111/ajd.12352

[14] Krishna, P. M., Rao, K. N. V., Sandhya, S., Banji, D. (2012). A review on phytochemical, ethnomedical and pharmacological studies on genus Sophora, Fabaceae. Revista Brasileira de Farmacognosia, 22 (5), 1145–1154. doi: http://doi.org/10.1590/s0102-695x2012005000043

[15] Phad, A. R., Dilip, N. T., Ganapathy, R. S. (2018). Emulgel: a comprehensive review for topical delivery of hydrophobic drugs. Asian Journal of Pharmaceutics, 12 (2), 382–393. doi: http://dx.doi.org/10.22377/ajp.v12i02.2366

[16] Yarema, I., Fedorovska, M. (2014). Development of the emulsion base composition when creating the medicinal cosmetic product used in androgenetic alopecia. News of Pharmacy, 2 (78), 15–19. doi: http://doi.org/10.24959/nphj.14.1938

[17] Yarema, I. O., Fedorovska, M. I., Kutsyk, R. V. (2016). Substantiation of antibacterial preservatives choice in remedies for androgenic alopecia topical treatment. Odes'kij medicnij zurnal, 2 (154), 20–24.

[18] Lanigan, R. S., Yamarik, T. A. (2002). Final Report on the Safety Assessment of BHT. International Journal of Toxicology, 21 (2), 19–94. doi: http://doi.org/10.1080/10915810290096513

[19] State Standard of Ukraine (2008) No. 4765: 2007 Cosmetic creams. General technical conditions. State Consumer Standard of Ukraine. Kyiv.

[20] Estanqueiro, M., Conceição, J., Amaral, M. H., Santos, D., Silva, J. B., Lobo, J. M. S. (2014). Characterization and stability studies of emulsion systems containing pumice. Brazilian Journal of Pharmaceutical Sciences, 50 (2), 361–369. doi: http://doi.org/10.1590/s1984-82502014000200016

[21] Strus, O., Polovko, N., Yezerska, O. (2019). Justification of technological parameters of the cream production with sapropel extract. Pharmacia, 66 (1), 19–25. doi: http://doi.org/10.3897/pharmacia.66.e35022

[22] Derzhavna Farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: Derzhavne pidpryiemstvo «Ukrainskyi naukovyi farmakopeinyi tsentr yakosti likarskykh zasobiv», 1128.

[23] Fedorovska, M., Polovko, N. (2016). Development of the composition of the gel base for treating telogen effluvium. News of Pharmacy, 4 (88), 38–42. doi: http://doi.org/10.24959/nphj.16.2097

[24] Fedorovska, M. I., Yarema, I. O. (2015). Technology development of herbal remedies for androgenic alopecia external application. The Pharma Innovation Journal, 4 (8), 26–28.

[25] Shpychak, O., Tikhanov, A., Musoev, S. (2014). The biopharmaceutical research of "protabent" ointmentin the experiments "in vitro". Bulletin of the Tajik National University. Series Medicine – Pharmacy, 1 (2 (130)), 217–221.

[26] Mohsin, S., Akhtar, N., Mahmood, T., Khan, H., Mustafa, R. (2016). Formulation and stability of topical water in oil emulsion containing corn silk extract. Tropical Journal of Pharmaceutical Research, 15 (6), 1115–1121. doi: http://dx.doi.org/10.4314/tjpr.v15i6.1

Received date 03.08.2020
Accepted date 16.09.2020
Published date 30.09.2020