DETERMINATION OF THE SHELF-LIFE AND STORAGE CONDITIONS OF THE GEL FOR TREATMENT OF WOUNDS IN THE II PHASE OF THE WOUND PROCESS

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Key words: gel; stability; organoleptic indicators; physical and chemical indicators; shelf-life; storage conditions

With the purpose of complex research of soft medicinal product – gel for treatment of wounds in the II phase of the wound process the assessment of the indicators, which are specified in the corresponding normative documents and allow to control comprehensively the quality of the product developed during its shelf-life, has been carried out. During the experiment the methods regulated by such normative documents as the SPhU and SUC 24.5-37-103:2004 “Cosmetic Gels” have been used. The gel developed was stable according to the experimental indicators within 2 years under the modes studied: the pH value was stable for all the series of the gel samples and was within the range of 5.0-7.5; the quantitative content of the substances was within the QCM project; the mass of a gel tube did not changed. After centrifugation the gel breaking was not observed, the temperature change did not also affect the stability of the product developed during the study. The data obtained allowed to recommend the shelf-life of 2 years at the room temperature in aluminium tubes. Based on the study of the structural-mechanical properties of the gel samples during storage the complete flow rheograms have been built, according to their data it can be seen that during the period under research the gel samples have not practically changed their rheological characteristics. It indicates the strength of the gel structure and the right choice of active substances and excipients, their concentrations, and the rational technology. The mechanical stability values of the product developed during the whole storage period have not practically changed, and it indicates the drug stability in the process of storage, as well as the absence of interaction between the active substances. According to the research data both after preparation and during the long storage of the gel the indicators obtained characterize it as a structured system with positive consumer and structural-mechanical properties.

A responsible stage when developing a new medicine is its standardization. It includes the assessment of the indicators (organoleptic, physical and chemical, microbiological, etc.), which are specified in the corresponding normative documents (SPhU, DSTU, SUC) and allows to control comprehensively the quality of the product developed during its shelf-life determined experimentally [1, 4, 12].

Additionally, with the purpose of the complex research of a soft medicine it is expedient to study its structural-mechanical parameters in the process of storage since these indicators also determine the level of completeness and the release rate of active substances from the base and affect the stability of the gel developed [6, 9].

During the experiment the methods regulated by such normative documents as the SPhU and SUC 24.5-37-103:2004 “Cosmetic Gels” have been used [2, 3].

Experimental Part

As the objects of the research we selected the gel samples with allantoin, glucosamine hydrochloride and lavender oil [5].

To determine the shelf-life, the gel was stored in 30 g aluminium tubes at temperatures (8-15) °C and (15-25) °C. The study of the gel stability was carried out on five series for 27 months analyzing the samples investigated every 6 months. As containers the aluminium tubes with the membrane and bouchons (TC U 25363020-01-98) with the internal coating polish of Paclac 11-15-000 type were used.

Results and Discussion

As we can see from Table 1, the gel developed was stable by the experimental indicators within 2 years under the modes studied (at the cool and room temperatures). The results of the stability study of other four test series of the medicine developed were identical.

It was experimentally proven that the pH value was stable for all the series of the gel samples and was within the given range of 5.0-7.5 over the estimated period of storage.

The research conducted showed that after centrifugation the gel breaking was not observed, the temperature change did not also affect the stability of the product developed within two years.

It has been noted that the quantitative content of such substances as glucosamine hydrochloride, allantoin, lavender oil, sodium benzoate and ethanol is within the limits of the QCM project.

We also observed the mass of the gel tube content during the period of storage. It has been noted that the samples have stable values, they do not dry up and break. Thus, the data obtained allow to recommend the shelf-life of 2 years at the room temperature in aluminium tubes.
### Table 1

#### Assessment of indicators of the gel for treatment of wounds in the II phase of the wound process during storage

| Name of the indicator | Requirements of the QCM | Shelf-life, months | Samples stored at the cool temperature | Samples stored at the room temperature |
|-----------------------|-------------------------|--------------------|----------------------------------------|----------------------------------------|
|                       |                         | Start              | 6                                      | 12                                     | 18                                      | 24                                      | 27                                      |
| **Appearance**        | Homogeneous opaque jelly-shaped mass without any foreign impurities | -/-                 | -/-                                    | -/-                                    | Heterogeneous mass                      | -/-                                    | -/-                                    | -/-                                    | Heterogeneous mass                      |
| **Colour**            | Should correspond to the product colour | Yellowish          | -/-                                    | -/-                                    | Yellowish                               | -/-                                    | -/-                                    | -/-                                    | Yellowish                               |
| **Odour**             | Should correspond to the product odour | Characteristic for lavender oil | -/-                                    | -/-                                    | Characteristic for lavender oil         | -/-                                    | -/-                                    | -/-                                    | Characteristic for lavender oil         |
| **Colloidal stability**| Stable                  | Stable             | -/-                                    | -/-                                    | Unstable                                | -/-                                    | -/-                                    | -/-                                    | Unstable                                |
| **Identification**    |                         |                    |                                        |                                        |                                        |                                        |                                        |                                        |                                        |
| – glucosamine         | Match the retention times of the reference solution peaks | Match the retention times of the reference solution peaks | -/-                                    | -/-                                    | –                                       | Match the retention times of the reference solution peaks | -/-                                    | -/-                                    | -/-                                    | –                                       |
| hydrochloride         |                         |                    |                                        |                                        |                                        |                                        |                                        |                                        |                                        |
| – allantoin           |                         |                    |                                        |                                        |                                        |                                        |                                        |                                        |                                        |
| – linalol             | not less than 0.8 mg/g  | not less than 0.8  | not less than 0.8                      | not less than 0.8                      | not less than 0.8                       | not less than 0.8                      | not less than 0.8                       | not less than 0.8                      | not less than 0.8                       | –                                       |
| – linalyl acetate     | not less than 1.0 mg/g  | not less than 1.0  | not less than 1.0                      | not less than 1.0                      | not less than 1.0                       | not less than 1.0                      | not less than 1.0                       | not less than 1.0                      | not less than 1.0                       | –                                       |
| – ethanol             | 4.5-5.5 mg/g            | 5.02±0.03          | 5.00±0.02                             | 4.80±0.03                             | 4.75±0.02                              | 4.65±0.04                             | –                                       | 5.02±0.05                             | 5.05±0.03                             | 4.80±0.04                                 |
| – sodium benzoate     | 0.8-1.1 mg/g            | 1.00±0.02          | 1.00±0.02                             | 0.95±0.03                             | 0.90±0.04                              | 0.87±0.04                             | –                                       | 1.00±0.02                             | 1.00±0.03                             | 0.94±0.02                                 |
| **pH of 10% solution**| 5.0-7.5                 | 6.95±0.3           | 6.93±0.2                              | 6.91±0.2                              | 6.86±0.2                               | 6.82±0.2                               | 4.85±0.2                               | 6.95±0.3                              | 6.90±0.3                              | 6.88±0.2                                 |
| **Mass of the tube’s content, g** | Permissible deviations from the nominal mass of 1.2 g (from 28.8 g to 31.2 g) | 30.3±0.5          | 30.2±0.4                              | 30.0±0.2                              | 29.7±0.4                               | –                                       | 30.3±0.5                              | 30.0±0.4                              | 29.8±0.4                              | 29.6±0.5                                 |

**Note:** h=5, P=95%.
Taking into account that the gel developed refers to a soft form it is reasonable to study additionally its structural-mechanical properties during the process of storage [8, 11]. The study of these properties was performed immediately after preparation and in every 6 months of storage at the room temperature within 24 months. On the basis of the data obtained the complete flow rheograms of the gel samples were built.

As we can see from Fig., the gel samples after preparation, as well as in the process of storage within the period under research did not practically change their rheological characteristics, the flow type remained plastic, the area of the hysteresis loop also did not change. It indicates the strength of the gel structure and the right choice of active substances and excipients, their concentrations, and the rational technology.

For additional determination of the gel stability in the process of storage the values of mechanical stability (MS) were calculated according to the measurement results immediately after preparation and in every 6 months [6, 11] (Tab. 2).

As we see from Tab. 2, the MS values of the product developed during the whole storage period have not practically changed, and it indicates the positive indicators of structural-mechanical properties, namely the drug stability in the process of storage, as well as the absence of interaction between the active substances.

Thus, based on the research data both after preparation and during the long storage of the gel for treating wounds in the II phase of the wound process the indicators obtained characterize it as a structured system with positive consumer and structural-mechanical properties.

CONCLUSIONS

The stability of the gel developed at the cool and room temperatures has been studied by the following indicators: appearance, colour, odour, colloidal stability, qualitative and quantitative content of active substances and the preservative, pH of 10% gel solution, mass of the tube content and some rheological indicators. The data obtained have been used when developing the QCM project. It has been determined that the products developed are structured systems with a non-Newtonian type of the flow and particular thixotropic properties. The indicators of the mechanical stability calculated confirm their stability during storage, and it allowed to recommend the shelf-life of 2 years at the room temperature in aluminium tubes.

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ВИЗНАЧЕННЯ ТЕРМІНУ ПРИДАТНОСТІ ТА УМОВ ЗБЕРІГАННЯ ГЕЛЮ ДЛЯ ЛІКУВАННЯ РАН У ЇЇ ФАЗІ РАНОВОГО ПРОЦЕСУ

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Ключові слова: гель; стабільність; органолептичні показники; фізико-хімічні показники; термін придатності; умови зберігання

З метою комплексного дослідження м'якого лікарського засобу гелю для лікування ран у двох фазах ранового процесу проведена оцінка показників, які вказані в відповідній нормативній документації та дозволяють відбачено проаналізувати кількість збережених в досліджуваному терміні придатності. Також визначено їх структурно-механічні параметри у процесі зберігання. При проведенні експерименту використовувалась методика, що регламентується наступними нормативними документами: ДФУ, а також СОУ 24.5-37-103:2004 «Гелі косметичні». За даними експерименту розроблений гель був стабільним за вказаними показниками протягом 2 років при досліджуваних режимах: значення рН було стабільним для всіх серій зразків гелю та знаходилось у межах 5,0-7,5; кількісний вміст речовин знаходився у межах, зазначених у проекті МКЯ; маса вмісту туби гелю не змінювалась. Після центрифугування не спостерігалось розщеплення гелю, зміна температури також не вплинула на стабільність розробленого засобу на протязі часу виявлення. Отримані дані дозволили рекомендувати термін зберігання 2 роки при кімнатній температурі у тубах алюмінієвих. На підставі проведеного структурно-механічного вивчення зразків гелів у процесі зберігання були побудовані реограми течії, за даними яких видно, що впродовж досліджуваного періоду змінилися не змінилися, що свідчить про стабільність препарату у процесі зберігання, а також про відсутність взаємодії між речовинами.

Матеріали та методи

ОПРЕДЕЛЕНИЕ СРОКА ГОДНОСТИ И УСЛОВИЙ ХРАНЕНИЯ ГЕЛЯ ДЛЯ ЛЕЧЕНИЯ РАН ВО II ФАЗЕ РАНЕВОГО ПРОЦЕССА

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Ключевые слова: гель; стабильность; органолептические показатели; физико-химические показатели; срок годности; условия хранения

С целью комплексного исследования мягкого лекарственного средства геля для лечения ран во второй фазе раневого процесса проведена оценка показателей, которые указаны в соответствующей нормативной документации и позволяют всесторонне проанализировать качество разработанного средства в течение всего срока годности. Также определены его структурно-механические параметры в процессе хранения. При проведении эксперимента использовались методики, которые регламентируются следующими нормативными документами: ГФУ, а также СОУ 24.5-37-103:2004 «Гели косметические». По данным эксперимента разработанный гель был стабильным по указанным показателям в течение 2 лет при исследуемых режимах: значение рН было стабильным для всех серий образцов и находилось в пределах 5,0-7,5; количественное содержание веществ находилось в пределах, заложенных в проекте МКК; масса содержимого тубы геля не менялась. После центрифугирования не наблюдалось расщепление геля, изменение температуры также не повлияло на стабильность разработанного средства на протяжении времени изучения. Полученные данные позволили рекомендовать срок хранения 2 года при комнатной температуре в тубах алюминиевых. На основании изучения структурно-механических свойств образцов гелей в процессе хранения, были построены полные реограммы течения, по данным которых видно, что на протяжении исследуемого периода образцы практически не меняли свои реологические характеристики, что свидетельствует о прочной гелевой структуре и правильном выборе активных и вспомогательных веществ, их концентрации, а также рациональной технологии. Значение механической стабильности разработанного средства на протяжении всего срока хранения практически не менялось, что свидетельствует о стабильности препарата в процессе хранения, а также об отсутствии взаимодействия между действующими веществами. По данным проведенных исследований как после приготовления, так и при длительном хранении геля полученные показатели характеризуют его как структурированную систему с положительными потребительскими и структурно-механическими свойствами.