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## STABILITY ESTIMATION OF THE WOOL FAT SUBSTANCE WHEN STORING IN THE PHARMACY

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*One of the main objectives for drug manufacturers is to study stability, which is the quality factor for any drug. The requirements of stability are imposed to the extemporaneous medicines too. The Guide for the Compounding Practitioner (USA) contains article "1191" "Stability considerations in dispensing practice" with recommendations to repacking of substances, which can be used in pharmaceutical compounding. The pharmacy receives the wool fat substance in the original packing with a large volume that causes the necessity of its opening and the substance repacking to the container of a smaller volume for direct use. The analysis of the wool fat substance stability under conditions of its repacking from original packing to the amber glass container during the research has been done. The research has shown its compliance with the parameters set. The repacked substance was stored at the temperature of + 25°C in the pharmacy conditions in the assistant room within four months. Re-analysis of the quality parameters indicates the compliance with the requirements of the "Quality control methods" (QCM) and the European Pharmacopoeia. It has been found that the acid and peroxide values have increased only a little, and the water absorption ability of the substance has decreased. The results obtained have shown that all quality parameters of the wool fat substance in relation to stability when storing in the pharmacy after its repacking from original packing to the amber glass container are preserved within four months.*

Stability is one of the main parameters of the drug quality, it provides preservation of its therapeutic and preventive properties during its storage period [2, 6, 7]. One of the main stages of drug manufacturing is the study of stability of drugs and determination of their expiration date [6].

Stability is the factor of the drug quality. The literal meaning of stability is the ability of a drug product to remain within the quality specifications to provide its identity, strength, and purity. Stability comes into focus when the quality, efficiency and safety of the drug are concerned. The main objective of the stability study is to determine its sensitivity to the different environmental factors and assess the shelf-life of the drug and the storage conditions recommended [4, 8, 9].

The requirements of stability to the extemporaneous medicines are contained in article "1191" "Stability considerations in dispensing practice" of the Guide for the Compounding Practitioner [10] developed on the basis of the US Pharmacopoeia requirements. It has the subsection "Responsibility of Pharmacists", which describes indicators of instability of all extemporaneous dosage forms. For semisolids the primary indication of instability is often either discoloration or a noticeable change in consistency or odour. The common signs of instability of ointments are the change in consistency and separation of excessive amounts of liquid and formation of granules or granularity [3, 10].

Stability of the base considerably influences on the quality of the dosage form. In the prescriptions of the compounding ointments wool fat is used as a base (with White soft paraffin or as an independent base). The phar-

macy receives the substance in the original packing and after its opening wool fat is stored in the amber glass or ceramic containers.

The aim of this work is to assess stability of the wool fat substance for compounding ointments within four months when storing in the amber glass containers in the pharmacy conditions.

### Materials and Methods

For our research the wool fat substance manufactured by "Lanolines Stella S. A.", Belgium; the amber glass containers; tableware and reagents corresponding to the requirements of the State Pharmacopoeia of Ukraine were used. The experimental work was carried out in the laboratory of the quality control of medicines of the State inspectorate of the quality control of medicines in the Donetsk region.

#### *Quality parameters of wool fat*

*Drop point* [1, 5]: 38°C to 44°C. Place the test sample into a metal cup, melt the wool fat on a water-bath, cool to about 50°C, pour into the cup and allow to stand at 15-20°C for 24 h.

*Water absorption ability* – Place 10 g of the molten wool fat into a mortar and allow to cool to the room temperature. Weight the mortar. Add water *R* in portions of 0.2-0.5 ml from a burette stirring vigorously after each addition to incorporate water *R*. Instead of a pestle, use a high-density polypropylene cylindrical rod. The end-point is reached when visible droplets remain and cannot be incorporated. Weight the mortar again and determine the amount of water absorbed by the weight difference. Not less than 20 g of water *R* should be absorbed [5].

Table

The results of stability studies of the wool fat substance during its storage period

Quality parameter	The research conducted*		Requirements	Results
	Experiment 1	Experiment 2		
Description	+	+	A yellow pasty substance, when melted it is a clear or almost clear, yellow liquid. The solution in light petroleum is opalescent (QCM, EP)	satisfied
Drop point	44°C	44°C	38-44°C (QCM, EP)	satisfied
Water absorption ability	29.2 ml	23.0 ml	not less than 20 ml (QCM, EP)	satisfied
Acid value	0.57	0.60	maximum 1.0 (QCM, EP)	satisfied
Peroxide value	12.0	16.6	maximum 20 (QCM, EP)	satisfied
Saponification value	90.7	90.8	90 to 105 (QCM, EP)	satisfied
Loss on drying	0.25%	0.27%	maximum 0.5% (QCM, EP)	satisfied
Sulphated ash	0.03%	0.03%	maximum 0.15% (QCM, EP)	satisfied
Paraffines	absent	absent	not more than 1.0% (QCM, EP)	satisfied
Chlorides	absent	absent	not more than 150 ppm (QCM, EP)	satisfied

\* – the average result of three measurements is given for each experiment

*Acid value* – not more than 1.0. Dissolve 5.0 g of the test sample in 25 ml of the mixture of equal volumes of ethanol *R* and light petroleum *R3* previously neutralized with 0.1 M potassium hydroxide [1, 5].

*Peroxide value* [1, 5] – not more than 20. Before adding 0.5 ml of saturated potassium iodide solution *R* cool the solution obtained to the room temperature.

*Saponification value* [1, 5] – from 90 to 105. Heat 2.00 g of the test sample under reflux for 4 h.

*Paraffines* [5] – not more than 1.0%. The stopper and cotton plugs used must be free from lubricants. Prepare a column with anhydrous aluminium oxide of 0.23 m long and 20 mm in diameter by adding a suspension of anhydrous aluminium oxide *R* and light petroleum *R1* to a glass tube fitted with a stopper (before use, dehydrate the anhydrous aluminium oxide by heating it in an oven at 600 °C for 3 h). Allow to settle and reduce the depth of the layer of the solvent above the column to about 40 mm. Dissolve 3.0 g of the substance to be examined in 50 ml of warm light petroleum *R1*, cool, pass the solution through the column at the flow rate of 3 ml/min and wash with 250 ml of light petroleum *R1*. Concentrate the combined eluate and the washing liquid to the small volume by distillation, evaporate to dryness on a water bath and heat the residue at 105°C for 10 min until the difference between two successive weighings will not exceed 1 mg. The weight of the residue should not exceed 30 mg.

*Chlorides* [5] – the content of chlorides does not exceed 150 ppm. Boil 1.0 g of the substance with 20 ml of ethanol *R* (90 % v/v) in a round-bottomed flask fitted with a reflux condenser for 5 min. Cool, add 40 ml of water *R* and 0.5 ml of nitric acid *R* and filter. To the filtrate add 0.15 ml of 10 g/l solution of silver nitrate *R* in ethanol *R* (90 % v/v). Allow to stand for 5 min protected from light. Opalescence in the test solution should not be more intense than that in the standard solution prepared at the same time by adding 0.15 ml of 10 g/l solution of silver nitrate *R* in ethanol *R* (90 % v/v)

to the mixture of 0.2 ml of 0.02 M hydrochloric acid, 20 ml of ethanol *R* (90 % v/v), 40 ml of water *R* and 0.5 ml of nitric acid *R*.

*Loss on drying* [5] – not more than 0.5 %. Dry 1.000 g of the substance under study in a drying cabinet at 105°C for 1 h.

*Sulphated ash* [5] – not more than 0.15 %. Ignite 5.0 g of the test sample and use the residue to determine the sulphated ash.

### Results and Discussion

The subsection “Responsibility of Pharmacists” of the article “1191” “Stability considerations in dispensing practice” of the Guide for the Compounding Practitioner (USA) [3, 10] contains recommendations about repackaging of substances, which can be used in pharmaceutical compounding. In general, repackaging is inadvisable. If repackaging is necessary, it is essential to use suitable containers. First of all, it must be made of a neutral material.

If stability data of the substance after its repackaging to the new container are not available, repackaging only the necessary quantities for use in a short period of time is recommended. On the label of the new package a series of substance and the expiration date must be specified. If a sterile product is repacked from a multiple-dose vial into unit-dose syringes, discard the latter if it is not used within 24 hours unless the data are available to support longer storage. If quantities are repacked in advance of immediate need, maintain suitable repackaging records indicating the name of the manufacturer, the lot number, date and persons that are responsible for repackaging and checking. If safety closures are required, use container closure systems that ensure compliance with compendial and regulatory standards for storage.

The pharmacies receive the wool fat substance in the original packing with a large volume that causes the necessity of its opening and the substance repackaging to the container of a smaller volume for direct use and subsequent storage. Since in the literature there is no

information about stability of the wool fat substance after its repacking from original packing, the aim of our further work was to study the stability parameters of the given substance.

Part of the wool fat substance from the original packing was bought for the research and dispensed into the amber glass containers. The analysis of the substance carried out in a week after repacking has shown its compliance with the QCM requirements (Table, experiment 1) containing the list of tests given to verify the quality of the wool fat substance in the European Pharmacopoeia [5].

After that wool fat was stored at temperature of + 25°C in the assistant room. The second analysis of the wool fat substance compliance with all quality parameters according to the QCM was conducted in four months (Table, experiment 2). The results obtained indicate the preservation of stability of the wool fat substance when storing in the pharmacy conditions in the amber glass container. Only the acid value (from 0.57

to 0.60) and the peroxide value (from 12.0 to 16.6) slightly increased a little, and the water absorption ability of the wool fat substance (from 29.2 ml to 23 ml) decreased. However, all quality parameters of the wool fat substance correspond to the parameters set in QCM and do not exceed them.

#### CONCLUSIONS

1. Stability of the wool fat substance during its storage in the amber glass container in the pharmacy conditions within four month has been studied.

2. During the period studied the water absorption ability of the wool fat decreased, and the acid and peroxide values e increased. However, all parameters are in compliance with the QCM requirements.

3. The results obtained have shown the possibility of repacking and storage of the wool fat substance in the amber glass containers in the pharmacy conditions.

4. Our further research will be devoted to the study of the microbiological purity of the bases to verify their compliance with the requirements set.

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#### ОЦІНКА СТАБІЛЬНОСТІ СУБСТАНЦІЇ ЛАНОЛІНУ ПРИ ЗБЕРІГАННІ В УМОВАХ АПТЕКИ

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**Ключові слова:** стабільність; мазеві основи; ланолін безводний; аптечне виготовлення

Однією з основних задач, яка стоїть перед виробником лікарського засобу, є дослідження його стабільності. Вона є одним із факторів якості препарату. Вимоги до збереження стабільності висуваються і до екстемпоральних лікарських засобів. До Керівництва для аптечних працівників США входить стаття «1191» «Поняття стабільності в аптечній практиці», в якій містяться рекомендації щодо перепакування субстанцій, які можуть використовуватись в аптечній практиці. Субстанція ланоліну надходить до аптечного закладу в заводських упаковках. Оскільки їх об'єм досить великий, необхідним є розфасування субстанції в тару меншого об'єму для безпосереднього використання. В процесі дослідження здійснено оцінку стабільності субстанції ланоліну безводного при його перепакуванні з заводської тари в аптечну скляну тару з темного скла. Проведений аналіз за всіма показниками якості субстанції ланоліну безводного свідчить про її відповідність встановленим параметрам. Розфасована субстанція зберігалась при температурі + 25°C в умовах аптеки в асистентській кімнаті впродовж чотирьох місяців. Повторне дослідження показників її якості свідчить про відповідність «Методам контролю якості» (МКЯ) та вимогам Європейської Фармакопеї (ЄФ). Встановлено, що дещо збільшились лише кислотне та пероксидне число, а також зменшилась водоабсорбційна здатність субстанції. Отримані результати свідчать про збе-

реження показників якості щодо стабільності субстанції ланолину при його перефасуванні та зберіганні в умовах аптеки в штангласах з темного скла впродовж чотирьох місяців.

#### **ОЦЕНКА СТАБИЛЬНОСТИ СУБСТАНЦИИ ЛАНОЛИНА ПРИ ХРАНЕНИИ В УСЛОВИЯХ АПТЕКИ**

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Одной из основных задач, которая стоит перед производителем лекарственного средства является исследование его стабильности. Она является одним из факторов качества препарата. Требования к сохранению стабильности выдвигаются и к экстремпоральным лекарственным средствам. В Руководство для аптечных сотрудников США входит статья «1191» «Понятие стабильности в аптечной практике», в которой содержатся рекомендации о переупаковке субстанций, которые могут использоваться в аптечной практике. Субстанция ланолина поступает в аптечное учреждение в заводских упаковках. Поскольку их объем достаточно большой, необходимым является ее расфасовка в тару меньшего объема для непосредственного использования. В процессе исследования осуществлена оценка стабильности субстанции ланолина безводного после его переупаковки с заводской тары в аптечную стеклянную тару из темного стекла. Проведенный анализ по показателям качества субстанции ланолина безводного свидетельствует о ее соответствии установленным параметрам. Расфасованная субстанция хранилась при температуре + 25°C в условиях аптеки в ассистентской комнате на протяжении четырех месяцев. Повторное исследование показателей ее качества свидетельствует о соответствии «Методам контроля качества» (МКК) и требованиям Европейской Фармакопеи (ЕФ). Установлено, что несколько увеличились показатели только кислотного и пероксидного чисел, а также уменьшилась водоабсорбционная способность субстанции. Полученные результаты свидетельствуют о сохранении показателей качества в отношении стабильности субстанции ланолина при его перефасовке и хранении в условиях аптеки в штангласах из темного стекла на протяжении четырех месяцев.