Fine Chemical Technologies, 2019, Vol. 14, No. 5, pp. 71–78.

SYNTHESIS AND PROCESSING OF POLYMERS AND POLYMERIC COMPOSITES

СИНТЕЗ И ПЕРЕРАБОТКА ПОЛИМЕРОВ И КОМПОЗИТОВ НА ИХ ОСНОВЕ

ISSN 2686-7575 (Online)

https://doi.org/10.32362/2410-6593-2019-14-5-71-78

UDK 691.175.2

Effect of polyethylene glycol mixtures as ointment base on the physicochemical properties of Lavsan atraumatic wound dressings

Anastasiya A. Korolchuk[1], Elena S. Zhavoronok[1], Olga A. Legonkova[2], Stanislav A. Kedik[1]

[1]MIREA – Russian Technological University (M.V. Lomonosov Institute of Fine Chemical Technologies), Moscow 119571, Russia

[2]A.V. Vishnevsky National Medical Research Center of Surgery, Moscow 117997, Russia
[@]Corresponding author, e-mail: nastya.corolchuk@yandex.ru

Objectives. *Modern atraumatic wound dressings are based on polyethylene terephthalate, or Lavsan, which is shaped to form threads. The aim of the study was to determine the reasons for Lavsan woven nets' hardening and becoming more trauma-prone during storage, and to find ways of eliminating these effects.*

Methods. *We used differential scanning calorimetry, performed on a NETZSCH DSC 204 F1 Phoenix device, in a dynamic mode with a temperature range from 20 to 300 °C in argon flow to determine phase states, glass transition temperatures, and melting temperatures of Lavsan fibers (including those treated with polyethylene glycol mixtures). We performed rheoviscometry studies on a Brookfield DV2TLV rotational viscometer, with a SC4-16 thermostatic control unit, at the following temperatures: 25, 36.6, 40, 45, 50, and 55 °C, with shear rates ranging from 120 to 200 s–1 to determine dynamic viscosity and investigate the mixing characteristics of polyethylene glycols with different molecular weights.*

Results. *We have established that samples of Lavsan woven nets, stored long-term in laboratory conditions (up to 2, 3, and 16 years), are in the crystalline state with a high degree of crystallinity. Upon heating these nets to 300 °C, it is possible to reduce the degree of crystallinity by 19–32%, but it does not completely eliminate the effect. Polyethylene glycols and their mixtures which exhibit non-Newtonian flow behavior and are used as an ointment base, have a significant effect on Lavsan's crystallinity. We have determined that the optimal ratio of polyethylene glycols for the modification of Lavsan nets is PEG-400:PEG-1500 = 80:20 wt %. Upon storing Lavsan woven nets in this mixture at room temperature, the Lavsan's crystallinity is greatly reduced, and upon heating the system, the crystallinity practically disappears.*

Conclusions. *The effect of polyethylene glycol mixtures (the base for therapeutic ointments) with various molecular weights on the phase organization of Lavsan has been evaluated. As a result of this study, we can offer a new approach to reduce the injuring effect of synthetic (Lavsan) bases of atraumatic wound dressings.*

Keywords: *wound dressing, ointment base, polyethylene terephthalate, polyethylene glycol, melting point, degree of crystallinity, viscosity.*

For citation: Korolchuk A.A., Zhavoronok E.S., Legonkova O.A., Kedik S.A. Effect of polyethylene glycol mixtures as ointment base on the physicochemical properties of Lavsan atraumatic wound dressings. *Tonkie Khim. Tekhnol.= Fine Chem. Technol.* 2019;14(5):71-78 (in Russ.). https://doi.org/10.32362/2410-6593-2019-14-5-71-78

Влияние смесей полиэтиленгликолей в качестве мазевой основы на физико-химические свойства лавсановых атравматичных раневых повязок

А.А. Корольчук[1], Е.С. Жаворонок[1], О.А. Легонькова[2], С.А. Кедик[1]

[1]МИРЭА – Российский технологический университет (Институт тонких химических технологий имени М.В. Ломоносова), Москва 119571, Россия
[2]Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского, Москва 117997, Россия
[@]Автор для переписки, e-mail: nastya.corolchuk@yandex.ru

Цели. *Основой современных атравматичных раневых повязок является полиэтилентерефталат (или лавсан), которому придают вид нитей. Целью работы являлось определение причин увеличения жесткости и травматичности лавсановых тканых сеток при хранении и поиск путей устранения этого эффекта.*
Методы. *Для определения фазового состояния, температуры стеклования и плавления лавсановых волокон, в том числе после обработки смесями полиэтиленгликолей, использовали дифференциальную сканирующую калориметрию, которую проводили на приборе NETZSCH DSC 204 F1 Phoenix в динамическом режиме в диапазоне температур от 20 до 300 °C в токе аргона. Для определения динамической вязкости и оценки характера смешения полиэтиленгликолей разной молекулярной массы применяли метод реовискозиметрии, которую осуществляли на ротационном вискозиметре Brookfield DV2TLV с термостатируемым рабочим узлом SC4-16 при температурах: 25, 36.6, 40, 45, 50 и 55 °C в диапазоне скоростей сдвига от 120 до 200 $с^{-1}$.*
Результаты. *Установлено, что длительно выдержанные в лабораторных условиях (до 2, 3 и 16 лет) образцы лавсановых тканых сеток находятся в кристаллическом состоянии с высокой степенью кристалличности. Прогрев этих сеток до 300 °C позволяет снизить степень кристалличности на 19–32%, но не устраняет ее полностью. Полиэтиленгликоли и их смеси, которые используют в качестве мазевой основы, проявляющие неньютоновское поведение при течении, оказывают заметное влияние на степень кристалличности лавсана. Установлено оптимальное соотношение полиэтиленгликолей для модификации лавсановых сеток: ПЭГ-400:ПЭГ-1500 = 80:20 мас. ч. После выдерживания лавсановой тканой сетки в этой смеси при комнатной температуре степень кристалличности лавсана сильно снижается, а после прогрева такой системы кристалличность практически исчезает.*
Заключение. *Оценено влияние на фазовую организацию лавсана смесей полиэтиленгликолей различной молекулярной массы, являющихся основой лечебных мазей. В результате проведенной работы предложен новый подход для уменьшения травматичности синтетических (лавсановых) основ атравматичных раневых повязок.*

Ключевые слова: *раневое покрытие, мазевая основа, полиэтилентерефталат, полиэтиленгликоль, температура плавления, степень кристалличности, вязкость.*

Для цитирования: Корольчук А.А., Жаворонок Е.С., Легонькова О.А., Кедик С.А. Влияние смесей полиэтиленгликолей в качестве мазевой основы на физико-химические свойства лавсановых атравматичных раневых повязок. *Тонкие химические технологии.* 2019;14(5):71-78. https://doi.org/10.32362/2410-6593-2019-14-5-71-78

Introduction

Atraumatic wound dressings is just one type of bandage material meant to gently protect wounds from exposure to harmful environmental factors [1]. Such dressings are based on fibers, threads, tissues, films, and nonwoven materials [2] and should prevent damaged areas from coming into contact with external irritants, foreign objects and infections, as well protect the wound from possible new injuries [2, 3].

Historically, the first materials used to stop bleeding and mechanically protect wounds, were cotton tissues [2]. However, this material has a

number of disadvantages, and a major one is the heterogeneity of cotton threads. Microscopic strands, which are characteristic for cotton, get into the wound, thus irritating the injured area and affecting the healing of the wound [3]. This has led to research on alternative dressings that could be chemically inert and have homogenous threads. Polymeric materials such as polyethylene terephthalate (PET) fulfill these requirements.

Polyethylene terephthalate, or Lavsan, is a complex polyester that is shaped as threads for convenience [4, 5]. The main reasons for Lavsan to be used as wound dressings are its mechanical characteristics and relatively low cost [5]. Lavsan fibers are very strong and durable, elastic and resistant to chemicals, and biocompatible; Lavsan is a polymer with a low rate of biodegradation [6, 7]. However, the prolonged storage of Lavsan nets makes them harder and more trauma-prone, which is unacceptable for wound dressings [8, 9]. The aim of this study is to investigate the reasons for Lavsan woven nets' hardening and becoming more prone to trauma during storage, and to find ways of eliminating these effects.

Materials and Methods

We used Lavsan woven nets made of polyethylene terephthalate with a nominal molecular weight of NMW = 30 kDa, stored in a laboratory for up to τ_{aging} = 2, 3, 16 years. The samples differed in their aging time, as well as in the weaving (see Table 1). To investigate the effect of ointment base on the nets, we used model oligomers: polyethylene glycols (PEGs) PEG-400, PEG-1500 and their mixtures in various ratios. The mixing of PEGs was performed at room temperature, followed by heating to 80 °C for 10 minutes until homogeneous viscous mixtures were obtained. The nets were soaked for 1, 7, or 28 days in PEG-400 or PEG-400:PEG-1500 = 80:20 wt % mixture, at room temperature, and subsequently studied.

Over the course of this work, we used differential scanning calorimetry (DSC) and rheoviscometry. Thermograms were recorded on a NETZSCH DSC 204 F1 Phoenix device, in a dynamic mode with the temperature range from 20 to 300 °C in argon flow. The dynamic viscosity of PEGs and their mixtures was studied on a Brookfield DV2TLV rotational viscometer, with a SC4-16 thermostatic operating unit, at the following temperatures: 25, 36.6, 40, 45, 50, and 55 °C, with shear rates ranging from 120 to 200 s^{-1}.

Results and Discussion

The results of DSC studies of Lavsan woven nets are shown in Fig. 1.

The analyzed samples have a clear endothermal peak in the 240–280 °C temperature range that can be interpreted as a melting of polyethylene terephthalate crystals, according to [10]. It is evident that this peak area becomes smaller in the second DSC experiment, but in the 60–80 °C temperature range there is a characteristic "step" indicating that devitrification occurs and an amorphous phase is present. In the second scanning, we observe an additional, sharp exothermal peak in the 140–160 °C temperature range, which can be interpreted as crystallization of the amorphous part of the sample, according to [10].

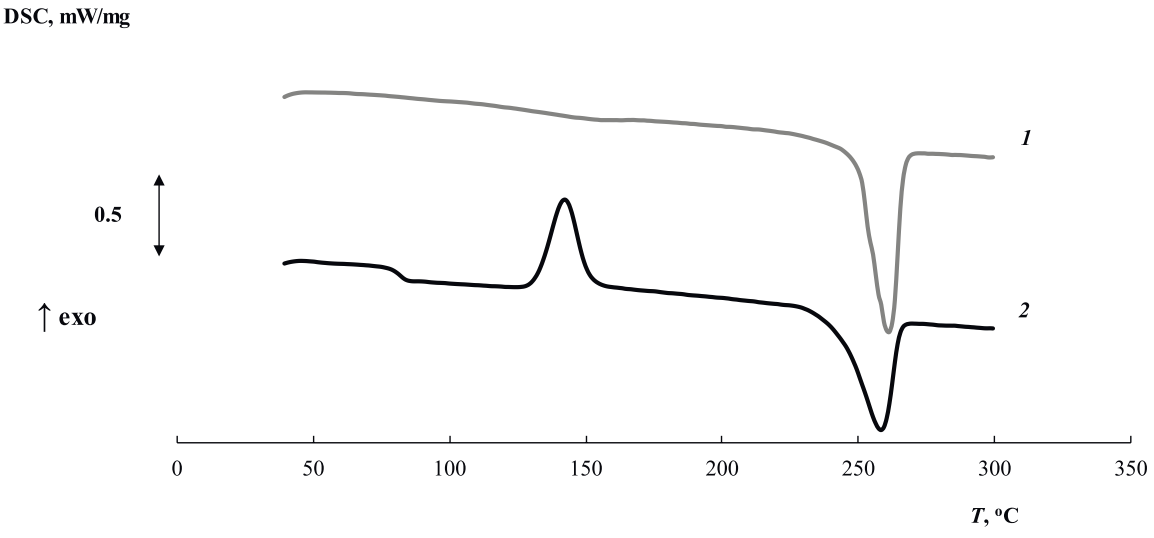

Fig. 1. Typical DSC diagram for Lavsan woven nets; shown here is the diagram for PET-207 at w^{+} = 10 K/min: *1* – initial heating; *2* – secondary heating.

The thermophysical characteristics of the studied samples are presented in Table 1. We may conclude that samples stored at room temperature for a long time are in crystallized state, and the amorphous phase content is very low, but it increases upon heating of the sample.

The areas of endothermal melting peaks allowed us to estimate the degree of crystallinity, in our first approximation. We set the degree of crystallinity at 100% for those samples that did not exhibit vitrification, according to their DSC thermograms, and calculated the degree of crystallinity of the re-heated samples using the following formula [11]:

$$\alpha = \frac{\Delta S''}{\Delta S'} \times 100\% , \quad (1)$$

where α is the crystalline phase content, ΔS′ is the melting peak area of the crystalline phase in the first scanning, ΔS″ is the melting peak area of the crystalline phase in the second scanning.

The calculated values of α are shown in Table 1. We can see that the degree of crystallinity is between 68% and 81% even for the re-heated samples.

The ointment base can have a significant effect on the phase state of polyethylene terephthalate; this is why we investigated some ointment bases. A common ointment base is PEG mixtures, with molecular weights of 400 and 1500, used in various ratios [11]. The experimental viscosity–velocity curves (Fig. 2) show the PEG mixtures that look homogeneous do exhibit non-Newtonian behavior.

When PEG-1500 concentration increases, we observe viscosity hysteresis (rheopexy type) that enhances over time. This may indicate that the PEG mixture has a heterogeneous structure, despite it looking homogeneous. Fig. 2 shows that when a PEG-1500 concentration in PEG-400 increases, the dynamic viscosity of the mixtures is elevated.

Temperature is an important parameter that influences the viscosity of oligomers and their mixtures. As we can see from experimental data in Fig. 3, the viscosity of the sample decreases when the temperature increases, and the non-Newtonian behavior becomes less obvious; for example, at 55 ºC we observe almost Newtonian behavior of the samples.

Our analysis of the results obtained at different temperatures allows us to estimate the activation energy of viscous flow for pure ethylene glycols and their mixtures using the Arrhenius–Frenkel–Eyring equation:

$$\eta = A \times e^{\frac{-E_a}{R}} , \quad (2)$$

where η is the effective dynamic viscosity at 55 s^{-1}; E_a is the activation energy of viscous flow; R is the universal gas constant; T is the absolute temperature; A is the pre-exponential factor that takes into account the probability that an elementary act of viscous flow happens.

The dependency of the apparent activation energy on the PEG ratio in their mixture is shown in Fig. 4. We can see that the activation energy of viscous flow is low and almost does not depend on the PEG mixture's composition. This indicates that the mixing of PEGs with different molecular weights (containing the same monomer) is athermal.

To sum up, when PEG-1500 content in PEG-400 is up to 50 wt %, the mixture of these oligomers

Table 1. Thermophysical parameters for Lavsan woven materials samples

Sample	τ_{aging}, years	T_g, ºC	T_{cryst}, ºC		$\lvert\Delta S_{cryst}\rvert$, J/g		T_{melt}, ºC		$\lvert\Delta S_{melt}\rvert$, J/g		α, %
			1 scan	2 scan	1 scan	2 scan	1 scan	2 scan	1 scan	2 scan	
PET-208*	2	80	–	145	–	36	261	256	62	44	71
PET-207**	3	80	–	–	–	–	262	257	79	54	68
PET-206*	3	80	–	148	–	69	260	257	115	90	78
PET-205**	16	83	–	–	–	–	262	258	74	51	69
PET-204*	16	82	–	142	–	37	261	258	72	58	81

* Weaving: "honeycombs".

** Weaving: "squares". Apparently, the difference in the weaving means the difference in the degree of Lavsan fiber elongation during the formation of the woven net, therefore the nets of the same age, but with different weaving have different properties.

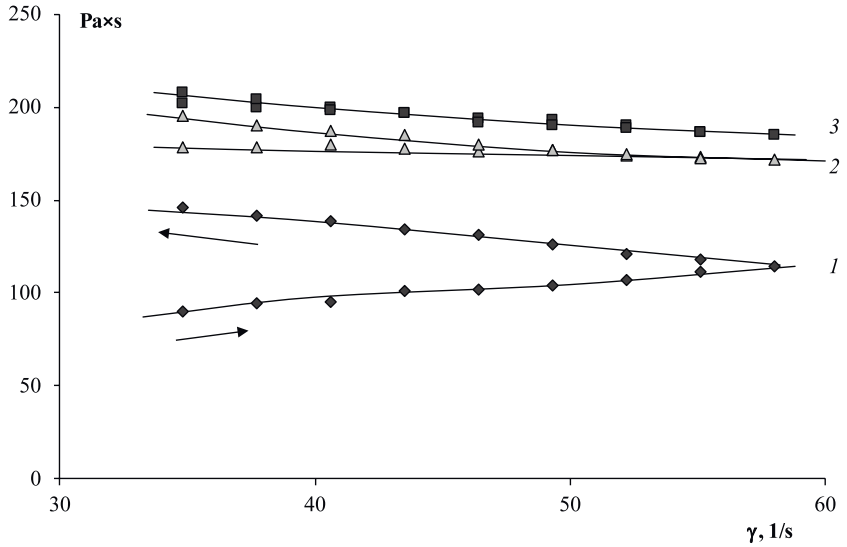

Fig. 2. Typical viscosity–velocity curves obtained at 25 ºC for PEG-400 and PEG-1500 mixtures, with PEG-400 content, wt %: 70 (*1*); 80 (*2*); 90 (*3*).

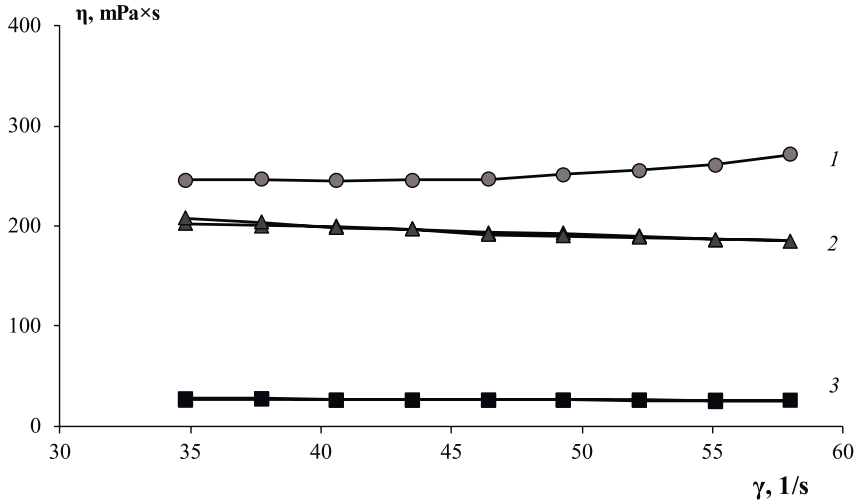

Fig. 3. Typical viscosity–velocity curves for the PEG-400:PEG-1500 = 80:20 wt % mixture, obtained at the following temperatures, ºC: 25 (*1*); 36.6 (*2*); 55 (*3*).

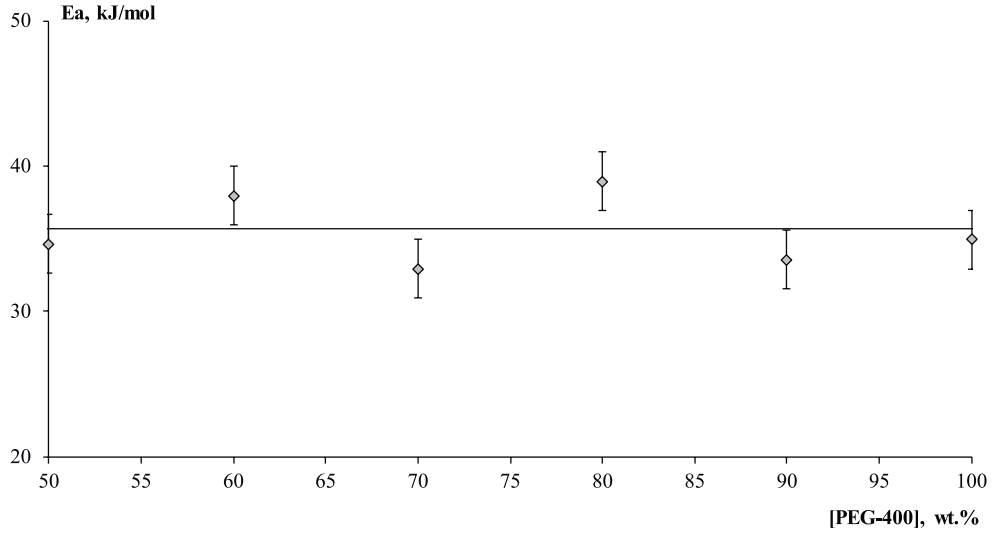

Fig. 4. Dependency of the apparent activation energy of viscous flow on the composition of PEG-400:PEG-1500 mixtures.

behaves the same. This is why we selected the PEG-400:PEG-1500 = 80:20 wt % composition for further study; this composition is widely used in ointment bases for atraumatic wound dressings, according to [12, 13]. We used the DSC method to investigate the effect of this composition on the phase state of Lavsan woven nets. The thermograms obtained are presented in Fig. 5.

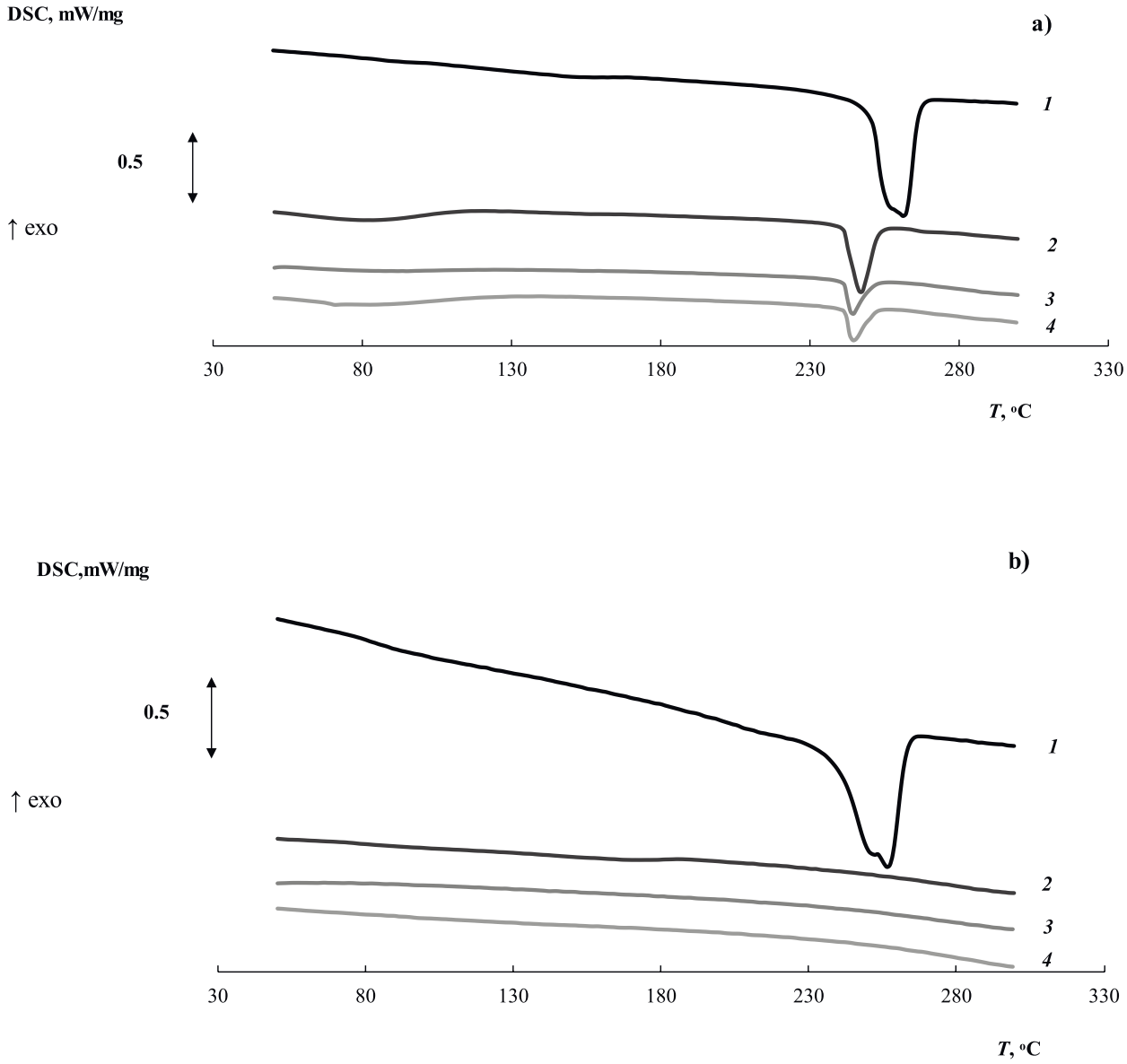

Fig. 5. Typical DSC thermograms for initial PET-204 (*1*) and for PET-204 incubated in the PEG-400:PEG-1500 = 80:20 wt % composition for 1 day (*2*), 7 days (*3*) and 28 days (*4*). Results of the first (a) and the second (b) scanning, at w^+ = 10 K/min, are shown here.

The analysis of these thermograms shows that the incubation of Lavsan woven nets in PEG mixtures results in an expected decrease in the area of the endothermal peak in the 250–280 ºC temperature range. At the same time, in the low temperature range (80–100 ºC) we observe a "step" resembling vitrification. It means that the degree of crystallinity decreases; calculations using formula (1) show that the degree of crystallinity for incubated samples goes down to 14% in 28 days (Table 2). However, even after this prolonged incubation the degree of crystallinity still remains significant. At the same time, the re-heating of such samples (Fig. 5b) leads to the complete disappearance of the endothermal melting peak. Clearly, it happens because PEG molecules penetrate into polyethylene terephthalate, but the woven net does not change its appearance and commercial properties.

Table 2. Thermophysical parameters for samples of PET-204 incubated in PEG-400 and its mixture with PEG-1500

Incubation time, days	PEG-400		PEG-400:PEG-1500 = 80:20 wt %	
	$\|\Delta S_{melt}\|$, J/g	α, %	$\|\Delta S_{melt}\|$, J/g	α, %
1	46	58	25	32
7	11	22	11	14
28	17	14	11	14

Conclusions

We have shown that Lavsan nets aged in natural conditions are partially crystallized, with a high crystalline content. Upon their incubation in PEG mixtures commonly used as ointment bases and whose optimal composition was selected based on rheoviscometry, the degree of crystallinity decreases significantly at room temperature, and the crystallinity almost disappears upon heating. This provides an opportunity to prolong the shelf life of Lavsan nets.

The authors declare no conflict of interest.

References:

1. Petrov S.V. Obshchaya khirurgiya [General Surgery]. Saint-Petersburg: Lan' Publ., 1999. 672 p. (in Russ.). ISBN 5-8114-0129-9
2. Kurinova M.A., Galbriah L.C., Skibina L.E. Modern wound dressings (review). *Sovremennaya meditsina: aktual'nye voprosy* = Modern Medicine: Topical Issues. 2015;48-49:137-145 (in Russ.).
3. Strukov A.I., Serov V.V. Patologicheskaya anatomiya [Pathological Anatomy]. 5th ed. Moscow: Litterra Publ., 2010. 880 p. (in Russ.).
4. Blatun L.A. Local medical treatment of wounds. *Khirurgiya. Zhurnal imeni N.I. Pirogova* = Pirogov Russian Journal of Surgery. 2011;(4):51-59 (in Russ.).
5. Mayorova A.V., Sysuev B.B., Khanalieva I.A., Vikhrova I.V. Morden assortiment, properties, and perspectives of dressings improvement of wound treatment. *Farmatsiya i farmakologiya* = Pharmacy and Pharmacology. 2018:6(1):4-32 (in Russ.). https://doi.org/10.19163/2307-9266-2018-6-1-4-32
6. Marichev S.N., Kalinin B.A. Polimery v meditsine [Polymers in medicine]. Vladimir: Vladimir State University Publ., 2001. 68 p. ISBN 5-89368-277-7 (in Russ.).
7. Legonkova O.A., Asanova L.Y. Linear polyesters in modern medicine. *Vysokotekhnologichnaya meditsina* = High-Tech Medicine. 2017;4(1):16-31 (in Russ.).
8. Waring M., Bielfeldt S., Springmann G., Ceo K-P.W. An instant tack wound dressing designed to reduce skin stripping. *Wounds UK*. 2012;8(2):60-67.
9. Tabaev B.V., Khlestkin R.N., Maslennikov E.I. Charecteristics of crystallization of amorphous polyethylene terephthalate in solid state under strain conditions. *Bashkirskii khimicheskii zhurnal* = Bashkir Chemical Journal. 2010:17(4):29-31 (in Russ.).
10. Bershtein V.A., Egorov V.M. Differentsial'naya skaniruyushchaya kalorimetriya v fizikokhimii polimerov [Differential Scanning Calorimetry in Polymer Physics and Chemistry]. Saint-Petersburg: Khimiya Publ., Leningrad section, 1990. 256 p. (in Russ.).
11. Menczel J.D. Thermal Analysis of Polymers. Fundamentals and Application. Ed. by J.D. Menczel, R.B. Prime. Hoboken (New Jersey): Wiley, 2009. 698 p.
12. Shikova Y.V., Kadyrov A.R., Zaytseva O.E., Simonyan E.V., Vasilyeva N.A., Soldatova E.S. The use of modern auxiliary substances of high molecular compounds in formulation of drugs. *Health and Education Millennium.* 2018;20(1):222-226. https://dx.doi.org/10.26787/nydha-2226-7425-2017-20-1.
13. Slivkin A.I., Krasnuk I.I. (Jr.), Belenova A.S., Diakova N.I. Farmatsevticheskaya tekhnologiya. Vysokomolekulyarnyye soyedineniya v farmatsii i meditsine [Pharmaceutical Technology. High-Molecular Compounds in Pharmacy and Medicine]. Ed. by I.I. Krasnuk (Sr.). Moscow: GEOTAR-Media Publ., 2017. 560 p. (in Russ.). ISBN 978-5-9704-3834-3
14. Weinstein V.A. Determination of structural-mechanical properties of soft drugs. *Razrabotka i registrtsiya lekarstvennyh sredstv* = Drug Development & Registration. 2017;3(20):70-78 (in Russ.).
15. Makarenko M.V., Kurchenko V.P., Usanov S.A. Modern approaches to the development of wound coverings. *Trudy Belorusskogo gosudartvennogo universiteta* = Proceedings of the Belarusian State University. 2016;11(1):273-279 (in Russ.).

About the authors:

Anastasiya A. Korolchuk, Student of the Chair of Biotechnology and Industrial Pharmacy, M.V. Lomonosov Institute of Fine Chemical Technologies, MIREA – Russian Technological University (86, Vernadskogo pr., Moscow 119571, Russia).

Elena S. Zhavoronok, Cand. of Sci. (Chemistry), Associate Professor of the Chair of Biotechnology and Industrial Pharmacy, M.V. Lomonosov Institute of Fine Chemical Technologies, MIREA – Russian Technological University (86, Vernadskogo pr., Moscow, 119571, Russia). Scopus Author ID 7801409746, ResearcherID H-9420-2013, https://orcid.org/0000-0002-7235-3361

Olga A. Legonkova, Dr. of Sci. (Engineering), Head of the Department of Dressings, Suture and Polymer Materials in Surgery, A.V. Vishnevsky National Medical Research Center of Surgery of the Ministry of Health of the Russian Federation (27, Bolshaya Serpukhovskaya ul., Moscow 117997, Russia). Scopus Author ID 18437207900

Stanislav A. Kedik, Dr. of Sci. (Engineering), Professor, Head of the Chair of Biotechnology and Industrial Pharmacy, M.V. Lomonosov Institute of Fine Chemical Technologies, MIREA – Russian Technological University (86, Vernadskogo pr., Moscow 119571, Russia). https://orcid.org/0000-0003-2610-8493

Об авторах:

Корольчук Анастасия Александровна, студент кафедры биотехнологии и промышленной фармации Института тонких химических технологий имени М.В. Ломоносова ФГБОУ ВО «МИРЭА – Российский технологический университет» (119571, Россия, Москва, пр-т Вернадского, д. 86).

Жаворонок Елена Сергеевна, кандидат химических наук, доцент кафедры биотехнологии и промышленной фармации Института тонких химических технологий имени М.В. Ломоносова ФГБОУ ВО «МИРЭА – Российский технологический университет» (119571, Россия, Москва, пр-т Вернадского, д. 86). Scopus Author ID 7801409746, ResearcherID H-9420-2013, https://orcid.org/0000-0002-7235-3361

Легонькова Ольга Александровна, доктор технических наук, руководитель отдела перевязочных, шовных и полимерных материалов в хирургии ФГБУ «Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского» Министерства здравоохранения Российской Федерации (117997, Россия, Москва, ул. Большая Серпуховская, д. 27). Scopus Author ID 18437207900

Кедик Станислав Анатольевич, доктор технических наук, профессор, заведующий кафедрой биотехнологии и промышленной фармации Института тонких химических технологий имени М.В. Ломоносова ФГБОУ ВО «МИРЭА – Российский технологический университет» (119571, Россия, Москва, пр-т Вернадского, д. 86). https://orcid.org/0000-0003-2610-8493

Submitted: May 29, 2019; Reviewed: July 10, 2019; Accepted: September 24, 2019.

Translated by