

Tracking the Physical Aging of Poly(ethylene oxide): A Technical Note

Submitted: February 23, 2006; Accepted: June 22, 2006; Published: December 15, 2006

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KEYWORDS: Poly(ethylene oxide), physical aging, positron annihilation lifetime spectroscopy, differential scanning calorimetry, amorphous

INTRODUCTION

Poly(ethylene oxide) (PEO) is a non-ionic linear homopolymer of ethylene oxide, which can be used as a matrix system for controlled release, a tablet binder for direct compression, a mucosal bioadhesive, a thickening agent, and a tablet coater.¹

Most of these applications require long-term stability, but amorphous and partially amorphous polymers are not in thermodynamic equilibrium and usually undergo physical aging manifested in volume and enthalpy relaxation causing serious structural changes in the material.² The plasticization effects of everyday materials are enough to change the crystallinity or the glass transition temperature (T_g) of the polymer significantly.³⁻⁵

Thermal techniques, such as differential scanning calorimetry (DSC), often prove to be time consuming or too complicated for the tracking of enthalpy relaxation, which underlines the importance of volume relaxation measurements, such as positron annihilation lifetime spectroscopy (PALS). PALS is a unique method because it is exceptionally sensitive to the free volume of substances.⁶ It is frequently used to determine the size distribution of free volume holes in polymers, which is reported to change when physical aging of the material occurs. All of these measurements are based on the interaction of the free volume holes and the so-called *ortho*-positronium (o-Ps) atom. In polymers, the formed o-Ps atoms tend to be trapped in free volume holes, and their lifetime is associated with the size of the free volume around them.^{7,8}

Although the blends of PEO with other different polymers have been studied from the point of physical aging,^{9,10} such investigations concerning the pure material are rather rare,¹¹ and the application of PALS for tracking the aging of PEO has not been reported so far.

The purpose of the present work was to follow the possible aging process of poly(ethylene oxide) by positron annihilation lifetime spectroscopy, differential scanning calorimetry, and scanning electron microscopy.

MATERIALS AND METHODS

Materials

Two grades of PEO with different molecular weights (M_w) (Polyox WSR N-12K – $M_w = 1 \times 10^6$ and Polyox WSR 303 – $M_w = 7 \times 10^6$) from The Dow Chemical Co (Midland, MI) were investigated. The polymer consists of ethylene oxide monomers, which can be described by the following structural formula: $(\text{CH}_2\text{CH}_2\text{O})_n$. The initial water content of the materials was below 1%.¹

Storage Conditions

Identical amounts of the 2 substances were placed into a desiccator and kept at $75\% \pm 5\%$ relative humidity (RH) and $40^\circ\text{C} \pm 2^\circ\text{C}$ temperature in an open container. The humidity of the desiccator was maintained using saturated NaCl solution. These circumstances are in accordance with those proposed by the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMA)^{12,13} for accelerated stability testing. Storage periods of 1, 2, and 4 weeks were chosen.

Positron Annihilation Lifetime Spectroscopy

The spectra of samples taken before storage and after 1, 2, and 4 weeks of storage were obtained. The positron source applied for the measurements was made of carrier-free $^{22}\text{NaCl}$ of the activity of 4×10^5 Bq. The active sodium chloride was sealed between 2 very thin polyimide foils. The source was then placed between 2 pieces of the sample treated

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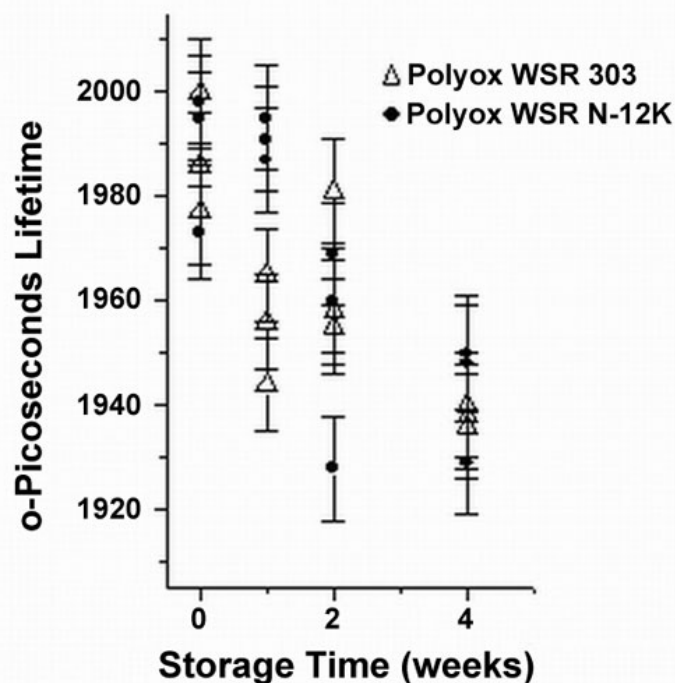


Figure 1. Ortho-positronium lifetime values of the investigated polymers.

identically before. Positron lifetime spectra were recorded by a conventional fast-fast coincidence system. The system was constructed from standard ORTEC electronic units, while the detectors were made up of BaF₂ scintillator crystals and XP2020Q photomultipliers. The time resolution of the system was ~200 picoseconds.

Differential Scanning Calorimetry

Five to six milligrams was weighed from each sample into an open aluminum pan and was heated in dry nitrogen atmo-

sphere using TA Instruments DSC 2920 unit (Newcastle, DE). Melting point and melting enthalpy values were determined from DSC scans performed from room temperature to 300°C with a heating rate of 10°C min⁻¹.

Scanning Electron Microscopy

Powder samples were fixed on the sample holder using double-adhesive tape, and gold coating was applied. Examinations were performed by means of a scanning electron microscope (SEM, Philips XL 30, Amsterdam, The Netherlands) at 12 kV and 20 kV accelerating voltage with a working distance of 11.1 to 11.9 mm. Original magnification ×1000 with an accuracy of ±2% was used.

RESULTS AND DISCUSSION

Figure 1 indicates the o-Ps lifetime values of the different samples as a function of storage time. The lifetime decrease indicates that the free volume of the studied polymers became smaller referring to volume relaxation because of physical aging initiated by the applied storage conditions. At 40°C (above its T_g and below its melting point [T_m]), the amorphous part of polymer is in the viscoelastic state, where the mobility of small segments of the molecules can lead to the reorientation of the chains. By this process, the structure of the polymer would become more ordered, causing the consequent decrease of the size of free volume holes of the polymer.

Figure 2 shows the obtained DSC curves, while Table 1 indicates the melting enthalpy and the calculated crystallinity of the substances. A characteristic melting peak can be observed on each thermogram at ~70°C, with enthalpy values increasing with storage. The crystallinity (X_c%) of the polymers was calculated from X_c% = ΔH/ΔH₀, where ΔH is the melting enthalpy of the sample and ΔH₀ is the

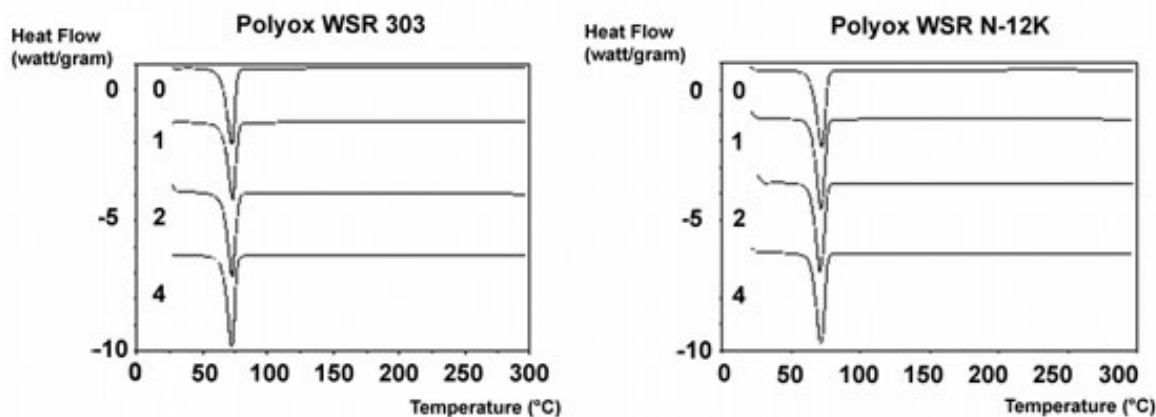


Figure 2. Differential scanning calorimetry curves of Polyox WSR 303 and N-12K before (0) and after 1 (1), 2 (2), and 4 (4) weeks of storage (exotherm up).

Table 1. Change of Melting Enthalpy, Crystallinity, and o-Ps Lifetime Values of the Examined Polymers After Different Storage Intervals

Storage Interval	Melting Enthalpy (J/g)		Crystallinity (%)		o-Ps Lifetime (ps)	
	PEO 303	PEO N-12K	PEO 303	PEO N-12K	PEO 303	PEO N-12K
0 weeks	149.8	151.4	73.8	74.6	1988	1989
1 week	154.8	169.8	76.3	83.6	1951	1991
2 weeks	169.0	167.0	83.3	82.3	1965	1952
4 weeks	173.9	172.2	85.7	84.8	1938	1942

equilibrium melting enthalpy of PEO crystals taken to be equal to 203 J/g.^{14,15} As the calculated crystallinity values show, almost three quarters of both polymers were crystalline originally, and the increasing melting enthalpies suggest that further crystallization of the amorphous part occurred along with storage. This crystallization process can be attributed to the reorientation of the macromolecular chains—also seen from the PALS results. The lower molecular weight

Polyox WSR N-12K exhibited faster crystallization. The explanation for this difference might be that in the case of polymers with equal polarity, water-absorbing ability increases with decreasing molecular weights.¹⁶ The plasticizing effect of the absorbed water could enhance the above-mentioned reorientation and crystallization, and this effect could develop earlier in the case of the lower molecular weight PEO.

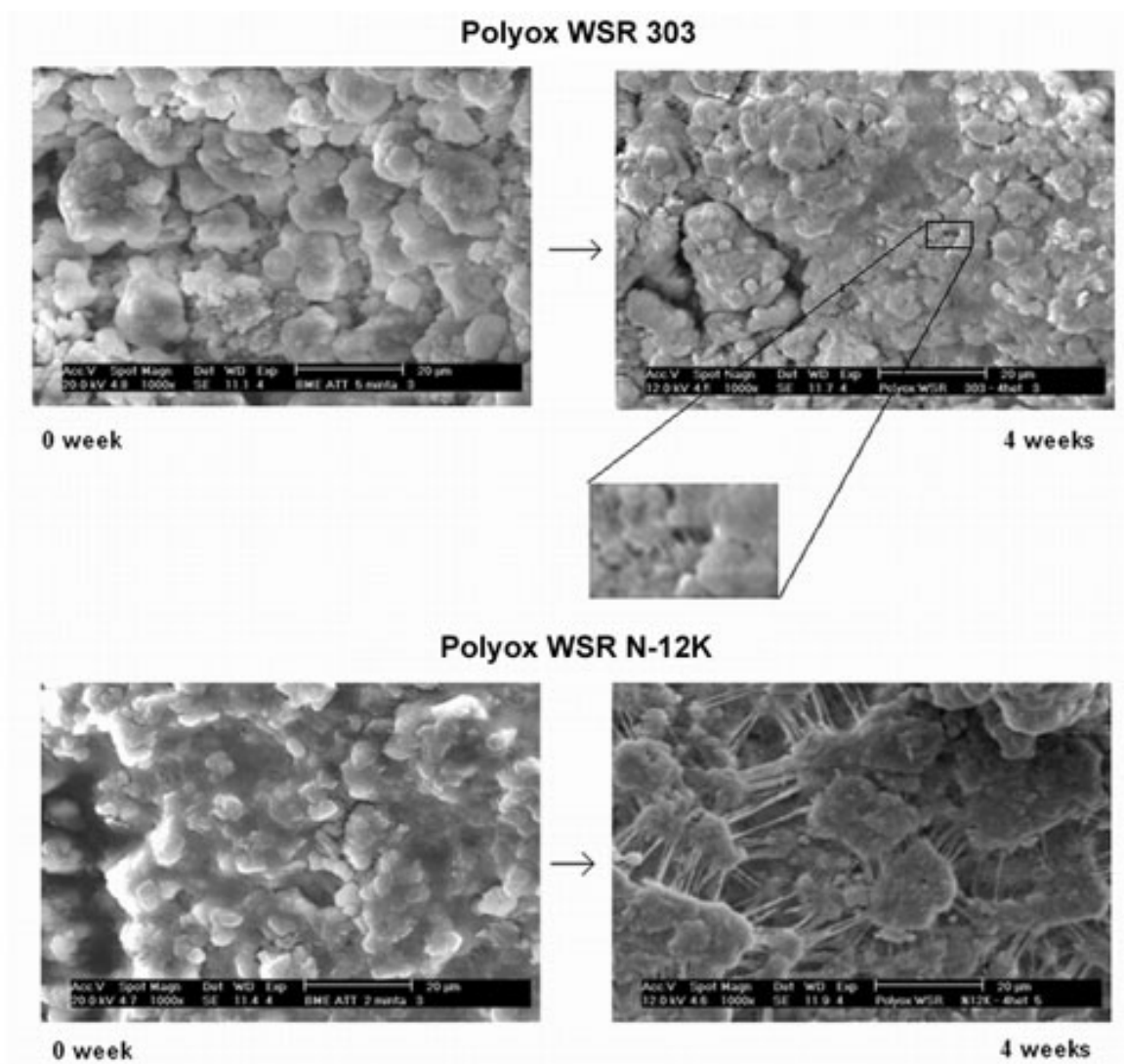


Figure 3. Photomicrographs of Polyox WSR 303 and Polyox WSR N-12K before storage (left) and after 4 weeks of storage (right) (original magnification $\times 1000$).

The faster crystallization of Polyox WSR N-12K could also explain the difference between the 2 polymers concerning the o-Ps lifetime values after 1 week. As positrons interact mainly with the amorphous part of the polymer, o-Ps lifetime did not change remarkably after 1 week in the case of Polyox WSR N-12K, because, during this period, the aging process was manifested mainly in crystallization. After this interval, however, crystallization slowed down, allowing the detection of the decrease of the free volume holes of the amorphous part of the polymer. In the case of Polyox WSR 303, crystallization proved to be slower, and the changes in the amorphous part could be followed more easily.

The usually monitored enthalpy relaxation and T_g values could not be tracked in this case because of the high crystallinity of the samples. This finding confirms the importance of the investigation of microstructural aspects by PALS measurements in monitoring physical aging of polymers.

As a result of water absorption by the materials, a glassy to rubbery transition can be observed on the SEM photomicrographs (Figure 3). The extent of this transition was again greater in the case of Polyox WSR N-12K.

These structural changes that might occur due to physical aging not only influence the pure substances but also have an effect on dosage forms. Because of these alterations, mechanical and drug release properties of the prepared dosage forms can change,⁸ which might result in stability problems in the course of long-term storage. In order to avoid the potential of the physical aging of polymeric excipients to become a formulation hurdle, it is advisable to monitor the possible structural changes.

SUMMARY AND CONCLUSIONS

Physical aging of 2 types of PEO could be tracked by the combination of PALS, DSC, and SEM methods. After storing the samples at $40^\circ\text{C} \pm 2^\circ\text{C}$ and $75\% \pm 5\%$ RH, a decrease in the o-Ps lifetime values and an increase in the melting enthalpies as a function of storage time indicated a reorientation of the polymer chains. The limitations of monitoring enthalpy relaxation confirm the importance of methods that track volume relaxation, such as PALS. Structural changes could be observed even after a short storage time (4 weeks), which highlights the effect of further investigations of the influence of physical aging on the properties of PEO-containing dosage forms.

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