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Effect of ethanol solution of iodine on degradation of poly(ε-caprolactone)

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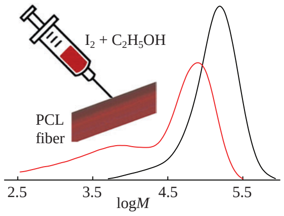
The study of the effect of iodine on the degradation of poly(ε-caprolactone) fibers has revealed a drastic decrease in their molecular weight upon 24 h exposure to a 10% iodine solution in ethanol. It has been assumed that the main mechanism of this degradation is alcoholysis which proceeds with an efficient rate constant of nearly 7.5×10^{-3} h^{-1}.



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Poly(ε-caprolactone) (PCL) belongs to the class of biodegradable aliphatic polyesters.[1] At present, this polymer is widely used in biomedicine to create three-dimensional scaffolds for tissue engineering, drug-delivery systems, implants with controlled release, bioresorbable surgical sutures, *etc*.[2] In spite of its biocompatibility, good mechanical properties, and simplicity of processing, this polyester has a number of drawbacks associated with its pronounced hydrophobicity and long degradation periods of 2–4 years depending on its molecular weight, degree of crystallinity, and other parameters.[3] To vary the degradation rate, ε-caprolactone is often copolymerized with lactides[4,5] and other lactones.[6] However, a more flexible approach may be an addition of fillers, including nanofillers, that modify the degradation profile of the polymer matrix. Previously,[7] it was found that introduction of iodine into polylactide fibers would substantially accelerate the hydrolytic degradation of the polymer in phosphate buffered saline (PBS) medium at 37 °C.

The goal of this work was to study the effect of iodine on the degradation rate of PCL and to determine the possible mechanism of this process. Since iodine is widely used in medicine as an antimicrobial[8] and a radiopaque substance,[9] such a study seems to be urgent for the search of low-cost and efficient fillers to control the degradation rate of polymers.

Iodine-containing PCL (pI_2-PCL) was prepared on the basis of porous fibers obtained as described previously.[10,11] For this purpose, initial isotropic PCL fibers (i-PCL) were preliminarily stretched in ethanol to a tensile strain of 100%; then they were annealed under isometric conditions at 40 °C. The resulting porous PCL fibers (p-PCL) with an effective bulk porosity of 28 vol% were impregnated with a 10% solution of iodine (reagent grade, ‘Ruskhim’) in 95% ethanol for 1 h; then, the solvent was removed. The pI_2-PCL fibers with 5 wt% of I_2 are characterized by a rather uniform distribution of iodine by volume [for details, see Online Supplementary Materials (OSM)].

Since PCL-based materials are, primarily, of interest for biomedical applications, we studied the hydrolytic degradation of the obtained pI_2-PCL fibers and for comparison unfilled i-PCL and p-PCL fibers in PBS (10 mM Na_2HPO_4 and 0.15 M NaCl; pH 7.4), which is often used as a model medium in biological studies. The experiments were performed at 37 °C for 10 weeks. It should be noted that during this time neither appearance nor molecular-weight and mechanical parameters of initial i-PCL and porous p-PCL fibers substantially changed (changes in the values of the characteristics were less than 15%). However, for iodine-containing samples, the changes appeared to be significant. The values of M_n and M_w determined by gel-permeation chromatography (GPC, for details, see OSM), dramatically decreased to 9–11 and 40–45 kDa, respectively, while $Đ$ increased to 4–5, and the fiber embrittlement was observed. The most pronounced changes in the molecular-weight characteristics were observed during exposition of p-PCL in an ethanol solution of iodine. The molecular-weight distribution curve (Figure 1, curve *2*) acquired a bimodal character and shifted to the region of lower molecular weights.

The exposure of the pI_2-PCL samples in PBS had a significant effect on the characteristics of the polymer only within the first 2 weeks (see Figure 1, curves *3*–*6*). This is most probably due to the washing out of iodine through the open porous structure of

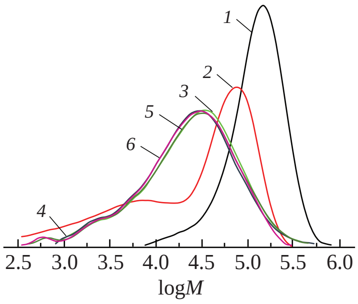

Figure 1 Molecular-weight distribution curves for (*1*) porous p-PCL fiber and (*2*)–(*6*) pI_2-PCL fibers containing iodine (5 wt%) after their exposure in PBS at 37 °C for (*2*) 0, (*3*) 2, (*4*) 4, (*5*) 8 and (*6*) 10 weeks.

the fibers into the PBS solution, as is evident from the sample by the gradual discoloration. This fact indicates that PCL degradation is accelerated only in the presence of iodine, and when it is removed from the bulk of the polymer, the decomposition rate decreases.

Since it has been found that the ethanol solution of iodine most significantly accelerates PCL degradation, the mechanism of this process has been carefully studied using isotropic i-PCL. For this purpose, the fibers were exposed in a 10% iodine solution for various periods of time. The maximum degree of PCL swelling in ethanol and the ethanol solution of iodine was reached in 1 h and was found to be 4%. The maximum I_2 content of about 5 wt% was reached in 24 h. GPC data (Table 1) revealed that, as the time of i-PCL exposure in the ethanol solution of iodine increases, the M_n and M_w values of the polymer would gradually decrease, which indicates the occurrence of degradation processes. Note that the exposure in pure ethanol caused no substantial changes in the characteristics of the polymer.

To determine the possible mechanism of the acceleration of polymer degradation in the presence of I_2, i-PCL samples were studied by ^{1}H NMR. Their integral intensities relative to that of the signal at 3.60–3.67 ppm of the terminal group for i-PCL samples are given in Table 2. It was assumed that the signals at 4.12 (q, 2H) and 1.25 ppm (t, 3H) are attributed to terminal ethoxycarbonyl groups $–C(O)O–CH_2–CH_3$, which should be formed in the course of transesterification (ethanolysis) of PCL in the presence of I_2 as a catalyst (for the spectra images, see OSM).

The probable scheme of the reaction mechanism is presented in OSM, Figure S4. As reported previously, iodine catalyzes esterification yielding esters[12] and the ring-opening polymerization of ε-caprolactone[13] due to the formation of a charge-transfer complex as an intermediate compound. This reaction may be promoted by the acidic medium of the alcohol solution of iodine, the pH of which is 3.4–4.1 (the pH of 95% ethanol is 6.9). The acidity of the medium seems to increase predominantly due to acetic and hydroiodic acids, which are the most probable products of the interaction between ethanol and I_2.[14] It is important to note that the rate of hydrolytic degradation of PCL at pH 3 increases insignificantly (the rate constant k is ~0 day^{-1}), as previously shown elsewhere.[15] The values of the number-average molecular weight of PCL determined by ^{1}H NMR (see Table 2) from the integral intensity ratio between the signals of methylene of the main chain and terminal groups of PCL are in good agreement with the GPC data (see Table 1).

The effective rate constant of PCL degradation *via* the alcoholysis reaction was determined (for details, see OSM). Since the weights of the samples remained unchanged within the experiment time (24 h), *i.e.*, low-molecular-weight reaction products were not washed out, it may be assumed that the concentration of the newly-formed chain ends is inversely proportional to the polymerization degree of the polymer and number-average molecular weight $1/M_n$. So, the dependence of $1/M_n$ *vs*. degradation time t (for details, see OSM, Figure S5) characterizes the process of the formation of degradation products. The rate constant calculated for the alcoholysis in the ethanol solution of iodine at 20–25 °C has appeared to be 7.5×10^{-3} h^{-1}, thus being two orders of magnitude higher than the rate constant previously determined for the hydrolytic degradation of PCL in the phosphate buffer (pH 7.6) at 37 °C.[4]

Table 1 Molecular-weight characteristics determined by GPC for i-PCL fibers exposed to different media.

Medium	t/h	M_n/kDa	M_w/kDa	M_w/M_n ratio
Air	24	112	169	1.51
EtOH	24	105	162	1.54
10% I_2 in EtOH	1	87	146	1.68
10% I_2 in EtOH	3	42	98	2.33
10% I_2 in EtOH	15	18	53	2.94
10% I_2 in EtOH	24	13	38	2.92

Table 2 Relative integral intensities of i-PCL signals and number-average molecular weights of the polymer exposed in the ethanol solution of iodine for different periods of time.

t/h	Signals of methylene groups/ppm					M_n/kDa
	3.60–3.67	1.50–1.80	1.25–1.50	2.15–2.45	3.90–4.20	
0	1	930	456	455	456	52
15	1	236	118	122	117	13
24	1	189	94	94	93	10

In conclusion, the PCL degradation is accelerated in an ethanol solution of iodine, which can be used when developing bioactive materials with programmed degradation profile. At the same time, when using iodine as an agent for low-temperature sterilization of devices made of PCL, it is necessary to consider the possible occurrence of side processes leading to the degradation and rapid embrittlement of the material.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.04.035.

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