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Effect of γ-irradiation on the structure of poly(ethyl acrylate-*co*-hydroxyethyl methacrylate) copolymer networks for biomedical applications

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Abstract The effect of the sterilization process by γ-irradiation on the structure of poly(ethyl acrylate-*co*-hydroxyethyl methacrylate) copolymer networks, P(EA-*co*-HEMA) is studied for a broad dose range (7, 15, 25 and 50 kGy) and copolymer composition interval (0, 0.3, 0.5, 0.7 and 1 weight fraction of HEMA in the copolymer). γ-irradiation promotes chain scission in PHEMA homopolymer but induces new crosslinking points in PEA homopolymer. Both effects are present in the copolymers, with a net result that depends on composition. For copolymers with high HEMA fractions chain scission predominates, while, as the amount of EA in the copolymer increases, the situation changes and the net effect turns out to be an increase in the number of elastically active chains. Further, γ-irradiation strengthens the γ relaxation in PHEMA homopolymer, what suggest that the number of interchain hydrogen bonds decreases. FTIR spectroscopy reveals no oxidation as a consequence of the sterilization process.

1 Introduction

Biomedical polymers either introduced in vivo in an organism or used for in vitro experiments (e.g. cellular culture supports) must be sterile to avoid subsequent infection that could lead to serious problems (illness or death in vivo, experiment failure in vitro). Some materials seem to be more sensitive to bacterial contamination because of their composition, microstructure, degree of porosity, or surface chemistry itself [1]. Among the methods of sterilization, the exposure to γ rays is one of the most employed. γ-irradiation is highly penetrating which represents an advantage with respect to other sterilization techniques for materials in which the existence of nanopores cannot be discarded [2, 3].

The minimum sterilization dose required by official authorities is 25 kGy [4]. Even though polymers undergo changes in both mechanical and structural properties when subjected to ionization, a wide range of materials are compatible with radiation sterilization, including polyethylene, polyesters and methacrylates [1, 5–7].

Molecular weight of a polymer, and its distribution, can be drastically altered by exposure to ionizing radiation [1, 8, 9]. These high-energy treatments result in free radical generation, main chain scission and crosslinking, and subsequently alter the distribution of chain size in the bulk polymer. Besides, the combined action of ionizing radiation and oxygen on polymers may rapidly lead to a severe deterioration of the polymer properties. The resulting effects are strongly dependent on the chemical structure of the polymer. The radiation damage and the oxidative degradation cause chemical changes in the polymer structure with build-up of variety of new functional groups as carbonyls, carboxyls, esters, hydroxyls, unsaturations; furthermore, chain scissions and cross-links are often induced [1–3, 10].

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Poly(ethyl acrylate-*co*-hydroxyethyl methacrylate) copolymer networks are known to exhibit nanophase separation into hydrophilic and hydrophobic domains [11]. This fact has been used for explaining its success in promoting cell adhesion and viability when used as materials for cell culture [12]. In this work we have studied the effect of γ-irradiation on the copolymer structure by Dynamic Mechanic Spectroscopy (DMS) and Fourier Transform InfraRed Spectroscopy (FTIR) in the whole copolymer composition range and in a broad dose range around the standard 25 kGy.

2 Materials and methods

2.1 Synthesis

Copolymer networks were prepared from a solution of both monomers ethyl acrylate, EA, and hydroxyethyl methacrylate, HEMA, with the desired proportion, using 0.1 wt% of benzoin (Scharlau 98% pure) as photoinitiator and 2% by weight of ethyleneglycol dimethacrylate, EGDMA (Aldrich 99% pure) as crosslinking agent. The copolymerization was carried out up to limiting conversion. Three monomer feed compositions were chosen, given by the weight fractions of HEMA in the initial mixture of 0.7, 0.5 and 0.3. Polymerization took place under the ultraviolet light for 24 h at room temperature and afterwards low molecular weight substances were extracted from the material by boiling in ethanol for 24 h and then drying in vacuum to constant weight. Besides, pure poly(hydroxyethyl methacrylate), PHEMA, and poly(ethyl acrylate), PEA, networks were prepared in the same way.

2.2 Gamma radiation

All samples were irradiated with a Cobalt-60 primary source for γ radiation (ARAGOGAMMA, S.A.), the doses used were 7, 15, 25 and 50 kGy. A sample not exposed to radiation was used for a comparison. The samples were packaged in air before the irradiation and their dimensions were approx. $30 \times 15 \times 1$ mm^3.

2.3 Dynamic Mechanical Spectroscopy

Dynamic mechanical spectroscopy (DMS) was performed at a heating rate of 1 °C/min in a Seiko DMS210 instrument from –150 to 200 °C at a frequency of 1 Hz. Samples for DMS experiments were rectangular approx. $10 \times 2.5 \times 0.8$ mm^3.

2.4 Fourier Transform Infrared Spectroscopy

Fourier Transform InfraRed spectroscopy (FTIR) was performed in a Nicolet Nexus spectrometer in the Attenuated Total Reflectance (ATR) mode. The average sample thickness was 1 mm. Thirty-two scans were taken for each sample.

3 Results and discussion

Figure 1 shows the dynamic-mechanical relaxation thermograms of the copolymers without irradiation. The pure PEA and PHEMA networks show a single maximum in the loss tangent at 9°C and 140°C, respectively, which corresponds to the main relaxation or α process. In addition PHEMA shows at lower temperatures, in the glassy state, a smooth shoulder in the loss tangent that is ascribed to the secondary relaxation associated to local movements of the side chains of the polymer: the β relaxation [13] and a low-

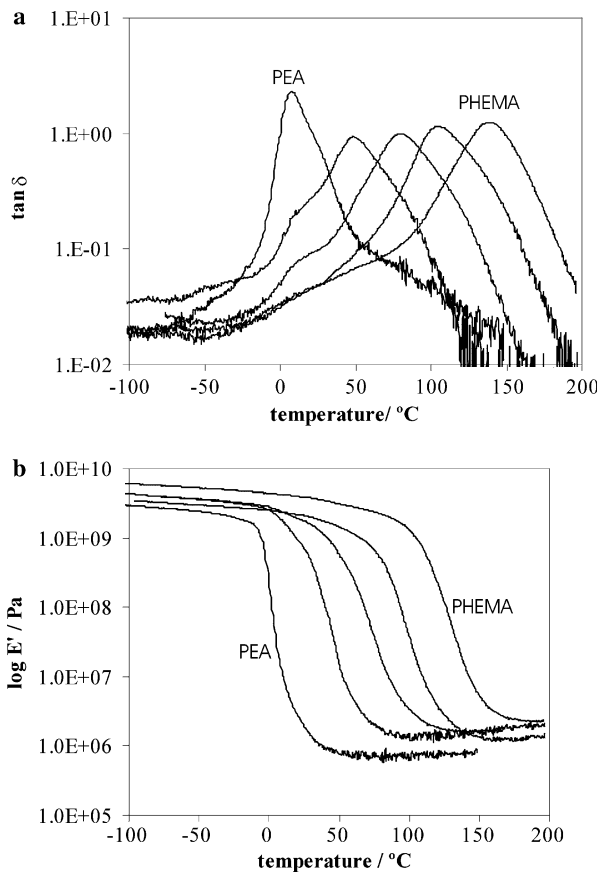

Fig. 1 Dynamic-mechanical relaxation thermograms of PEA, PHEMA and their copolymers (0.7/0.3, 0.5/0.5, 0.3/0.7) measured at 1 Hz. (**a**) Mechanical loss tangent. (**b**) log E'

temperature γ relaxation around –70 °C that will be analysed below.

DMS experiments on copolymers show two relaxation processes of different intensity located between the temperatures of the main relaxation of the pure polymers. The bigger one is at higher temperature and its intensity is similar to that of the pure PHEMA network independently of the copolymer composition. On the contrary the second one is much smaller, and it is revealed as a shoulder in the low-temperature side of the main peak, in the temperature range of the α relaxation of the PEA network; its intensity depends on composition: the higher the amount of HEMA in the copolymer the lower the magnitude of this relaxation process (Fig. 1a).

The different reactivity [14] of the two comonomers in the copolymerization of EA and HEMA makes that P(EA-*co*-HEMA) are not random copolymers but their chains are formed by long blocks of HEMA and some EA, and some pure PEA chains are also formed in the latter stages of the polymerization when all the HEMA monomer has been consumed. As a consequence the copolymer networks present two separated phases with nanometric dimensions. One of them consists in a copolymer richer in HEMA than the average composition and the other is formed by pure PEA. This picture of the structure of the copolymer networks is supported by DSC experiments [11]. The high-temperature relaxation appearing in the mechanical loss tangent of the copolymers can be ascribed to the main relaxation of the copolymer chains and its position depends on the average copolymer composition, the higher the amount of HEMA the higher the temperature of the maximum. The low-temperature relaxation process can be ascribed to the relaxation associated to the glass transition of the pure PEA domains. It is worth noting that this low-temperature shoulder cannot be due to the β relaxation of PHEMA since its strength would decrease with an increasing content of EA in the copolymer and the experiments show the contrary.

Figure 2 shows the DMS spectra of the PHEMA and PEA homopolymers after radiating at different doses. The effects of the irradiation are subtle but nevertheless significant.

Figure 3 shows the relative variation of the rubber modulus of the homopolymers as a function of the doses employed in the sterilization process.

As the radiation doses increases, the modulus increases in the PEA homopolymer and decreases in the PHEMA homopolymer when compared with the corresponding sample without irradiation. The value of the rubber modulus is related to the structure parameters of the network by the theory of rubber elasticity [15],

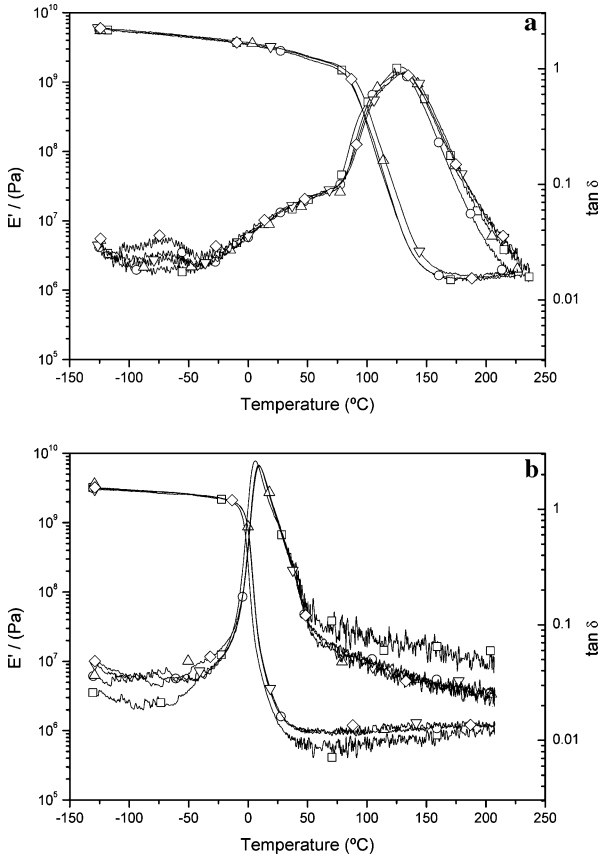

Fig. 2 Dynamic-mechanical relaxation thermograms of the homopolymers at different radiation doses. (**a**) PHEMA homopolymer (**b**) PEA homopolymer; non-irradiated sample (square), 7 kGy (circle), 15 kGy (triangle), 25 kGy (inverted triangle), 50 kGy (diamond)

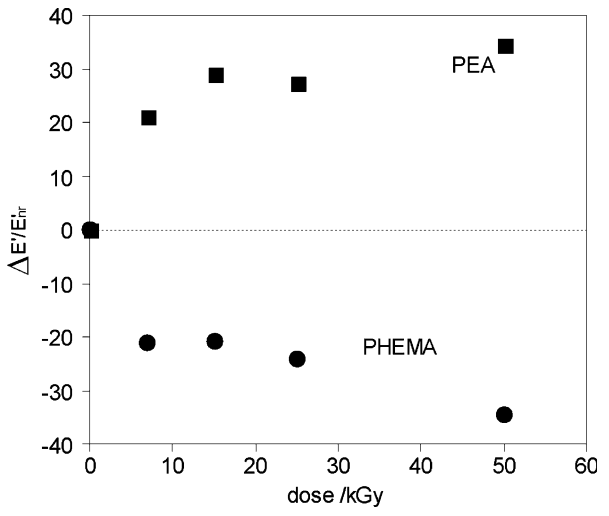

Fig. 3 Relative variation (to the non-radiated sample) of the rubbery modulus at different radiation doses for the PEA and PHEMA homopolymers

Table 1 Density of elastically active chains (n_c/V) and average molecular weight between crosslinks ($\bar{M}_c$) as a function of radiation doses

Samples	Doses (kGy)									
	0		7		15		25		50	
	$\frac{n_c\,(\text{mol})}{V\,(\text{cm}^3)}$	$\bar{M}_c$ (g/mol)	$\frac{n_c\,(\text{mol})}{V\,(\text{cm}^3)}$	$\bar{M}_c$ (g/mol)	$\frac{n_c\,(\text{mol})}{V\,(\text{cm}^3)}$	$\bar{M}_c$ (g/mol)	$\frac{n_c\,(\text{mol})}{V\,(\text{cm}^3)}$	$\bar{M}_c$ (g/mol)	$\frac{n_c\,(\text{mol})}{V\,(\text{cm}^3)}$	$\bar{M}_c$ (g/mol)
PHEMA	2.73E–04	4457	2.15E–04	5650	2.16E–04	5636	2.07E–04	5863	1.79E–04	6801
PEA	1.14E–04	9993	1.38E–04	8243	1.46E–04	7747	1.45E–04	7848	1.53E–04	7425

$$E' = \frac{3 \cdot n_c \cdot R \cdot T}{V_0}, \quad (1)$$

In this equation T is the temperature at which the rubbery modulus E' is measured, R is the gas constant, V_0 the volume of the sample and n_c the mole number of elastically active chains. The effect of γ-irradiation on E' (Fig. 3) can thus be explained by a change in the volume density of elastically active chains (n_c/V). Table 1 shows the effect of radiation dose on this structural parameter of the homopolymer networks. n_c/V decreases as the radiation doses increase for the PHEA homopolymer due to chain scission, but increases for the PEA homopolymer due to the radiation-induced new cross-links. Besides, the average molecular weight between crosslinks,

$$\bar{M}_c = \frac{\rho}{n_c/V} \quad (2)$$

can be calculated from n_c/V and the density ρ (the measured density of the radiated samples shows no change relative to the non-radiated ones). The result is also shown in Table 1. As expected, the average molecular weight between crosslinks increases in the PHEMA homopolymer and decreases in the PEA one.

It has been described [1] that polymers of the type (CH_2-CR′R″), such as PHEMA, will undergo under radiation predominantly chain scission, while polymers of type (CH_2–CHR), such as PEA, will be susceptible to crosslinking. In general, polymers with high concentrations of quaternary carbon atoms along the chain undergo scission while in polymers lacking this feature, crosslinking is the main effect of radiation. The presence of insaturation in the polymer chain promotes this effect and enhances the yield of crosslinking (natural rubber is an example) [1]. Even though PEA and PHEMA seem to be quite similar in their backbone chemistry, there are subtle differences that render very different reactions to ionizing radiation. PEA undergoes crosslinking when exposed to radiation, while PHEMA degrades very rapidly through chain scission. The number of both main chain scissions and crosslinkings is proportional to radiation dose (Fig. 3 and Table 1).

The relative variation of the rubbery modulus of the radiated samples relative to the non-radiated sample has been calculated from the DMS spectra and is shown in Fig. 4.

The values obtained for the copolymers are in-between those of the corresponding homopolymers. Pure PEA shows an increase of approx. 30% in E' as a consequence of new crooslinking induced by radiation. On the contrary, pure PHEMA shows a decrease in E' because radiation gives rise to chain scission. As the amount of HEMA in the copolymer increases the relative variation in E' decreases in an almost linear way. The variation is nil for 50% HEMA content in the copolymer, i.e. chain scission and new crosslinking creation take place in such a way that the density of elastically active chains is approximately the same as that of the copolymer without radiation. For higher HEMA contents in the copolymer the variation in E' turns out to be negative, and the chain scission mechanism predominates. The relative variation of E' in the copolymers agrees with the molecular architecture of this system [11]: even though copolymerization takes place from a random solution of both monomers,

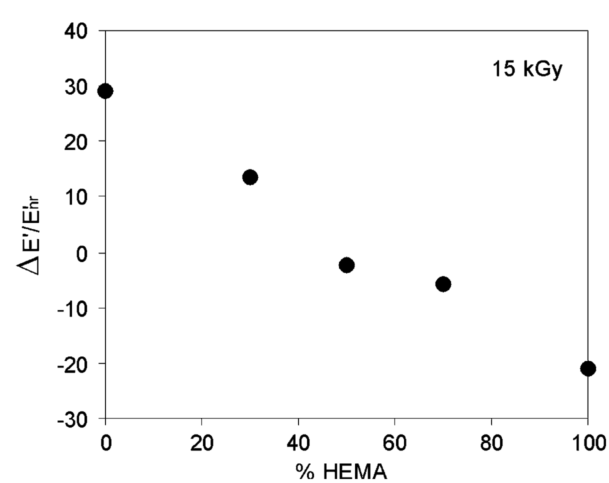

Fig. 4 Relative variation of the rubbery modulus for the EA/HEMA copolymers at a fix dose 15 kGy

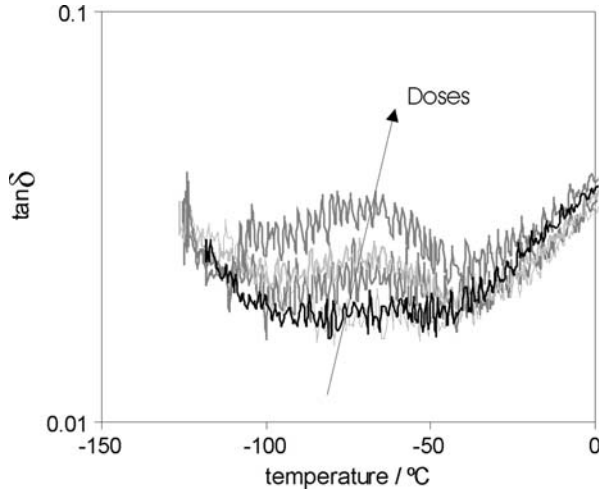

Fig. 5 Mechanical loss tangent for the PHEMA homopolymer at different radiation doses. Only the γ-relaxation temperature interval is shown

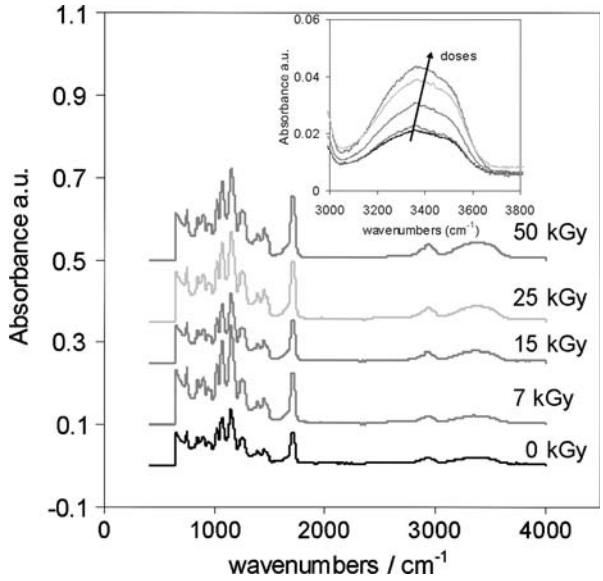

Fig. 6 FTIR spectrum for the PHEMA homopolymer at different radiation doses. The insert shows the magnification of the O–H band

the copolymer chain obtained after copolymerization keeps a certain order. HEMA units are predominantly joined together in the chain, which gives rise to a heterogeneous material at the nanoscale, with HEMA rich domains and pure PEA domains. The effect of radiation can be seen as a linear superposition of effects directly related to the copolymer composition.

The existence of scissions in the PHEMA homopolymer chains is also reflected in the dynamic mechanical thermograms. Figure 5 shows a magnification of the loss tangent for the PHEMA homopolymer networks at different radiation doses in the low temperature range.

It is clearly observed that the intensity of this low temperature, γ, relaxation increases as the doses level does. The γ relaxation in PHEMA is associated to the rotation of the hydroxyethyl group attached to the ester side chain [16, 17]. Rotation of $-CH_3CH_2OH$ side group in PHEMA must be observed as a result of slow viscoelastic deformation on the application of a mechanical load. Even though the γ relaxation has been accounted for by dielectric spectroscopy in the temperature range of –147 °C to –60 °C (0.1–100 KHz) [18, 19], some previous reported mechanical spectroscopy data on PHEMA reported the absence of γ relaxation above –160 °C [20]. An increase in the intensity of tan δ for this relaxation process means that there are side groups able to overcome interchain hydrogen bonds as a consequence of higher mobility due to chain scission. The effect of irradiation on hydrogen bonding is observed also in FTIR data on the O–H band. The insert in Fig. 6 shows higher intensity of the O–H stretching band for the PHEMA homopolymer as the radiation doses increases, which supports the influence of γ-irradiation on the interchain-hydrogen bonding mechanisms.

The existence of oxidative processes within the material is characteristic of γ-irradiation sterilization processes [4], which results in new infrared absorbance bands in the wave number range of 1680–1800 cm^{-1}, due to carbonyl-containing chemical species such as ketones, esters, aldehydes, and acids [21]. This is not the situation for the copolymer networks studied in this work. Figure 6 shows the FTIR spectra in the Attenuated Total Reflectance (ATR) mode for the PHEMA homopolymer. There is no qualitative change in the spectra as the dose changes and no oxidative process is induced in the material as a consequence of sterilization. The FTIR spectra for the other compositions and the pure homopolymers behave in a similar way, i.e. no signal of oxidation appears as the sterilization dose increases.

4 Conclusions

The effect of γ-irradiation on the structure of P(EA-*co*-HEMA) copolymer networks has been studied. The rubbery modulus of PEA homopolymer increases as a consequence of new crosslinks induced by radiation. On the contrary, in PHEMA, chain scission predominates and E' decreases as the sterilization dose increases.

The effect of radiation on the copolymers is a superposition of the corresponding homopolymers,

which agrees with the previously nanoheterogeneity reported for this system

Radiation has also an effect on the intensity of the relaxation mechanism associated to the movement of the $-CH_3CH_2OH$ group. The number of interchain –OH bonds decreases as a consequence of γ-irradiation, the more the higher the radiation dose.

Finally, FTIR has confirmed the absence of any kind of oxidative process in the samples induced by the sterilization process.

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