Degradation of $\gamma$-irradiated polyethylene-ethylene vinyl alcohol-polyethylene multilayer films: An ESR study
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A B S T R A C T

The present work aims to investigate by ESR the effects of γ-irradiation on antioxidants and on solid multilayer films used in biomedical applications. The multilayer films analyzed here are mainly composed of polyethylene and ethylene vinyl alcohol. Radical species are monitored over time after γ-irradiation at several doses (30, 50, 115 and 270 kGy) using ESR to assess the impact of the dose-value on the formation of the radicals.

Keywords:
Electron spin resonance investigation
γ-irradiation
Polyethylene
Ethylene vinyl alcohol
Antioxidants
Additives

1. Introduction

The preparation, storage, mixing, freezing, transportation, formulation, and filling of biopharmaceutical solutions are performed in sterile single-use plastic bags. The sterilization is achieved through γ-irradiation, which generates modifications of the materials, as reported in the literature [1]. The integrity and the security of packages rely on the appropriate flexible and barrier polymeric materials such as polyethylene (PE) and ethylene vinyl alcohol (EVOH) [2]. γ-sterilization of single-use systems initiates chemical reactions inside the plastic material, leading to either an increase or a decrease in the molecular weight of the polymers [3,4]. In our work, we focused on the effects of γ-irradiation on the solid state of a multilayer PE/EVOH/PE polymer film, named film A, and on additives commonly used in this type of film [5–7]. The manufacturing of polymeric films is carried out by extruding the resin granulates. To allow the robust transformation of the resin granulates into films and to aid further manufacturing through to the finished products, additives are used to adjust the characteristics of the resin. PE has interesting water barrier properties and mechanical properties [8,9]. EVOH is remarkable for its barrier properties to CO2 and O2 gases [2].

The classical γ-irradiation dose range used in the biopharmaceutical industries is between 25 and 45 kGy [10]. In this study, γ-irradiation doses up to 270 kGy were investigated in order to enhance the effect of the γ-irradiation and to therefore better emphasize and investigate the modifications induced by γ-rays.

The γ-sterilization of these systems affords complex modifications inside the materials, leading to modifications of the additives or to damage in the polymers themselves [11–13]. The modifications probably induce the formation at the surface and in the core of the material of radical species that are detected by ESR (Electron Spin Resonance). The radical species are generated despite the presence of antioxidants in the films, which raises questions about the localization and the nature of these radical species. The radicals generated during the irradiation process should be quickly scavenged by the antioxidants in the layers where these additives are present [14]. The presence of oxygen-containing organic molecules results from the competition between the free-radical scavenging by antioxidants and the reaction of O2 with the hydrocarbon chains [15]. This competition may depend on the γ-irradiation dose rate.

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and on the direct availability of oxygen and antioxidants [15]. The generation of oxygen-containing organic molecules on the surface of the films should be higher than in their core, due to the direct contact with air, while the permeation of oxygen through the polymers is rather a slow migration process. The generation of free radicals and their diffusion in the polymers are therefore two independent phenomena resulting in different radical lifetimes, depending on which layer the radicals originate from.

The localization, nature and lifetime of the radicals generated during the γ-irradiation stage were investigated on film A. Film A, as well as some antioxidants and additives (Fig. 1) commonly used in plastic films [56–7], was investigated under different conditions: irradiated at different γ-doses under air and degassed.

2. Experimental

The films and resins investigated in this study – the three-layer film A, the monolayer PE film, the monolayer EVOH film and EVOH resins with different grades of EVOH – were provided by Sartorius Stedim FMT (Aubagne, France). It is worthy to note that the thickness of the EVOH layer is not homogeneous in the overall film. Molecules 1–6 were purchased from Sigma Aldrich, stored at room temperature, and used as received. Molecules 1–4 and 6 are generally used in manufacturing of plastic films. The internal layer is the side of film in contact with the solution when the bag is filled, and the external layer is the side of film in contact with air. Unlike in the case of a previous investigation [16], this information is not crucial as the radicals generated do not depend on the side.

Additives, films and resins were irradiated at room temperature by a 60Co γ-source under air or degassed conditions. Under air, sheets of film were packed in plastic bags (made of PE) and additives or resins were introduced in glass bottles. Under vacuum, pieces of film, additive 6 or resins were all introduced in glass tubes, which were then degassed ($P = 10^{-5}$ Torr). Table 1 summarizes the mass and the conditions for each sample.

The 60Co γ-source (Synergy Health company, Marseille, France) provided doses of 30 (±1), 50 (±1), 115 (±2) and 270 (±5) kGy, at a dose rate of 8–13 kGy/h. To obtain the target dose, it was necessary to perform several sterilization cycles, including a waiting time not controlled between each cycle as well as in non-controlled storage conditions.

Air irradiated samples were transferred into ESR probes (masses are reported in Table 1). The samples irradiated under vacuum conditions were quickly transferred under argon atmosphere in ESR probes, and again degassed ($P = 10^{-5}$ Torr). The additives, in pure solid form or in solution in toluene, were oxidized by PbO2 (masses reported in Table 1).

ESR measurements were carried out on a Bruker EMX X-band spectrometer operating at 9.5 GHz and equipped with a high sensitive rectangular microwave cavity. The first spectra were recorded at room temperature a few days after γ-irradiation and the others over time.

The spectroscopic parameters were: modulation amplitude 2 G or 0.5 G (for solid and liquid additives oxidized by PbO2, respectively), magnetic field sweep 500 G, receiver gain 104, resolution 1024 points, power 20.12 mW and sweep time of 20.972 s or 83.89 s (for solid and liquid additives oxidized by PbO2, respectively). One scan was performed to record each ESR signal.

Nitroxide 7 (see Fig. 1) was prepared according the reported procedures [18]. 45.4 mg of pure 7 were solved in dichloromethane in order to prepare a concentration of 1016 molecules. The stock solution was diluted to 1015, 1016, 1017, 5·1016, 4·1016, 3·1016, 2·1016 and 1016 molecules. Then 300 µl of these solutions were poured on silica gel to achieve a homogeneous powder in the ESR probe. The tubes were left open so that the dichloromethane could evaporate. Then, the ESR signals were recorded: modulation amplitude 2G, magnetic field sweep 500 G, receiver gain 102, resolution 1024 point, power 20.12 mW and sweep time 20.972 s.

Masses of silica gel $m$, double integrals $I_1$ and normalized double integral $I_2$ are reported in Table 2. As displayed in Fig. 2, a nice correlation ($R^2 = 0.9996$) was obtained on the concentration range investigated (Table 2) affording a reliable titration curve. Nevertheless, the accuracy limit for the titration was set at 5·1016 molecules and the detection threshold above 1016 molecules.

The calibration line is given by Equation (1), with $y$: the number of molecule/mg, and $x$: the double integral normalized with the amount of material.

$$y = -3.914\cdot10^{15} + 1.292\cdot10^{14}\cdot x$$

Fig. 1. Structures of additives, TEMPO derivative and film A. 1: 2,6-Di-tert-butyl-p-cresol, 2: Pentaeerythritol tetralak (3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate), 3: Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate, 4: Tris (2,4-di-tert-butylphenyl)phosphate, 5: 2,4-di-tert-butylphenol, 6: N,N-Ethylenebis (stearamide).
Table 1
Mass of additives, resins and films γ-irradiated (left part) or oxidized by PbO2 (right part) introduced in the ESR tube.b

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mass for γ-irradiation (mg)</th>
<th>Mass (mg)</th>
<th>Mass of PbO2 (mg)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>30 kGy</td>
<td>50 kGy</td>
<td>115 kGy</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>219.2</td>
<td>215.2</td>
<td>197.5</td>
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<td>3</td>
<td>181.7</td>
<td>190.0</td>
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<td>4</td>
<td>199.5</td>
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<td>254.0</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>82.5</td>
<td>-</td>
</tr>
<tr>
<td>6 under air</td>
<td>-</td>
<td>197.3</td>
<td>-</td>
</tr>
<tr>
<td>6 degassed</td>
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<tr>
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<tr>
<td>PE film</td>
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<td>-</td>
</tr>
<tr>
<td>EVOH fi</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Film A degassed</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EVOH resin A (71% VOH) under air</td>
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<tr>
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<td>-</td>
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<tr>
<td>EVOH resin A (56% VOH) under air</td>
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<td>EVOH resin A (56% VOH) degassed</td>
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<td>-</td>
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<tr>
<td>EVOH resin C (38% VOH) under air</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>EVOH resin C (38% VOH) degassed</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>EVOH film (68% VOH) under air</td>
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<td>-</td>
</tr>
<tr>
<td>EVOH film (68% VOH) degassed</td>
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</tr>
<tr>
<td>PE film under air</td>
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<td>-</td>
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<tr>
<td>PE film degassed</td>
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</table>

<table>
<thead>
<tr>
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<th>Number of nitroxides 7m, double integral I1, mass of 7m, and normalized double integral I2.</th>
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</thead>
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<tr>
<td></td>
<td>Number of nitroxides 7m</td>
</tr>
<tr>
<td>10⁰⁷</td>
<td>775,000</td>
</tr>
<tr>
<td>10⁰¹⁶</td>
<td>91,000</td>
</tr>
<tr>
<td>10⁰¹⁹</td>
<td>10,000</td>
</tr>
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<tr>
<td>5·10¹⁶</td>
<td>800</td>
</tr>
<tr>
<td>4·10¹⁶</td>
<td>600</td>
</tr>
<tr>
<td>3·10¹⁶</td>
<td>800⁸⁷</td>
</tr>
<tr>
<td>2·10¹⁶</td>
<td>600⁸⁷</td>
</tr>
<tr>
<td>10¹⁶</td>
<td>-</td>
</tr>
</tbody>
</table>

- a.u. for arbitrary unit.
- b Degassed at P = 10⁻³ Torr.
- c ca. 100 mg.
- d Dashed symbol — is for not investigated possibility.
- e Integration of traces.
- f No signal.

All data corresponding to the quantification of ESR signals are reported in Tables SI 1-7.

3. Results and discussion

3.1. ESR investigation of additives

Taking into account the broad linewidth (ΔHpp ≈ 4 G) [19], the hyperfine coupling of the aromatic hydrogen atom aH,m (aH,m = 1.1 G) at the meta position was not detected for 1• – 3•, and 5• (Fig. 3a, d, g and j). Moreover, the signals expected — quadruplet for the methyl at the para position, triplet for the methylene at the para position, and doublet for the aromatic H atom at the ortho position — were observed for 1• – 3• and 5• in toluene, with aH value close to 10 G (Table 3). For 4•, only traces of a species exhibiting likely an aH value close to the one observed for 5• are observable (Fig. 3j and m). Indeed, PbO2 is not expected to oxidize 4 into a phosphoniumyl radical [20]. As expected, 2• and 3• exhibit similar signals, as 2 is roughly composed of 4 unimers of 3. The similarities in signals for 2• and 3• mean that either only one phenoxy moiety was oxidized in 2• (which we chose to display in Fig. 1 for the sake of simplicity) or no spin exchange interaction occurred between the phenoxy moieties when several phenoxy moieties were oxidized in 2. Thus, the ESR signals observed for the solid solution prepared by mixing PbO2 and 1–3, and 5 were
Fig. 3. ESR spectra observed after oxidation of 1–5 (top to bottom) recorded at RT. From left to right: oxidation by PbO₂ in toluene, oxidation in solid solution with PbO₂, and γ-irradiated at 115 kGy for c, i and l spectra, and at 50 kGy for o spectrum. Arrows for signals other than the signal expected for the phenoxyl radical. Signals in (a)–(c), (d)–(f), (g)–(i), (m)–(o) are ascribed to 1a, 2a, 3a, and 5a.
Table 3: Coupling constants \(^a\) and \(g\) factors of \(1\ast - 3\ast\) and \(5\ast\) in liquid solution with PbO\(_2\).

<table>
<thead>
<tr>
<th></th>
<th>(1\ast)</th>
<th>(2\ast)</th>
<th>(3\ast)</th>
<th>(5\ast)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\Delta H_1)</td>
<td>11.0</td>
<td>8.8</td>
<td>8.6</td>
<td>/</td>
</tr>
<tr>
<td>(g)</td>
<td>2.0047</td>
<td>2.0049</td>
<td>2.0049</td>
<td>2.0039</td>
</tr>
</tbody>
</table>

\(^a\) In G.

\(^b\) Structures given in Fig. 1.

The Landé factors for \(1\ast - 3\ast\), and \(5\ast\) in toluene are around 2.0048, as expected for phenoxyl radicals (\(g = 2.0045\)) [23,24]. Assuming a weak anisotropy of signals for the PbO\(_2\) oxidized powder as well as for the \(\gamma\)-irradiated powder, the \(g\)-factors were straightforwardly determined and reported as 2.0048, 2.0043, 2.0044 and 2.0042, 2.0044, and 2.0046, respectively, confirming that the radical is a phenoxyl type radical. The spectra for irradiated additive \(6\ast\) under air and degassed are displayed in Fig. 4. The strong anisotropy of the signal for \(6\ast\) hampers its simple analysis.

Table 3: Coupling constants \(^a\) and \(g\) factors of \(1\ast - 3\ast\) and \(5\ast\) in liquid solution with PbO\(_2\).

<table>
<thead>
<tr>
<th></th>
<th>(1\ast)</th>
<th>(2\ast)</th>
<th>(3\ast)</th>
<th>(5\ast)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\Delta H_1)</td>
<td>11.0</td>
<td>8.8</td>
<td>8.6</td>
<td>/</td>
</tr>
<tr>
<td>(g)</td>
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<td>2.0049</td>
<td>2.0049</td>
<td>2.0039</td>
</tr>
</tbody>
</table>

\(^a\) In G.

\(^b\) Structures given in Fig. 1.

Ascribed to the corresponding radicals \(1\ast - 3\ast\), and \(5\ast\) (Fig. 3b, e, h and n). As expected, no signal (Fig. 3k) was observed for the solid mixture of 4 and PbO\(_2\). The ESR signal for 1 observed after \(\gamma\)-irradiation is in nice agreement with the literature data. Importantly, the shape of the ESR signal was not dependent on the \(\gamma\)-irradiation dose for \(1\ast - 5\ast\). Interestingly, the shapes of the ESR signals corresponding to the \(\gamma\)-irradiated additives and to the PbO\(_2\) oxidized additives in solid phase are very close, confirming the identical nature of the radical observed, e.g., the phenoxyl radical \(1\ast\) of additive 1. The splitting between the major lines corresponds to the \(\Delta H_1\) values in toluene. \(\gamma\)-irradiation of 2 and 3 affords the same ESR doublet signal exhibiting broad lines. Although less obvious than for \(1\ast\), \(\gamma\)-irradiated ESR signals for \(2\ast\) and \(3\ast\) are similar to the signals observed for the PbO\(_2\) oxidized powder. Indeed, for this powder, an asymmetrical single line can be observed in place of the expected doublet. The better resolution for the \(\gamma\)-irradiated sample is likely due to the depletion of oxygen under the experimental conditions [21]. For \(5\ast\), the unsymmetrical structure affords a signal exhibiting an anisotropy which is similar to that of the EPR signal observed for the PbO\(_2\) oxidized powder. In sharp contrast to the results obtained for 4 either in liquid or powder form with PbO\(_2\) as oxidant, a clear ESR signal was recorded for powder 4 after \(\gamma\)-irradiation. The non-symmetric signal observed for 4 after \(\gamma\)-irradiation, is due to the presence of two species: one species, corresponding to \(5\ast\) (very similar signal, right part of signal in Fig. 3l, see overlay in Fig. 1 SI, and \(g = 2.0044\) for the right hand side of the signal), and an unknown species (left broad line in Fig. 3l, see overlay in Fig. 1 SI). Nevertheless, no phosphorus centered radicals were detected [22], meaning they were either not generated (unlikely) or too unstable to be detected (more likely). Moreover, the amount of degraded product was too small to be detected by \(^{31}\)P NMR.

The \(g\)-factors for \(1\ast - 3\ast\), and \(5\ast\) in toluene are around 2.0048, as expected for phenoxyl radicals (\(g = 2.0045\)) [23,24]. Assuming a weak anisotropy of signals for the PbO\(_2\) oxidized powder as well as for the \(\gamma\)-irradiated powder, the \(g\)-factors were straightforwardly determined and reported as 2.0048, 2.0043, 2.0044 and 2.0042, 2.0044, and 2.0046, respectively, confirming that the radical is a phenoxyl type radical. The spectra for irradiated additive \(6\ast\) under air and degassed are displayed in Fig. 4. The strong anisotropy of the signal for \(6\ast\) hampers its simple analysis. Nevertheless, the same signal is observed under air and vacuum conditions although the signal observed under air is weaker [25]. No ESR signal is detected for molecule 6 in solid or liquid solution with PbO\(_2\) as expected (not shown).

At this time, \(6\ast\) has not been identified. However, its kinetic behavior denotes the presence of a radical highly reactive to O\(_2\), which is expected from alkyl, aminyl or aminiumyl radicals. As far as we know, the time evolution of \(\gamma\)-irradiated additives has only been reported for additive 1. The time evolutions at room temperature of irradiated additive radicals 1\ast to 4\ast and 6\ast are reported in Fig. 5 (Fig. 3SI) and Fig. 6 (Fig. 4SI). Concerning Fig. 5, it can be seen that radicals 1\ast to 4\ast are rather stable over time. The ESR signals are at least 3 orders of magnitude above the limit of detection and quantification. Radical \(6\ast\) (Fig. 6a) is highly unstable under air and disappears totally after two weeks, in sharp contrast to radicals 1\ast–4\ast, whereas \(6\ast\) is stable over time in the thoroughly degassed sample (Fig. 6b). A 3-fold increase in concentration for irradiation at 30 and 50 kGy was observed during the first two months after irradiation, as reported in the literature [26]. ESR signals of samples irradiated at 115 and 270 kGy were always recorded on the same day, so the sharp decrease in signal that can be observed at 6 and 8 weeks is likely due to an experimental problem. Moreover, the intensity of this signal rises back to the level it reached before the 6\(^{th}\) week.

3.2. \(\gamma\)-irradiation of PE film

Under air as well as under vacuum, no ESR signals were detected in PE upon \(\gamma\)-irradiation, whatever the doses received (Fig. 7a and b respectively). Obviously, the generated radicals are not stable in air at room temperature and in degassed conditions (\(P = 10^{-5}\) Torr), even though they are trapped in a matrix.

3.3. \(\gamma\)-irradiation of EVOH film and resins

Whatever the conditions (under air or vacuum), the ESR signals (Fig. 8d and h) recorded on a film exhibit a nice 1:4:1 triplet, as reported [27–30] and ascribed to the EVOH\(^\ast\) species (Fig. 1). However, the wings of this triplet are very weak when recorded for three types of resin (Fig. 8a–c, e–g). This difference is ascribed to the shape of the materials, that is, the polymer chains in resins [31] are likely folded and randomly oriented whereas in films the polymer chains are expected to be unfolded and oriented [32]. The hyperfine coupling of 30.4 G observed for the 1:4:1 triplet of film is very close to the 32 G reported by Rao et al. [27].

The \(g\)-factors are listed in Table 4 and are all around an average value of 2.0038, which is in the expected range for hydroxyl alkyl radicals (\(g = 2.0030\)) [33–38].

Whatever the conditions (air or vacuum), the EVOH\(^\ast\) generated by \(\gamma\)-irradiation at 50 kGy are stable for at least 3 months (Fig. 9 and Fig. 5SI).

Interestingly, \(\gamma\)-irradiation of EVOH under air did not generate radical species stable enough to be detected by ESR, except EVOH\(^\ast\) (Fig. 9). Moreover, the same amount of radicals was generated under air and in vacuum conditions. Furthermore, EVOH\(^\ast\), which is a C-centered radical, was as stable under air as it was in vacuum (Fig. 9).

These results nicely highlight the O\(_2\)-barrier properties of EVOH materials.

3.4. \(\gamma\)-irradiation of film A

Film A was investigated after two sterilization campaigns. For the first campaign, film A was irradiated at 30, 50, 115 and 270 kGy,
and for the second one, at 50 kGy (Film A50).

3.4.1. Under vacuum

In order to compare our results to literature results, and to be in the absence of O2, samples were degassed under high vacuum ($P = 10^{-5}$ Torr). It should be mentioned that the vacuum measurement values found in the literature are around 1 mTorr [28].

The ESR signal observed for film A50 as well as film A at other doses is strikingly different from those observed for EVOH resins and film, i.e., no wings and splitting of the central line. This ESR signal is not due to the PE layers (no ESR signal for PE, vide supra). It is likely that the ESR signal for 6 superimposed upon the signal for EVOH. This signal disappears under O2 bleaching (vide infra). Interestingly, the signal changes during the first month, the extra coupling almost disappears (Fig. 10c). After a 42% signal loss in 2 weeks, the amount of radicals remained constant over 11 weeks (Fig. 10b and Fig. 6SI). The second radical likely generated by γ-irradiation of 6 was less stable under vacuum, in contrast to Fig. 6b, probably because of the presence of several additives in the EVOH layer. When γ-irradiation was performed at 30, 50, 115 and 270 kGy on film A, the results were similar to those obtained for 50 kGy, whatever the dose.

Low variations in the amount of radicals with time and sharp signal changes are observed (Figs. 10c and 11b) meaning that the other species was generated in small amount but exhibited a strong signal. This agrees with the assumption of a species being generated by γ-irradiation of 6.

3.4.2. Under air

Films A and A50 exhibit ESR signals (1:4:1) (Fig. 12a and Fig. 13b, respectively) similar to those reported for EVOH film and resins. Film A is a 3 layer PE/EVOH/PE material containing various types of additives able to provide ESR signals. The $g$ factor was roughly estimated as $g_{iso} = 2.0036$, in nice agreement with the $g$ factor reported for EVOH resins and film (Table 4). The wing line/central line ratio is constant over time, pointing that the wing and central lines belong to the same species. As observed with EVOH resins and film, the ESR signal for film A50 was stable for 13 weeks (Fig. 12b).
Fig. 6. Time evolution of $G^*$ at RT in semi-log scale for a dose of 50 kGy: (a) under air, (b) degassed. Dotted line for quantification limit at $5.5 \times 10^{14}$ molecules/mg, dashed line for detection limit at $1.2 \times 10^{14}$ molecules/mg.

Fig. 7. ESR spectrum of contact layer (PE) irradiated at 50 kGy (a) under air, (b) degassed at RT.

Fig. 8. ESR spectra for EVOH resins and film irradiated at 50 kGy and at RT under air: (a) resin A, (b) resin B, (c) resin C, (d) film; and under vacuum: (e) resin A, (f) resin B, (g) resin C, (h) film.
and Fig. 8SI). Accordingly, the ESR signal observed for film A is ascribed to radical R—CH₂—C(OH)—CH₂—R from EVOH. On the other hand, film A, when irradiated at either 50, 115 or 270 kGy, displays an ESR signal up to 1 month, whereas when irradiated at 30 kGy, it displays a signal up to 10 weeks. Moreover, more radicals are observed in film A (10^{17}–10^{18} molecules/mg) than in film A_{50} (10^{16} molecules/mg). This discrepancy between the two series of irradiation is likely due to both the experimental conditions of irradiation, leading to a difference in concentration, and the heterogeneity of film A, i.e., the thickness of the EVOH layers varying by several micrometers. Nevertheless, the same qualitative comments hold for both series.

4. Conclusion

It is clear that γ-irradiation affords hydroxyalkyl radicals in

<table>
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<tr>
<th>Landé factor</th>
<th>Resin A</th>
<th>Resin B</th>
<th>Resin C</th>
<th>Film</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Under air</td>
<td>Degassed</td>
<td>Under air</td>
<td>Degassed</td>
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<tr>
<td>(g_x)</td>
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<td>(g_{iso})</td>
<td>2.0039</td>
<td>2.0037</td>
<td>2.0042</td>
<td>2.0039</td>
</tr>
</tbody>
</table>

\(g_{iso} = (g_x + g_y + g_z)/3\).

*Fig. 9. Quantity of radical species in EVOH resins and film over time (in week) in semi-log scale (a) under air (b) under vacuum (resin A ■, resin B ●, resin C ▲, film ▼) at RT. Dotted line for quantification limit at 5.5 \(10^{14}\) molecules/mg, dashed line for detection limit at 1.2 \(10^{14}\) molecules/mg.*

*Fig. 10. Film A_{50} (degassed) irradiated at 50 kGy: (a) ESR spectrum, (b) quantity of radical species over time in semi-log scale. Dotted line for quantification limit at 5.5 \(10^{14}\) molecules/mg, dashed line for detection limit at 1.2 \(10^{14}\) molecules. (c) ESR spectra of over time.*
Fig. 11. (a) Quantity of radical species in film A (degassed) over time in semi-log scale at different doses: 30 kGy ■, 50 kGy ●, 115 kGy ▲, 270 kGy ◆. Dotted line for quantification limit at 5.5 x 10^{14} molecules/mg, dashed line for detection limit at 1.2 x 10^{14} molecules. (b) ESR spectra of film A (degassed) irradiated at 270 kGy over time.

Fig. 12. Film A_{50} (under air): (a) ESR spectrum, (b) quantity of radical species over time. Dotted line for quantification limit at 5.5 x 10^{14} molecules/mg, dashed line for detection limit at 1.2 x 10^{14} molecules. (c) Wing line decay over time ■, central line decay over time ●, solid line corresponds to wing/central line ratio.

Fig. 13. (a) Quantity of radical species of film A (under air) over time (30 kGy ■, 50 kGy ●, 115 kGy ▲, 270 kGy ◆). Dotted line for quantification limit at 5.5 x 10^{14} molecules/mg, dashed line for detection limit at 1.2 x 10^{14} molecules. (b) ESR spectra for film A irradiated at 270 kGy over time.
EVOH, whatever the doses and the experimental conditions. Hydroxalkyl radicals are probably 3rd generation radicals from the primary oxoniumyl radical, as depicted in Scheme 1. Indeed, the oxoniumyl radical spontaneously releases a proton to generate an oxyl radical, which in turn generates a hydroxalkyl radical by H-abstraction either from another chain or through an intramolecular process (1,4-H-transfer). The 1:4:1 pattern requires a conformation with an H atom either eclipsed or anti to the C–O–H bond (Scheme 2). The stability of EVOH to O2-bleaching confirms the low permeability of the EVOH layer to O2.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.polymdegradstab.2015.10.021.

References

[17] Film A50 is the film A irradiated at 50kGy. Another Steriliz. campaign was performed 30, 50, 115 and 270 kGy doses.
[19] Solutions of toluene were not degassed.
[20] If such oxidation would have been occurred, the generated phosphoniumyl radial is not expected to be stable enough to be detected and the degradation processes are expected to afford in detectable amounts 55.
[21] The γ-ray-irradiation of materials is likely to generate alky radicals or hydrogen atoms which are prone to react quickly with O2 leading to a depletion of its interaction and then less spin-spin interactions with the phenoxyl radical affording narrower lines.
[23] For C15H23O2 in Landolt-Börnstein II/9c2. 79.
[29] To compare the effect of irradiation, signal under air was recorded with the same acquisition parameters than the signal degassed. Due to the very low concentration of radicals, the signal has a very poor signal/noise ratio (Fig. 4a).
[33] The ESR signal do not depend on the amount of EVOH in materials (Table 1).
[34] For their experiments, Rao et al. used powder of EVOH and 60Co source at 4 kGy/h.
[37] F.P. Sargent, Electron spin resonance studies of radiation damage. Part I. An alternating linewidth effect for the (CH3)2CO radical in gamma-irradiated

