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Effect of ionizing radiation on the thermal oxidative stability of medical polymers

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Abstract

In the medical-device industry, most products need to be sterilized prior to use. Sterilization by ionizing radiation is fast becoming the preferred method on account of its effectiveness and economy. However, energetic secondary electrons released from the primary irradiation event can cause significant damage and degrade the polymer. We have undertaken a study on the thermal oxidative stability of several medical polymers as measured by the oxidative induction time (OIT) on radiation exposures. It was found that, in selected cases with polyolefins, active antioxidants can be completely consumed during the sterilization process, leaving the polymer unprotected for the required shelf life. In addition, comparison between γ- and electron-beam irradiation sources revealed major differences on OIT reduction, primarily due to the dose rate effect.

Keywords: Degradation; Electron beam; Gamma-irradiation; Ionizing radiation; Oxidative induction time

1. Introduction

Ionizing sterilization is gaining popularity in medical-device and packaging industry, because of its convenience and lower cost. Concerns over worker exposure to ethylene oxide and temperature constraint of medical materials for high-temperature steam autoclaving have made radiation sterilization more preferable. The mode of sterilization is a consequence of the high-energy electrons released from the interaction of the γ-ray photons or electron-beam particles with the materials been sterilized. These high-energy electrons, in turn, interact with the DNA sequences in the microbiological burdens, through permanent alteration in their chemical structures, to render them innocuous.

The high-energy electrons, however, can also initiate ionization events in the material being sterilized. It can create peroxy and hydroperoxy free radicals in the presence of oxygen, and start the degradation cascade. This could result in unacceptable color formation, excessive pH shifts and high extractibles. Furthermore, the degradation could also lead polypropylene (PP) to the well-publicized catastrophic failures during post-radiation shelf-life storage. From product quality and application viewpoints, it is highly desirable to develop simple and very rapid systems to characterize radiation-sterilized packaging materials.

In this study, we have examined some of the widely used medical packaging materials for their radiation compatibility. Since different materials degrade via separate mechanisms, leading to various failure modes, we need to take them into account to gain proper understanding for broad applications. Accordingly, the objective of this study is to develop simple (minimum sample preparation) and rapid (minutes) techniques to characterize the radiation-sterilized packaging material properties. Specifically, oxidative

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induction time (OIT) will be used to identify radiation-sterilization compatibility.

2. Experimental and materials

The technique used in this study includes ASTM D3895-92 isothermal OIT from Dupont 1090 thermal analyzer with a 910 differential scanning calorimetry (DSC) cell. The stabilizer concentration was determined by high-performance liquid chromatography (HPLC) from established calibration curves. The materials studied consist of polypropylene (PP), high-density polyethylene (HDPE), low-density polyethylene (LDPE), and flexible polyvinyl chloride (PVC) with various stabilizer systems. γ-Ray exposure at various doses was conducted in a laboratory gamma cell at dose rates of $\approx$6 kGy/h.

3. Results and discussion

Confirming what has been widely reported in the literature [1], we also found the OIT at various temperatures to be an excellent linear function of active antioxidant content (Fig. 1). The exceptionally linear response of OIT at multiple temperatures strongly indicates the potential of the method as a simple (minimum sample preparation), and rapid (within minutes), albeit non-specific assay for active antioxidants.

Recent publications [2], using chemiluminescence as the detecting scheme also yielded linear responses of the induction time with respect to antioxidant concentration, but an inverse exponential dependence with respect to initial hydroperoxide concentrations (Figs. 2 and 3).

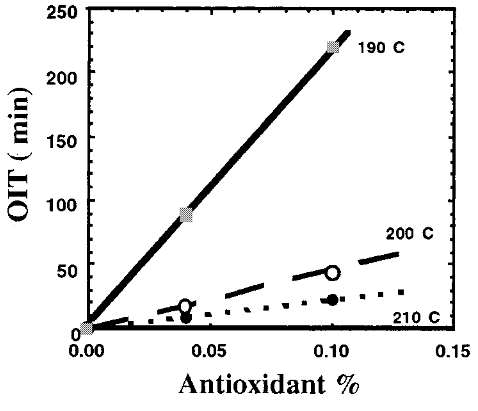

Fig. 1. OIT dependence on antioxidant concentration.

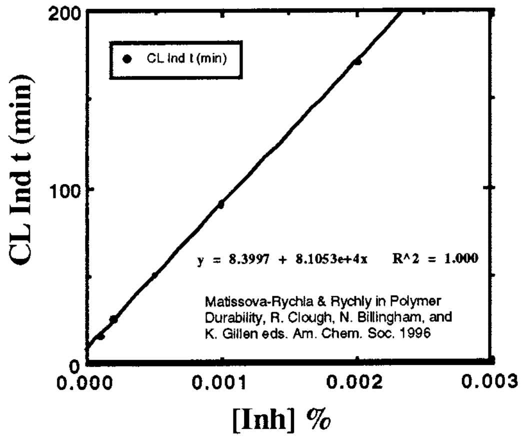

Fig. 2. Chemiluminescence induction times.

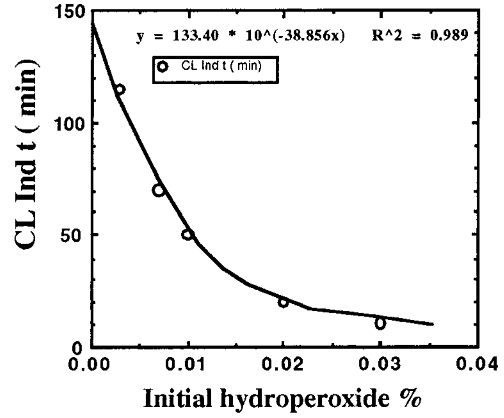

Fig. 3. Hydroperoxide effect.

Both, the OIT and chemiluminescence data support the general mechanism of degradation, where the primary alkyl-free radicals are propagated through atmospheric oxygen diffusing into the polymer via the formation of peroxy and hydroperoxy free radicals (Fig. 4). In this regard, the action of the phenolic antioxidant is mainly that of a hydrogen donor in eliminating organic free radicals, and becomes sacrificially consumed in the process.

PVC thermal stability, measured as OIT in Fig. 5, has been reported to exhibit a rather sharp maximum

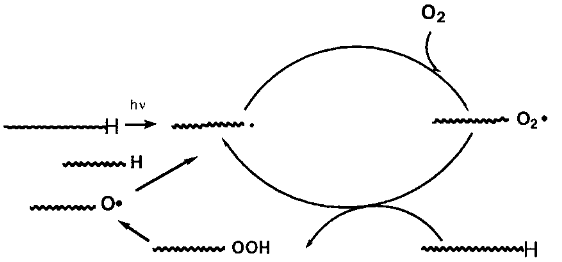

Fig. 4. Oxidative kinetic chain reaction.

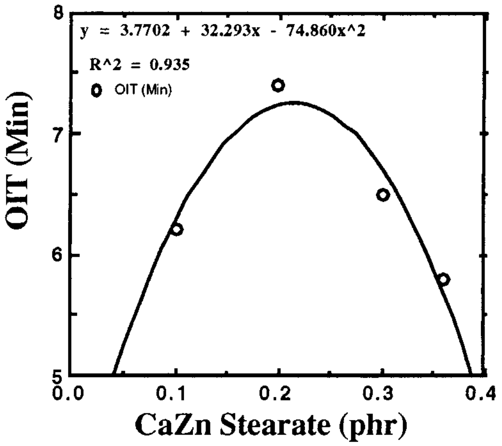

Fig. 5. PVC OIT dependence on CaZn stearate.

with respect to the concentration of a primary stabilizer, CaZn stearate at ca. 0.2 phr or ca. 0.13% for the system studied [3]. It was also noted that an extremely linear relationship existed for the secondary stabilizer, an epoxidized oil. Combined together, Fig. 6 shows that the PVC stability function spanned a three-dimensional design space.

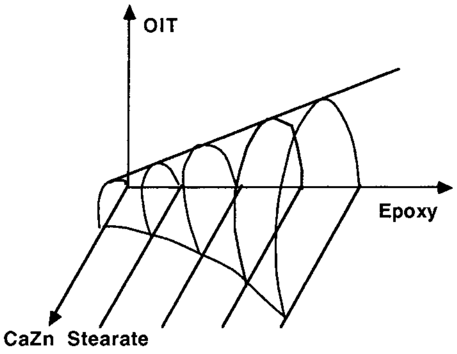

Fig. 6. Three-dimensional schematic of PVC stability.

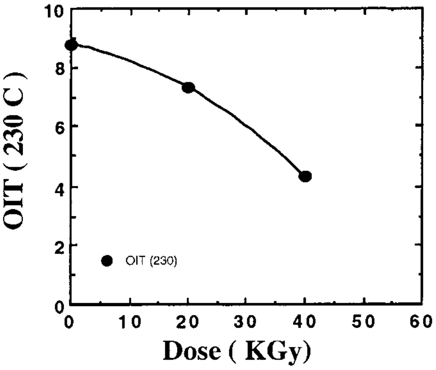

Fig. 7. Effect of radiation dose on PVC stability.

The OIT response of a PVC formulation at 230°C as a function of the sterilization dose is shown in Fig. 7 with a dose rate of approximately 6 kGy/h. From the zero dose OIT of ca. 9 min, a steady reduction in total stability was seen. In addition, the slope (rate of OIT decrease) appeared to increase from 20 to 40 kGy, indicating a non-linear response that accelerates the degradation reaction at high doses. Fig. 7 also indicates that, after 40 kGy, the formulation lost more than half of the initial total stability, limiting the maximum dose this particular formulation was capable of sustaining.

Radiation also alters polyolefin stability. In a hindered phenol stabilized HDPE film system, the film OIT at 200°C was determined for dose levels of 0, 20 and 40 kGy. Results in Fig. 8 clearly indicated a dramatic antioxidant annihilation during sterilization.

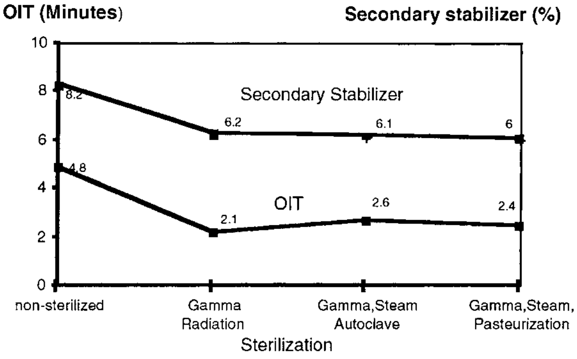

Fig. 8. PVC OIT and secondary stabilizer.

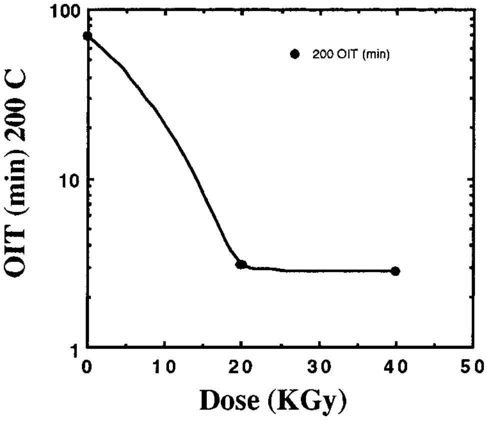

Fig. 9. Effect of radiation dose on HDPE stability.

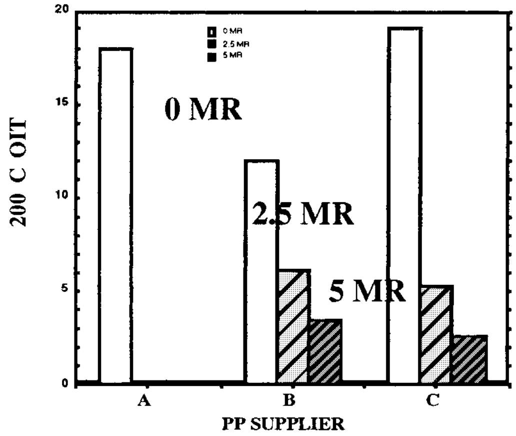

Fig. 10. Dose effect on various PP's.

It was also noted that the OIT was nearly flat between 20 and 40 kGy. This suggests that the antioxidant in question did not provide additional protection even when the radiation dose was reduced from 40 to 20 kGy, or alternatively, a fraction of the antioxidant was not accessible to provide protection during the irradiation (Fig. 9).

Comparing the packaging materials studied in Figs. 7 and 8, it was noted that PVC has a slower overall stability reduction than HDPE when subjected to radiation. Part of this can be attributed to a higher concentration of a secondary stabilizer in PVC, which can be as high as 10 wt%. This may explain why PVC medical products seldom encounter catastrophic failures after radiation. However, there is frequently a steady color formation accompanying the OIT reduction with dose, thus limiting the maximum dose for PVC formulations.

In Fig. 8, where the OIT and the secondary stabilizer content are plotted along the manufacturing processing steps, it is seen that the irradiation step is the most severe for degradation. Coincidentally, the apparent *increase* in OIT at the post-γ–steam autoclave step is quite reproducible. It is suspected that this effect originated from the dissolution of soluble zinc chloride, a potent Lewis acid for catalyzing PVC degradation formed during γ-irradiation.

In contrast, catastrophic failures have been reported during the PP shelf life. Intense investigation has led to the following conclusion: long-life free radicals trapped in the crystalline domains slowly migrate toward the crystalline/amorphous interface where they react with available oxygen to form peroxy and hydroperoxy radicals and initiate degradation near the interface [4,5]. When a sufficient number of the tie molecules between crystallites were cut through this chain-scission process, PP's elongation reduced dramatically and catastrophic failures followed.

In view of the fact that antioxidants in PP resides primarily in the amorphous phase, its effectiveness to react with primary free radicals preferentially governs the overall post-irradiation stability of the material. Accordingly, it is interesting to assess the correlation between OIT and radiation dose based on different suppliers.

Fig. 10 shows PP from three different suppliers, and their OIT at 200°C at 0, 25 and 50 kGy of doses. It is clearly seen that supplier A's formulation, where the OIT vanishes after only 25 kGy of dose, was not as stable or effective toward γ-radiation as the other two formulations. On the other hand, although PP formulations from suppliers B and C had experienced sizable OIT reductions, a significant fraction of antioxidant remained to protect against further degradation.

Fig. 11 shows the plot of OIT from various PPs at different doses with the phenolic primary antioxidant assayed by HPLC. An excellent correlation between the OIT and the assayed antioxidant concentration indicates the promise of using this simple procedure as an early screening tool for evaluating PP radiation stability. In other words, the stability of a radiation

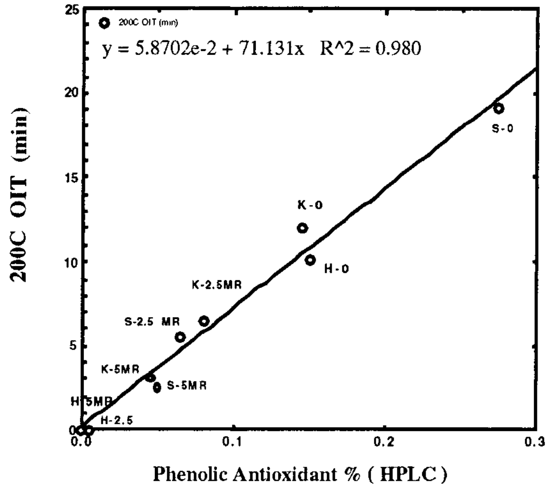

Fig. 11. PP OIT vs. antioxidant by HPLC.

sterilized PP can be simply and rapidly determined by OIT, and the remaining antioxidant level of sterilized PP can be easily determined from Fig. 11. Moreover, Fig. 10 also indicates that the stability of sterilized PP is dependent on the concentration and effectiveness of the suppliers' stabilizer package.

In a separate study, a radiation grade PP OIT under air-flow conditions of 100 ml/min was determined and the result compared with the same film sample (ca. 130 μm in thickness) after 20 kGy of gamma exposure at ca. 6 kGy/h dose rate. The data was tabulated in the Arrhenius form in Fig. 12. It is clearly seen that the gamma exposure has significantly reduced the OIT throughout the temperature range studied. In addition, the reduction factor appeared to be relatively constant over the entire temperature range. To access still lower temperatures, where the OIT detection becomes difficult, the gamma-exposed films were subjected to oven aging at 90° and 60°C and their failure times noted. Fig. 13 indicates a significant reduction in oven stability at higher temperatures.

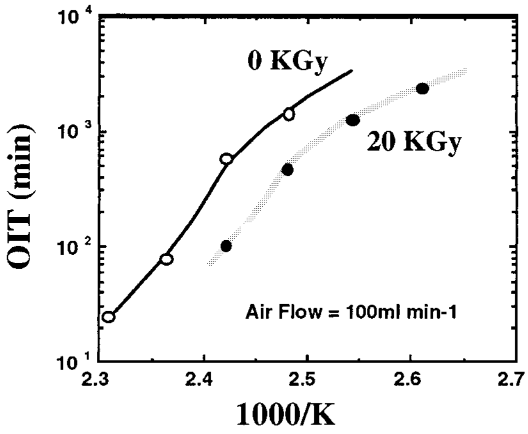

Fig. 12. Radiation grade PP OIT at 0 and 20 kGy.

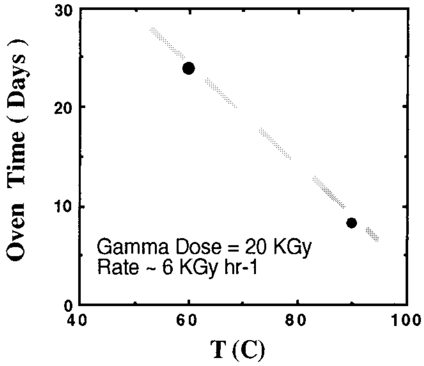

Fig. 13. Post-gamma exposure oven failure times.

More interestingly, when the oven failure times were plotted onto the Arrhenius plot with the gamma samples, a continuous curve with downward slope toward lower temperatures emerges (Fig. 14). This kind of continuity of functional behavior of OIT data at higher temperatures and oven stability data closer to ambient could, at least in principle, produce long-term property prediction based on OIT data, provided that the rate of slope change can be determined separately. Further experiments along this line of reasoning are being currently carried out so as to explore the boundary of validity for several polymer systems.

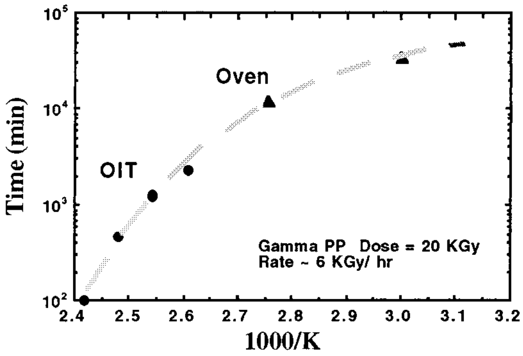

Fig. 14. Combined Arrhenius plot of OIT and oven times.

4. Post-irradiation aging

Since a significant fraction of antioxidant is lost during irradiation, and possibly alkyl peroxide and hydroperoxides are deposited in the polymer, it is interesting to monitor the remaining thermal oxidative stability as a function of storage time. The residual stability has undoubtedly great influence over the shelf-life stability of irradiated polymer devices. In addition, various polymers with entirely different oxidation mechanisms could degrade at different rates. Two polymer films were selected for this study. The first was a polypropylene (PP) random copolymer of about 2 wt.% ethylene content, the other a low-density polyethylene (LDPE) film. OIT data were first determined soon after the irradiation event. After several storage-time periods up to about 10 months at ambient temperatures, the OITs were determined as a function of storage shelf life. Figs. 15 and 16 depict data from the LDPE and the PP samples. For LDPE, a common temperature of 170°C was used, while normalized OIT fractions compared to time zero data were used for PP.

For the LDPE, it appears that for both the radiation doses of 30.6 and 57.3 kGy, over about 10 months of storage time, the OIT remained nearly constant, subject only to the normal degradation in air, and uncertainties of the instrument's long-term stability. However, for the case of PP, significant time dependence is seen. The reason is the steady oxidative reaction leading to the constant loss of antioxidants in the polymer. This observation is, as expected, yet another evidence supporting the view that there are significant oxidation initiation reactions taking place long after the irradiation event. Hence, the model that long-life free radicals migrate from crystalline domains toward the amorphous interface is supported.

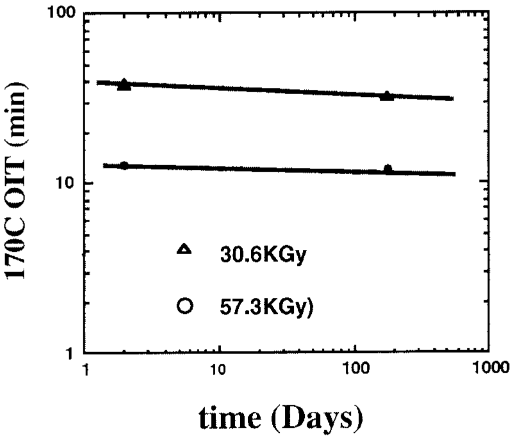

Fig. 15. LDPE OIT post-irradiation.

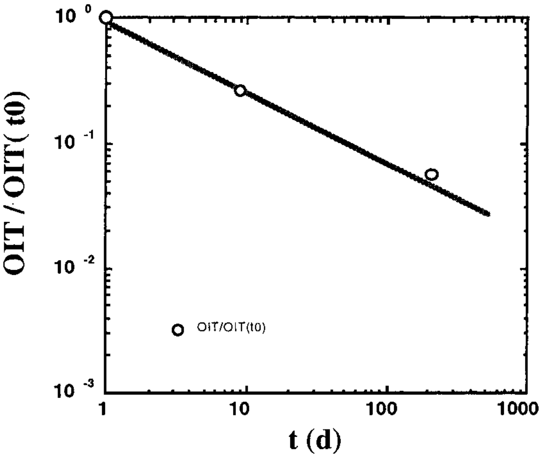

Fig. 16. PP OIT post-irradiation.

5. Comparison between γ- and electron-beam irradiations

Recently, electron-beam accelerators of sufficiently high energy and reliability are becoming available, and are gaining increasing popularity for sterilizing medical devices. The main benefits of electron beams are seen as process economics due to the availability of the radiation source on demand versus the constant (cannot be turned off) radioactivity from nuclear isotope decay. Also, advances in accelerator design have led to very compact and energy-efficient sources. The main difference between the two sources is the dose rate or exposure time where the dose is delivered. For the γ-source, a typical dose rate of ca. 1–10 kGy/h is very common. However, for the electron beam, dose rates as high as 20 kGy/s are possible. This difference of up to ten-thousand-fold in dose rate can be translated into lower exposure times. While it normally takes from one to several hours to accumulate the required 25 kGy sterilizing dose in γ-irradiation, electron-beam sources accomplish the task in seconds. During exposure, two simultaneous processes are

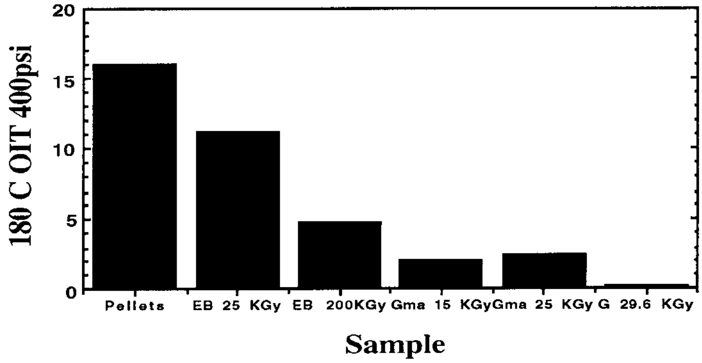

Fig. 17. EVA sample; comparison between γ- and electron-beam irradiation.

taking place: a constant generation of free radicals, and oxygen diffusion which can combine with the primary alkyl radicals to form peroxy radicals and thus propagate the degradation chain reaction. If, at equal dose, the exposure time is drastically reduced due to the higher dose rate, less oxygen diffusion should take place. Therefore, it is of interest to compare the effect on the thermal stability of the material from these two sources. For the electron beam, a 10 KW source was used. Sample of an ethylene vinyl acetate copolymer (EVA) was used. Data from Fig. 17 clearly indicates the dose rate and the corresponding oxygen diffusion effects. It appears, in terms of OIT reduction, or depletion of antioxidants, electron-beam doses of 200 kGy were milder than those of gamma doses of 15–30 kGy. In addition, at least in one instance, the gamma dose at about 29.6 kGy nearly depleted the antioxidants in the polymer.

6. Summary

Ionizing radiation for sterilizing medical products was found to reduce the oxidative stability of most medical polymers. The reduction in OIT was due primarily to the depletion of antioxidants. However, different polymers responded very differently. For example, phenolic antioxidants can be totally consumed in some polypropylenes during a typical sterilizing dose of 25 kGy, whereas for flexible PVCs, significant fractions of the stabilizer remained. The OIT test was found to be a simple (minimum sample preparation) and rapid (minutes) technique for active antioxidant analysis. Significant differences were also found among materials time-dependent post-irradiation degradation. Polypropylene revealed continuous reduction in oxidative stability, while confirming the model of long-life free radicals continually initiating oxidations. A comparison between high-dose-rate electron beam and γ-irradiation also detected significant oxygen diffusion effect.

References

[1] G.N. Foster, in J. Pospisil, P. Klemchuk (Eds.), Oxidation Inhibition in Organic Materials, vol. 2, CRC Press, Boca Raton, 1989.

[2] L. Matisova-Rychla, J. Rychly, in R. Clough, N. Billingham, K. Gillen (Eds.), Polymer Durability, Am. Chem. Soc., Washington, DC, 1996.

[3] L. Woo, Michael T.K. Ling, Eddie Chan, Application of the oxidative induction test to medical polymers, Thermochim. Acta 192 (1991) 209–219.

[4] R.J. Rolando, Radiation resistant polyprophylene: new development, J. Plast. Film & Sheeting 9(4) (1993) 326.

[5] L. Woo, J. Palomo, Michael T.K. Ling, E. Chan, C. Sandford, Shelf-life prediction methods and applications, Medical Plast. and Biomat. 3(2) (1996) 36.