PERGAMON

Radiation Physics and Chemistry 63 (2002) 845–850

Radiation Physics and Chemistry

www.elsevier.com/locate/radphyschem

Comparison of electron beam irradiation with gamma processing for medical packaging materials

Lecon Woo*, Craig L. Sandford

Corporate Research and Technical Services, Baxter International, Round Lake, IL 60073-0490, USA

Abstract

Ionizing radiation is known to degrade materials and in the meantime is capable of novel property creation. In the medical device industry, sterilization by ionizing radiation has become increasingly popular. In particular, the beta or electron beam irradiation has been adopted along with the traditional gamma radiation from Cobalt or Cesium sources. Of course, the ionizing radiation which disrupts bio-macromolecular structures in bio-burdens can damage polymer chains. Although the mode of radiation interaction is similar, gamma and high-energy electrons differ in several subtle ways: dose rate, sample temperature rise, oxygen availability and treatment duration.

We have conducted a comparative study on material interactions due to e-beam irradiation and treatment with gamma. A similarity between the two processes as well as significant differences will be presented.

1. Introduction

Recent advances in electron beam technology has made this mode of sterilization a worthy competitor to the traditional gamma processing. Increased available energy, compact design, improved reliability, and the absence of a source that steadily depletes with time, are some of the factors. Although the primary event of interaction with matter is different between gamma radiation and electrons, the major interaction is still Compton scattering for both cases. It is mainly the shower of secondary electrons that initiated the ionization events which activates numerous chemical reactions, many of which lead to oxidative degradation.

Although the main interaction with matter is basically the same for gamma and high-energy electrons, minor differences between the two modes remain. It is therefore the objective of this study to quantify these differences, especially towards material degradation.

In this study, doses higher than those employed for sterilization were used to explore and accentuate minor differences. However, doses higher than that of the sterilizing dose are commonly encountered in medical device manufacturing. For instance, rework calls for a minimum doubling of the dose. Dose variations under a given exposure condition would also increase the upper dose limit to achieve the minimum dose required. Also, biological indicators with more resistant strains would likewise increase the required nominal dose. Table 1 lists the pertinent comparison between the two sources.

From Table 1, it is seen that the principal difference lies in the charge and the rest mass. The absence of both the rest mass and charge gives gamma radiation a far greater penetration power than the accelerated electrons, whose penetration is primarily dependent on kinetic energy or the potential difference through which the electrons were accelerated.

In this initial study, we rely mainly on thermal and rheological techniques to monitor the interaction between these radiations with several common medical packaging materials. In the first approximation, at equally absorbed doses, assuming adequate penetration for the electrons, the number of chemical initiation events should be roughly equal. However, there is another major distinction between the two sources, which is that of the dose rate. Typical gamma irradiator delivers dose rates approximately between 5 and 20 kGy/h,

*Corresponding author. Fax: +1-847-270-6341.
E-mail address: wool@baxter.com (L. Woo).

0969-806X/02/$ - see front matter
PII: S0969-806X(01)00664-8

Table 1

	Electron	Gamma (^{60}Co)
Charge	−1	0
Rest mass	9e–28 gm	0
Energy	0.1–15 MeV	1.2 MeV
Velocity	0.3–0.99 C	C
Bond energy	3–10 eV	
UV source	4–5 eV	

while electron accelerators could deliver dose rates as much as ten thousand times higher. Under such high dose rate conditions, significant thermal effects could arise in order to modify the material's reaction pathways. Secondly, due to this huge dose rate disparity, irradiation exposure times are also vastly different. While it is not uncommon for a gamma facility to deliver the sterilizing dose in several hours, the electron accelerator would take mere seconds for the same dose delivery. The availability of oxygen diffusion and oxidative degradation during the exposure times would constitute another factor (Gillen and Clough, 1991).

2. Experimental

2.1. Rheological characterization

A Rheometrics Model RFR rheometer was used for rheological characterization of an ethylene vinyl acetate copolymer (EVA) of about 28% VA content by weight, in the parallel plate geometry 25 mm in diameter and about 3 mm in sample height. Thin film samples of about 300 μm in thickness were stacked and cut to 25.4 mm diameter size with a punch cutter. Prior to the experiment, samples were heated to about 180°C under moderate normal force of about 0.5 kg to ensure reproducible adhesive contact between sample layers and the rheometer fixture plates, even for highly crosslinked samples.

Two types of experiments were conducted with the EVA sample: dynamic frequency sweep and stress relaxation, both at temperatures far above the crystalline melting point of about 75°C. In the frequency sweep, angular frequencies from about 0.02–200 radian/s were covered with 3 points per decade and a strain amplitude of about 2% to insure linear response. For the dynamic experiment, the G' and G'' crossing frequency, where $\tan\delta$ equals unity was used as a relative measure of crosslink density.

For the stress relaxation, a step shear strain of about 5% is manually activated at time zero and the resultant stress response monitored as a function of time. The stress relaxation time constant τ is determined when the stress decay reaches $1/e$ or about 36.8% of the initial value. The stress relaxation time constant τ is taken as a measure of the increases in molecular weight as the crosslinking reaction proceeded.

2.2. Thermal analysis

Isothermal oxidative induction time (OIT) ASTM Procedure D3895-92 was followed mailyn, except that air was used instead of pure oxygen. The oxidative induction test was conducted on a Dupont 1090 thermal analyzer with 910 differential scanning calorimetry (DSC) cell (Fig. 1). For this test, usually a thin and flat specimen, typically about 5 mg or less, was prepared and placed in an open aluminum sample pan and secured on the thermoelectric disk of the DSC cell. The sample was then scanned under inert nitrogen purge of 100 ml/min at a rate of 20°C/min from ambient to the preset temperature. Once temperature equilibrium has been established, the controller automatically switches purge gas to air or oxygen at the same purging rate. The change-over point to air or oxygen purge is taken as the zero time of the experiment. The oxidative induction stability is assessed by monitoring an abrupt exotherm or endotherm departure from the baseline as indicated by Fig. 2 (ASTM, 1992). Often, if the reaction follows a simple zero-order kinetics, induction time measured at various temperatures can be used to construct an Arrhenius plot, expressed as $\log(\mathrm{OIT}^{-1})$ vs. T^{-1}, to obtain information on the oxidation reaction kinetics. Mathematically, the rate constant K, which is proportional to OIT^{-1}, may be expressed in the Arrehnius form as:

$$K = K_o e^{(-\Delta E/RT)}, \quad (1)$$

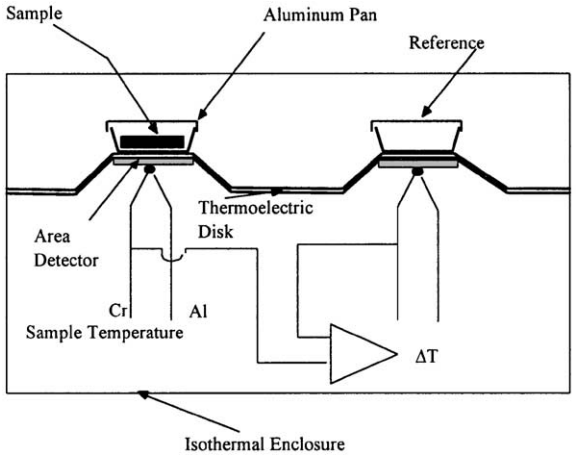

Fig. 1. Heat flow DSC.

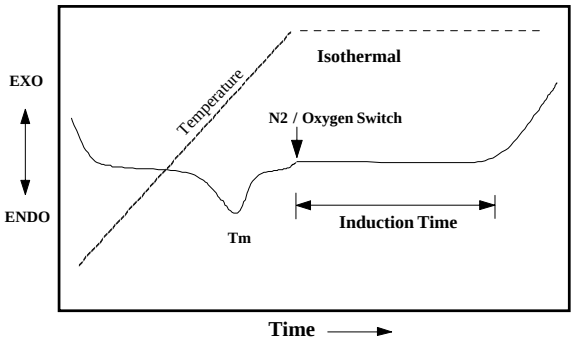

Fig. 2. Oxidative induction test.

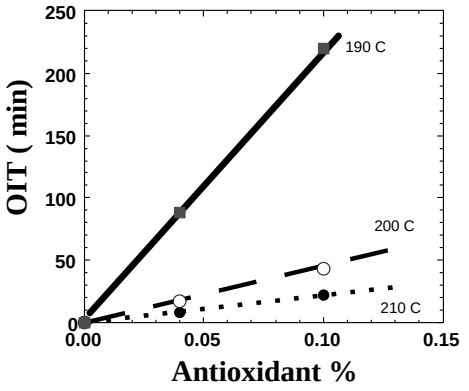

Fig. 3. OIT antioxidant response.

where K_o is the pre-exponential factor, ΔE is the activation energy of the reaction, R is the gas constant, and T is the absolute temperature in degrees Kelvin. The slope of the $\log K$ vs. T^{-1} plot is then the activation energy divided by R.

Specimens $<350\,\mu m$ in thickness were used throughout this study to ensure homogenization. Inhomogeneity could result in multiple oxidative transitions, and therefore, in normal cases, should be avoided. Inhomogeneity usually arises from the skin and core of molded sections, spatial variations in composition or thermal histories. With thin sections and small sample sizes, all inhomogeneity are likely to be resolved, and differentiation of skin and core, thermal histories is made possible and meaningful.

Confirming what has been widely reported in the literature (Foster, 1989; Matisova-Rychla and Rychly, 1996; Woo et al., 1991; Bair, 1981), we also found that the OIT at various temperatures is an excellent linear function of active antioxidant content (Irganox-1010).[1] The exceptionally linear response of OIT at multiple temperatures (Fig. 3) strongly indicates the potential of the method as a simple (minimum sample preparation), and very rapid (within minutes), albeit non-specific assay for active antioxidants.

Several common medical packaging materials in the thin film form was used in this study: (1) an ethylene vinyl acetate (EVA) film with 28% VA content by weight, (2) a 130 μm propylene ethylene random copolymer film of approximately 2% ethylene content and a melt flow of 1.5, and (3) a 100 μm medium density polyethylene film of about 0.94 kg/l density and a melt index of about 1.0. The gamma exposures were conducted at 30, 60 and 100 kGy in a laboratory gamma cell at a dose rate of about 6 kGy/h. The electron beam accelerator used in this study was a commercial 75 kW facility with 300 keV energy with dose delivery rates of about 7–22 kGy/s.

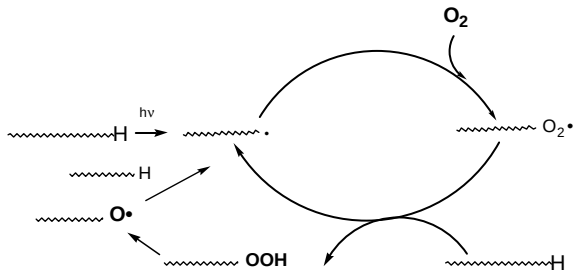

Fig. 4. Oxidative reaction kinetic pathways.

3. Result and discussion

The oxidative degradation pathway for organic polymers typically follows an initiation, propagation, and termination sequence. The initiation, in this case the ionizing radiation, is followed by the propagation steps with atmospheric oxygen (Fig. 4). It is noted that for a single initiation event, through the cyclic propagation cycles and available oxygen, many peroxy radical and hydroperoxide species can be generated. In addition, there are unimolecular and bimolecular termination reactions, where free radicals recombine or disproportionate themselves into neutral or inactive species (Eqs. (2)–(4)). At or near room temperature and under low dose rates, the active species concentrations are quite low; hence, the termination reactions are relatively unimportant. However, at higher temperatures where the main polymer chains are quite mobile or under high dose rate conditions, through the high initiation rate, the active species concentration can be quite high and thus the termination reactions can be very important.

[1] Ciba Geigy. Trade mark.

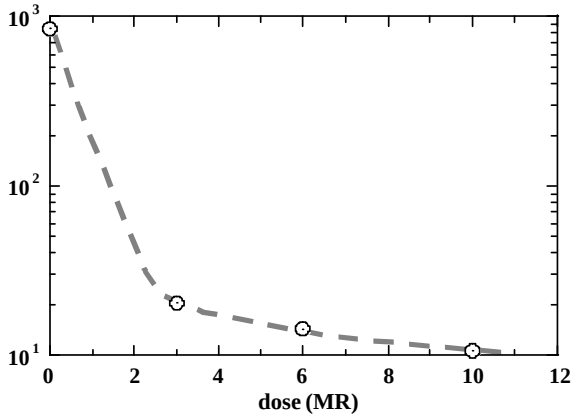

Fig. 5. MDPE film gamma.

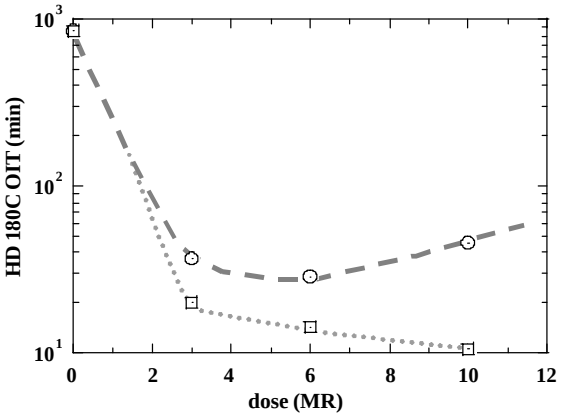

Fig. 6. Gamma e-beam (upper trace) comparison.

Termination reactions :

$$R\bullet + R\bullet \rightarrow R - R \text{ (inactive)}, \quad (2)$$

$$RO_2\bullet + R\bullet \rightarrow ROOR \text{ (inactive)}, \quad (3)$$

$$RO_2\bullet \rightarrow \text{Inactive species}. \quad (4)$$

The medium density polyethylene film underwent a drastic reduction in OIT or antioxidant potency even at a near-sterilizing dose of 30 kGy from almost 900 min of induction time to about 20 min at 180°C. Subsequent additional doses resulted in a near-linear decline in OIT on the logarithmic scale (Fig. 5).

A very significant reduction in OIT stability was also seen in the electron beam samples at 30 kGy, although a slightly better retention of antioxidants (about 40 min vs. 20 min for gamma) can be clearly seen (Fig. 6). From 60 to 100 kGy, a distinct upturn in OIT is plainly evident. This upturn is most likely caused by thermal and exposure time effects under high dose rates from limited oxygen availability and accelerated free-radical termination reactions favored at higher temperatures.

For the PP sample, again, a drastic OIT reduction is evident, with even greater depletion ratios under gamma irradiation. Once more, the OIT upturn at higher dose rates is very pronounced under an electron beam (Fig. 7). Most likely, a similar dose-rate-related exposure time and thermal effects are the causes.

The significant departure towards greater overall stability and the upturn at 100 kGy could be rationalized by the extremely high dose rate and the resulting temperature rise. At these high doses, dose rates of over 20 kGy/s or 72,000 kGy/h are encountered, or about 4 orders of magnitude higher than that of the gamma irradiation. In terms of the irradiation time, instead of nearly 17 h for 100 kGy, it is about 0.5 s for the electron beam. These high dose rates would invariably lead to much higher free-radical concentrations during the exposure and much higher recombination reactions discussed earlier. Since recombination reactions result in harmless neutral species, higher recombination would lead to less antioxidant consumption and polymer degradation.

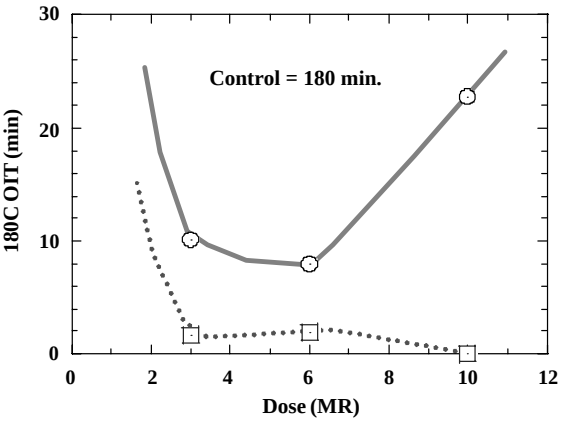

Fig. 7. PP gamma e-beam (upper trace) comparison.

Using a standard specific heat, at room temperature, of about 1.7 J/°C for polypropylene, and assuming no external heat loss (adiabatic), temperature rises for PP are shown in Fig. 8. It is seen that especially for 100 kGy, temperatures over 85°C are reached. At the higher temperatures, the free-radical recombination and termination reaction is expected to be much faster than that at near room temperatures, hence, less polymer degradation.

In addition, the much shortened irradiation duration would limit significant oxygen migration into the sample, compared with 17 h for gamma irradiation. Less oxygen availability would naturally lead to less oxidative degradations.

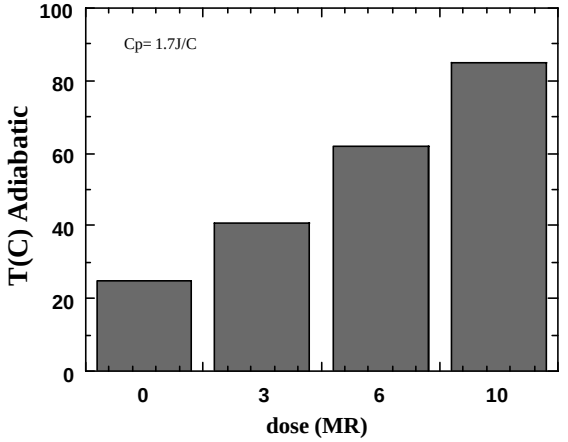

Fig. 8. PP temperature estimates.

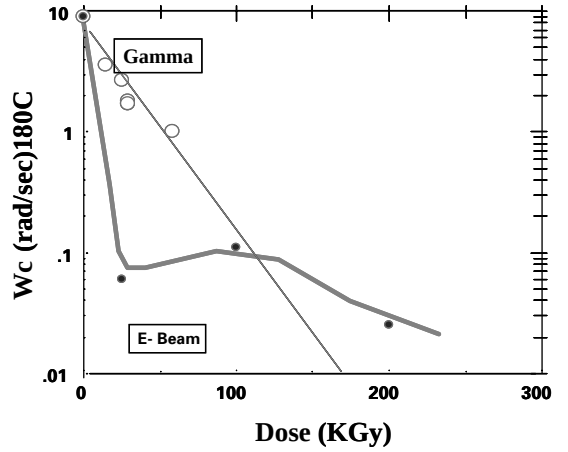

Fig. 9. EVA crossing frequency vs. dose.

In Fig. 9, dramatic differences were seen on the crossing frequencies between these two modes of irradiation. Although both gamma and electron beam radiations-induced reduction in ω_c, indicative of crosslinking reaction, the electron beam results were much more pronounced. During the first 25 kGy of dose, electron beam reduced ω_c by more than 2 orders of magnitude (>100 fold), while only about 5-fold reduction was seen for the gamma irradiation. This substantial departure can only be attributed to dose rate and associated thermal effects. Functionally, the gamma results appeared to follow a linear straight line at a reduced slope. However, after the initial drastic reduction, the electron beam results appeared to level-off between 25 and 100 kGy, and reduced slightly further at 200 kGy. The reason for the plateau response is not entirely clear.

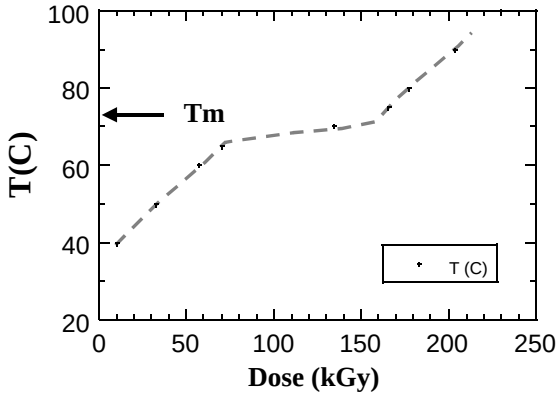

Fig. 10. EVA temperature rise vs. dose.

One possible explanation could be the melting of the sample and maintenance of constant temperature during high dose irradiation. Rapid heating and melting of crystallites can substantially increase chain mobility and probability of recombination reactions, thereby reducing the total concentration of free radicals. In this scenario, during the melting regime, additional free radicals generated from increasing doses were balanced by greater termination rates discussed above. Thus, the net crosslinking reactions could remain relatively constant while the sample went through the melting regime. Another way of looking at the situation is during melting, the sample's temperature remained constant at the melting point with additional radiation energy inputs consumed by material's enthalpy of fusion. Also the constant temperature contributed to the limiting reaction. Using approximate specific heat and melting enthalpy for the sample, temperature rise of the sample was calculated using an adiabatic assumption and the result is presented in Fig. 10. It is seen that the temperature plateau corresponded roughly to the plateau in ω_c.

In the second rheological experiment, the measured stress relaxation time constants followed linear dependence with dose for both gamma and electron beam irradiation, with the electron beam exhibiting a slope approximately twice that of gamma. Interestingly, the break for electron beam between 25 and 100 kGy was not detected (Fig. 11).

4. Summary

A comparitive study was carried out on several medical packaging materials such as EVA, MDPE. and PP, and on their relative stability retention upon gamma and electron beam irradiations. Although the doses went beyond what is requirred for a sterilzing dose, it is felt that higher doses can amplify and create

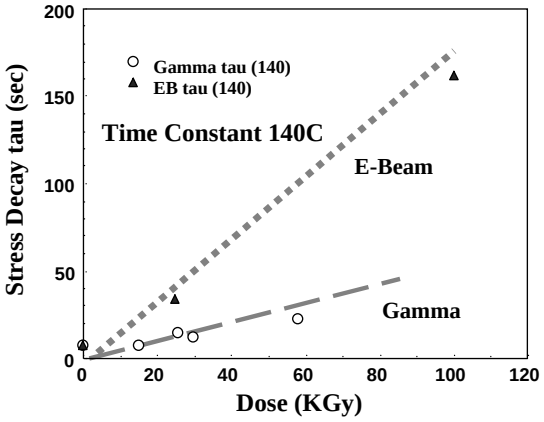

Fig. 11. EVA stress decay time constant.

greater differentiation among the two methods. In addition, an overdose is frequently encountered in medical device manufacturing. A simple ASTM OIT test was used to assess relative retention of stability and oxidative degradation.

For both MDPE and PP, a drastic reduction in oxidative stability was seen at the lowest dose of 30 kGy, possibly due to the very low antioxidant loadings in polyolefins. At higher doses, an anomalous upturn in stability was seen for both MDPE and PP samples. This behavior was explained by invoking the very high dose rates of the electron beam process and the accompaying temperature rise, relatively free from atmospheric oxygen reactions due to the very short irradiation durations.

References

ASTM, 1992. Standard D-3895-95.

Bair, H.E., 1981. In: Turi, E. (Ed.), Thermal Characterization of Polymeric Materials. Academic Press, New York, pp. 869.

Foster, G.N., 1989. In: Pospisil, J., Klemchuk, P. (Eds.), Oxidation Inhibition in Organic Materials, Vol. 2. CRC Press, Boca Raton, FL.

Gillen, K., Clough, R., 1991. In: Clegg, D.W., Collyer, A.A. (Eds.), Irradiation Effects on Polymers. Elsevier, New York.

Matisova-Rychla, L., Rychly, J., 1996. In: Clough, R., Billingham, N., Gillen, K. (Eds.), Polymer Durability. American Chemical Society, Washington, DC.

Woo, L., Michael T.K., Ling, Eddie Chan, 1991. Application of the oxidative induction test to medical polymers. Thermochim Acta 192, 209–221.