

REFERENCES

- (1) Kligman, A. M., *Am. Perfumer Cosmet.*, **78**, 51(1963).
- (2) Bell, K. W., *ibid.*, **81**, 25(1966).
- (3) Rothman, S. R., *J. Am. Med. Assoc.*, **178**, 38(1961).
- (4) Welsh, A. L., "The Dermatologist's Handbook," Charles C Thomas, Springfield, Ill., 1957.
- (5) Dubos, R. J., "Bacterial and Mycotic Infections of Man," J. B. Lippincott, Philadelphia, Pa., 1958.
- (6) Catalfomo, P., and Schultz, H. W., *J. Pharm. Sci.*, **55**, 117(1966).
- (7) Reddish, G. F., "Antiseptics, Disinfectants, Fungicides and Chemical and Physical Sterilization," Lea & Febiger, Philadelphia, Pa., 1957.
- (8) Cooper, K. E., in "Analytical Microbiology," Kavanagh, F., Ed., Academic Press, New York, N. Y., 1963.



Keyphrases

Dermatomucosal agents—antimicrobial activity
 Antimicrobial activity—small tube, disk methods
 Cosmetic products—antimicrobial activity

Effects of Heat and Ultraviolet Radiation on the Stability of a Polypropylene–Polyisobutylene Alloy

By ROBERT K. O'LEARY, WALLACE L. GUESS, and JOHN AUTIAN*

Polypropylene and blends of polypropylene are or may be utilized in medical items of equipment, containers, and various devices. Changes in properties of the material may negate its value when used for these purposes. This paper deals with the assessment of the stability of a polypropylene–polyisobutylene alloy when exposed to heat and ultraviolet radiation. Evaluation of stability was based upon (a) differential thermal analysis, (b) tensile properties, and (c) infrared spectroscopy. Results of the study revealed that considerable degradation of the material had occurred when exposed to a combination of heat and radiation, but relatively little degradation when the plastic was exposed to heat only.

PRESENTLY, polypropylene is enjoying widespread use in many applications in pharmacy, dentistry, and medicine as such items as disposable syringes, various types of containers, protective sheets, and a host of other devices. Addition of relatively small concentrations of a second polymer, polyisobutylene, gives added advantages for certain applications, the chief of which is a reduction in water vapor transmission.

Polypropylene is generally less stable to heat than polyethylene, for the most part due to the methyl side groups attached to every other carbon in the polymer (1). These tertiary carbons serve as active sites for oxidative degradations leading to chain scission and embrittlement. Incorporation of small quantities of antioxidants or combinations of antioxidants with other agents into the polymer increases the long-term stability of the final item.

Received July 17, 1967, from the *Materials Science Toxicology Laboratory, College of Dentistry and College of Pharmacy, University of Tennessee Medical Units, Memphis, TN 38103, and the Drug Plastic Research and Toxicology Laboratories, University of Texas, Austin, TX.

Accepted for publication June 11, 1968.

This study supported in part by contract No. DA18-035-AMC-391 (EA), Research Laboratories, Edgewood Arsenal, Md.

Appreciation is extended to Mr. Glynn R. McDonald for technical assistance during the study.

In recent years, the authors have become interested in various man-made polymeric materials as protective barriers against harmful chemicals. It has become clear, however, that depending upon the inherent properties of the polymeric material and the types of stabilizers employed, the shelf-life of the plastic will be a function of time and the environmental conditions imposed upon the item. A protective coating which is initially found to prevent the penetration or permeation of a chemical poison might become, depending upon its storage conditions, sufficiently altered to permit the passage of the contaminating agent.

To gain some knowledge as to the stability of polymeric materials which might be used in medical items, containers, and various devices, a study was initiated to evaluate the properties of a specific material, polypropylene–polyisobutylene alloy, when exposed to heat and ultraviolet radiation.

EXPERIMENTAL

Materials and Apparatus—Polypropylene–polyisobutylene alloy¹ (Pro-Fax N400), 10 mil thick—

¹ Five percent polyisobutylene.

ness (Hercules Chemical Co., Wilmington, Del.); Differential thermal analysis instrument, model KA-2-HD (Rogert L. Stone, Austin, Tex.); Instron apparatus, model TM (Instron Engineering Corp., Canton, Mass.); Infrared spectrophotometer, model 337 (Perkin-Elmer Corp., Norwalk, Conn.).

Heat and Ultraviolet Radiation—Samples of polypropylene alloy were exposed to heat alone and to a combination of heat and ultraviolet radiation. Figure 1 shows a diagram of the system employed to supply the heat and radiation. A G. E. sunlamp which emits only light rays greater than 2800 Å. was used for both heat and radiation sources. The temperature at the surface of the plastic samples was continually monitored and was found to average $82 \pm 2^\circ$. In the case of heat treatment alone, a thin cardboard 0.5 mm. thick (0.02 in.) was inserted above the sample, thus effectively shielding the plastic from the radiation without diminishing the heat intensity striking the plastic. The sunlamp was approximately 20 cm. above the samples.

At 24-hr. intervals or at other time periods, depending upon the experiment to be performed, samples were removed from both the heat-treated and heat-ultraviolet treated conditions for analysis, utilizing three techniques: (a) differential thermal analysis, (b) tensile properties, and (c) infrared spectroscopy.

Differential Thermal Analysis (DTA)—The DTA apparatus used in this study has been described in a previous paper (2). In this study, DTA was employed to characterize the thermal behavior of the plastic prior to any type of treatment, and at various time periods under the two types of treatment.

Initial experiments were conducted on 10 samples of plastic in order to establish the temperature at which transitions occurred. Samples were heated in the DTA instrument at a programmed rate of 12.6°/min. until a temperature of 200° was reached. The sample weight was approximately 1.5 mg., while the alumina (Al_2O_3) reference weight was 3.0 mg. To prevent oxidation of the samples during any DTA run, a nitrogen atmosphere was maintained. Figure 2 represents a typical thermogram on an untreated polypropylene-polyisobutylene alloy. In this case, both a heating and a cooling sequence were used, giving rise to an endothermic melt starting at 140° and peaking at 167°. The cooling curve demonstrates an exothermic peak (crystallization) beginning at approximately 119°, and peaking at 107°.

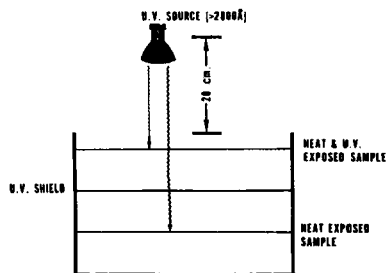


Fig. 1—Diagram showing method of heat and ultraviolet radiation treatment of plastic samples. Distance between samples exposed to radiation and exposed to heat is approximately 20 cm.

At the various time periods and for each of the treatments (heat and radiation), at least three samples of plastic were examined by the procedure described above. Only the DTA heating sequence was employed. From the various thermograms, the onset temperature and peak temperatures were recorded. The areas under the curve representing the melt were converted to standard heats of fusion (ΔH). Table I incorporates the temperature values and constants obtained from the DTA experiments. Figure 3 demonstrates the influence time and treatments have on the peak temperature (melt), while Fig. 4 is a similar relationship except heat of fusion values are plotted against time.

Tensile Properties—Test specimens were prepared from the samples of plastic taken from the hood at the various time periods and stress-strain curves obtained using an Instron instrument, follow-

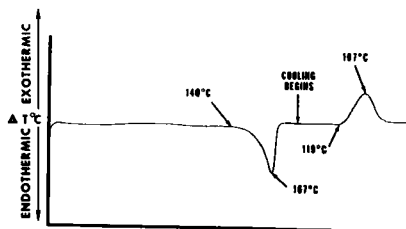


Fig. 2—Typical thermogram of untreated polypropylene-polyisobutylene alloy. A heating and cooling sequence is shown. The curve at the left represents the melt area; the curve at right represents the area associated with crystallization (on cooling).

TABLE I—SUMMARY OF DTA DATA FROM HEAT-TREATED (82°) POLYPROPYLENE ALLOY AT VARIOUS TIME PERIODS

Hr. Exposed	Melt Onset, °C.	Melt Peak, °C.	ΔH° cal./g.
0	122.4	165.0	16.1
48	128.1	164.5	16.4
96	130.9	166.7	14.7
120	132.6	165.3	14.6
192	130.9	164.2	16.6
240	131.3	165.3	15.5
264	129.8	165.1	16.5
288	131.8	165.1	16.1

* An average of 10 samples used at zero time with a standard deviation of ± 1.1 cal./g. All other values based upon an average of three samples with an average deviation falling within ± 1.5 cal./g.

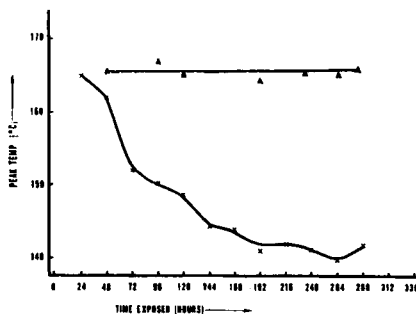


Fig. 3—Comparison of DTA melt peaks of heat-treated and heat-radiation treated samples. Key: ▲, heat treated; ×, heat and UV treated.

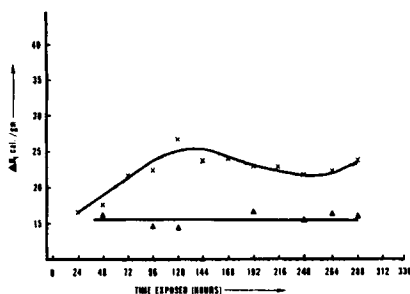


Fig. 4—Comparison of DTA ΔH of heat-treated and heat-radiation treated samples. Key: Δ , heat treated; \times , heat and UV treated.

TABLE II—SUMMARY OF DTA DATA FROM HEAT-RADIATION TREATED POLYPROPYLENE ALLOY AT VARIOUS TIME PERIODS

Hr. Exposed	Melt Onset, °C.	Melt Peak, °C.	ΔH° , cal./g.
0	122.4	165.0	16.1
24	126.9	164.9	16.9
48	127.0	163.8	17.7
72	104.9	152.0	21.8
96	109.8	150.3	22.5
120	96.9	148.8	26.8
144	99.2	144.4	23.8
168	96.1	144.0	24.1
192	87.5	141.1	23.2
216	94.5	142.0	23.0
240	96.4	141.7	21.9
264	95.8	139.8	22.4
288	91.8	141.6	23.7

^a An average of 10 samples used at zero time with a standard deviation of ± 1.1 cal./g. All other values based upon an average of three samples with an average deviation falling within ± 1.5 cal./g.

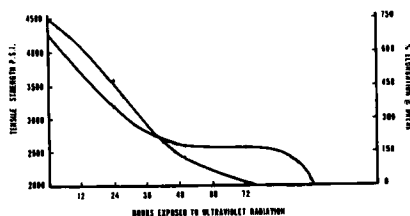


Fig. 5—Effect of heat-radiation treatment on tensile properties of polypropylene-polyisobutylene alloy. Key: \circ , tensile strength; Δ , % elongation.

ing the standard ASTM method.² From the various curves, tensile strength and percent elongation were evaluated. Three samples were used for each run for any one period and condition. Table II includes the results while Fig. 5 is a plot of the data.

Infrared Spectroscopy—The appearance of carbonyl bands and the intensity of these bands are indications of oxidation of the olefinic polymers such as polypropylene, and for these reasons infrared spectra were taken of samples of plastic exposed to the two treatments at various time periods. Prior to IR analysis, the films were mounted between KBr salt disks. These spectra were examined and the salient features noted in the 1750 cm.^{-1}

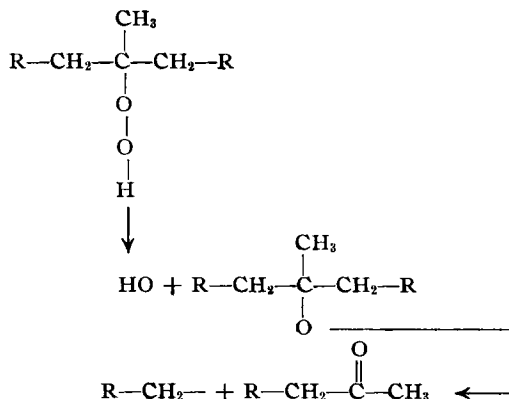
² Die is No. ASTM 1708-59T, determinations made at 25° , 52% RH on a full load of 10 lb., 23 mm. (0.9 in.) gauge length, drive speed of 12.7 mm. (0.5 in.)/min. and a chart speed of 127 cm. (50 in.)/min.

wavelength region (corresponding to carbonyl band). Figure 6 includes three spectra representing the carbonyl band of samples removed at several time periods from the heat-radiation treatment.

RESULTS AND DISCUSSION

Figure 2 illustrates a typical thermogram for the polypropylene-polyisobutylene alloy and includes the peak area for the melt and the peak area representing the crystallization phase after cooling. The two areas should theoretically correspond, but as is evident from the thermogram, this was not the case. The area under the curve for the crystalline phase was slightly larger than for the melt area. More dramatic, perhaps, is the peak temperature difference for the melt (167°) as compared to the crystallization peak (107°). Heat history plays an extremely important role on transition temperatures, and this, no doubt, was the case with what has been reported here. In one case (melt area), the sample has had a heat history quite different from that of the plastic after it is heated above its melting point and then cooled down in a short time period in the DTA instruments. In the melted state the polymers are all in a random motion with little orientation, but as the sample is cooled the chains start sorting out in a fashion to favor orientation with subsequent crystallization. Even though the degree of crystallization is slightly greater for the sample after the cooling treatment (in DTA instrument), the size of the individual crystallites are much smaller, reflected by the much lower onset and peak temperatures. For the purposes of this study, it was felt more advantageous to examine the area corresponding to the endothermic melt (heating sequence).

Stability studies on polypropylene by several workers have shown that this plastic is quite susceptible to oxidative degradation (3-5). The tertiary carbons in the molecule are active sites for the formation of hydroperoxides which then decompose into alkoxy and hydroxy free radicals. Chain scission takes place when the alkoxy radical at the tertiary carbon atom stabilizes through disproportionation into an alkyl radical and a ketone as shown below (6):



The reaction continues until two radicals combine, terminating chain scission. Other possible reactions are occurring during the degradation, and one or more of these can lead to cross-linking. It is, however, believed that the chain scission is most

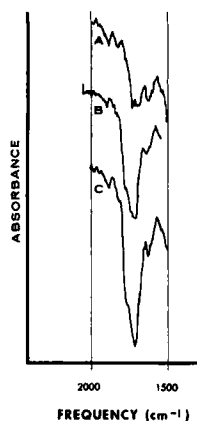


Fig. 6—Effect of heat radiation on IR absorption curve of polypropylene-polyisobutylene alloy (carbonyl formation observed at 1750 cm^{-1}). Key: A, 24 hr.; B, 48 hr.; C, 72 hr.

TABLE III—TENSILE PROPERTIES OF HEAT-TREATED AND HEAT-RADIATION TREATED SAMPLES OF POLYPROPYLENE ALLOY AT VARIOUS TIME PERIODS

Time, hr.	Treatment	Tensile Strength ^a	% Elongation at Break ^a
0	None	4,380 ± 271	746 ± 37
24	Heat	3,830 ± 281	649 ± 35
	Heat and radiation	3,207 ± 291	475 ± 100
50	Heat	3,646 ± 622	654 ± 70
	Heat and radiation	2,578 ± 86	121 ± 101
72	Heat	3,817 ± 194	550 ± 7.8
	Heat and radiation	2,688 ± 36	4 ± 0.3
91.5	Heat	3,718 ± 674	575 ± 96
	Heat and radiation ^b	—	—
117	Heat	3,860 ± 544	592 ± 101
	Heat and radiation ^b	—	—

^a Tensile properties based upon the average of three samples \pm the difference between the lowest and highest values. ^b Tensile properties could not be determined due to brittleness of samples.

likely favored over the cross-linking, at least in the initial phases of oxidative degradation.

Table I, Figs. 3 and 4 reveal that heat treatment alone has very little effect on the property of the alloy. Combined heat and radiation, however, has a dramatic effect on the material. As may be noted in Table II and Figs. 3 and 4, there is an appreciable drop in both the melt peak temperature and the heat of fusion (ΔH) during the time the plastic is exposed to the combined heat and radiation condition. A decrease in tensile properties (Table III and Fig. 5) also suggests that polymer alteration is occurring. Infrared studies (Fig. 6), in fact, confirm that oxidative degradation has taken place in the alloy and that this effect increases with time.

Figure 3 shows that the peak temperature (melt) decreases with time for the heat-radiation treated samples of plastic while Fig. 4 shows an increase in the heat of fusion (ΔH) with time. These results may be interpreted in the following manner: with chain scission there is a decrease in molecular weight; these short chains, as well as the possible broad molecular weight distribution of the polymers, create smaller crystallite regions which are more susceptible to melting at lower temperatures.

The increase in the heat of fusion (ΔH), demonstrated in Fig. 4, may be attributed to the formation of more crystallite regions in the previously amorphous zones, due to either rearrangements of the existing polymer chains into a more ordered system or to the degraded polymer chains forming new crystallites. Evidence from Fig. 3 (decrease in melt temperature), Fig. 5 (decrease in tensile properties), and Fig. 6 (decrease in carbonyl function favors the formation of new crystallite regions from the degraded polymers. Oswald and Turi have also noted that density (crystallinity) increases with oxidative degradation for polypropylene (6).

The decrease in tensile properties (Table III and Fig. 5) with time for the heat-radiated samples of alloy may be interpreted as being due to chain scission occurring in the amorphous regions of the material. The polymers in the amorphous region essentially "tie" the various crystallites into a unified structure having various degrees of toughness and elasticity. Any altering of these ties, such as chain scission, will help collapse the structure with eventual breaking or shattering of the material. It is also possible that a point of degradation may occur where cross-linking in the amorphous zone

becomes important and adds to the destruction of the material when some minor force is applied.

In this particular study, it was not possible to assess to what extent the relatively small concentration of polyisobutylene (5%) took part in the degradation. It is felt that this specific polymer would follow the same general chain scission reaction as is the case for polypropylene.

One important aspect of the study reported here is that storage of a protective barrier such as a plastic film may become altered sufficiently to malfunction, causing possible harm or damage to personnel or equipment. It appears that conditions of storage should be established for items to be used as protective devices and that this same concept should extend to all items to be used to protect health and life, as is the case for various devices used in medical and *para*-medical applications.

SUMMARY AND CONCLUSION

Polypropylene and alloys of polypropylene are being used with greater frequency for a number of applications in medical and *para*-medical applications. When the polypropylene alloy is used as a protective film to prevent harm to medical equipment, even slight alterations of the properties of the material due to storage may negate the value of the item. The results reported here for one alloy of polypropylene demonstrate that heat alone (82°) had no significant effect upon the material up to 300 hr. Under similar conditions, except in the presence of ultraviolet rays, the alloy was rapidly destroyed as measured by (a) DTA, (b) tensile properties, and (c) infrared. There appears to be a need for the establishment of storage profiles for certain plastic items if the value of the item is not to be lost with subsequent injury or damage to personnel or equipment.

REFERENCES

- (1) Madorsky, S. L., "Thermal Degradation of Organic Polymers," Interscience Publishers, New York, N.Y., 1964, p. 115.
- (2) O'Leary, R. K., Foy, J., Guess, W. L., and Autian, J., *J. Pharm. Sci.*, **56**, 494 (1967).
- (3) Hansen, R., DeBenedictis, T., and Martin, W. M., *Polymer Eng. Sci.*, **5**, 3 (1965).
- (4) Fitton, S. L., and Taylor, W., *Plastics*, 1966, 1139.
- (5) Gordon, D. A., and Rothstein, E. C., *Polymer Eng. Sci.*, **6**, 1 (1966).
- (6) Oswald, H. J., and Turi, E., *ibid.*, **5**, 152 (1965).



Keyphrases

Polypropylene-polyisobutylene alloy—stability

Heat effect—polypropylene alloy

UV radiation effect—polypropylene alloy

Thermal analysis—differential

Tensile properties—polypropylene alloy

IR spectrophotometry—analysis.

Characterization of Complex Formation Between Small Molecules by Membrane Permeation Measurements

By RICHARD H. REUNING* and GERHARD LEVY†

A membrane permeation technique is described which permits characterization of complex formation between small molecules. The method is applicable if the components of the complex diffuse across a nonporous membrane at markedly different rates. The procedure may be used (a) to determine the stoichiometry and stability constant of a complex, (b) to verify values of stability constants obtained by other methods, (c) to check assumptions concerning the stoichiometry of a complex, and (d) to determine the degree of complexation of a compound in systems complicated by the existence of two or more simultaneous equilibria, where other methods of determination may fail or be very time consuming. The membrane permeation technique has been applied to the characterization of the complex formation between salicylamide and caffeine at concentrations where appreciable self-association of caffeine occurs.

MANY TECHNIQUES have been developed in recent years for the characterization of drug complexes. Among the methods which have been most commonly used for the analysis of drug interactions are partitioning (1), spectrophotometric (2), equilibrium dialysis (3), dialysis rate (4, 5), and solubility techniques (6). All of the methods available for the study of complex formation are subject to certain limitations peculiar to the particular technique. Some of these limitations which were encountered in the present study are: the partitioning method requires that at least one of the uncomplexed species does not partition into one of the two solvent phases; the spectrophotometric method cannot

be applied to systems involving relatively weak molecular interactions and to those which do not manifest a pronounced change in spectral characteristics upon complex formation; the dialysis techniques are limited to the study of interactions between drugs which diffuse across a dialysis membrane and macromolecules which do not; the solubility method does not permit a determination of the stoichiometry of the complex with respect to the less soluble component, if the complex itself is very soluble.¹ Connors and Mollica (8) have recently pointed out that some of the experimental approaches mentioned above may not always yield the same values for an equilibrium constant and that comparative studies with several techniques may yield valuable information concerning the nature of a complex.

Complex formation between salicylamide and caffeine has been detected recently in this laboratory. The salicylamide-caffeine complexing system was used in studies concerning the effect of complex formation on drug absorption, which are

Received April 15, 1968, from the Biopharmaceutics Laboratory, Department of Pharmaceutics, School of Pharmacy, State University of New York at Buffalo, Buffalo, NY 14214.

Accepted for publication June 4, 1968.

This investigation was supported in part by grant RO1 AM 08753-03 PET from the U. S. Public Health Service, Bethesda, Md., and by Public Health Service Predoctoral Fellowship No. F1-GM-24,005 (for RHR) from the National Institute of General Medical Sciences.

The authors wish to thank Dr. H. B. Kostenbauder for making available the results of his extensive study of the permeation characteristics of synthetic membranes.

* Present address: School of Pharmacy, University of Missouri at Kansas City, Kansas City, MO 64110.

† To whom requests for reprints should be addressed.

¹ It is sometimes possible to reverse the system and thereby determine the stoichiometric ratio of the complex (7).