Acrylonitrile Copolymer Films: Influence of Modification by Reaction with Ethylene Oxide on Biological Degradation

J. M. COURTNEY, R. G. HOOD, and J. M. EWART, *Bioengineering Unit, University of Strathclyde, Glasgow, Scotland, and Edinburgh School of Agriculture, Edinburgh, Scotland*

Synopsis

The biological degradation of acrylonitrile–dimethylaminoethyl methacrylate and acrylonitrile–acrylic acid copolymers has been studied by evaluating copolymer films in a continuous in vitro rumen system. The copolymer films were examined before and after modification by reaction with ethylene oxide gas. The degradation of the acrylonitrile–dimethylaminoethyl methacrylate copolymer followed a pattern similar to that occurring on thermal degradation. Modification by reaction with ethylene oxide gas, which induces C=N conjugation, did not improve the resistance to degradation. The acrylonitrile–acrylic acid copolymer films disintegrated, but on prior modification by reaction with ethylene oxide they remained virtually unaltered. Modification of the acrylonitrile–acrylic acid copolymer results in crosslinking with an absence of C=N conjugation, leading to improved resistance to biological degradation.

INTRODUCTION

In a previous publication[1] the chemical modification of copolymers of acrylonitrile (AN) and dimethylaminoethyl methacrylate (DMAEMA) by reaction with ethylene oxide gas was described. An evaluation of AN–DMAEMA copolymer films showed that chemical modification with ethylene oxide at 30° and 60°C resembles thermal degradation in that it results in the development of a yellow color, insolubility, and the presence of an infrared absorption peak at 1590 cm^{-1}. This behavior is consistent with the formation of C=N conjugation. Chemical modification with ethylene oxide differs from thermal degradation in that it gives rise to an increase in the hydrophilicity of the AN–DMAEMA copolymer and the presence of an infrared absorption peak at 3300 cm^{-1}. This is attributed to the formation of CH_2CH_2OH groups. Therefore, the net result of reacting AN–DMAEMA copolymers with ethylene oxide gas is the formation of a hydrophilic ladder polymer. Since the properties of the modified copolymer are dependent on reaction time and temperature,[2] it is possible to alter and control AN–DMAEMA films with respect to dialysis, ultrafiltration and mechanical properties,[3] and blood compatibility.[4]

AN–DMAEMA copolymer films before and after reaction with ethylene oxide have now been evaluated in an *in vitro* rumen system. The objectives were to investigate the possibility of using AN–DMAEMA membranes as a replacement for the regenerated cellulose films generally used in such systems and to examine the degradation behavior of AN–DMAEMA films in this biological environment.

Copolymers of AN and acrylic acid (AA) were included in the evaluation.

Journal of Applied Polymer Science, Vol. 23, 1449–1452 (1979)

0021-8995/79/0023-1449$01.00

Since the initiation of the ladder structure during thermal degradation is enhanced by electrophilic groups,[5] AN–AA copolymers and AN–DMAEMA would be expected to behave differently during thermal degradation. It was of interest to establish whether this difference in behavior extended to modification by reaction with ethylene oxide and performance in the in vitro rumen system.

EXPERIMENTAL

Polymer Preparation. AN and AA were supplied by British Drug Houses Ltd. and DMAEMA, by Rohm and Haas (U.K.) Ltd. The copolymers were produced by free-radical redox polymerization from monomer weight ratios AN:DMAEMA or AN:AA of 85:15.

Film Formation. Polymers were produced in film form by solvent casting from solutions in dimethylformamide (DMF). The casting substrate was glass, and the solution concentrations were 10% w/v for AN–DMAEMA and 3% w/v for AN–AA. Films were exposed to the *in vitro* rumen system in two ways:

1. As strips 10 cm × 2.5 cm, corresponding to those generally used in the evaluation of mechanical properties.[6]
2. The films were converted into lay-flat tubing 4 cm wide by heat sealing, and an inlet and outlet of 2-mm-bore poly(tetrafluoroethylene) were sealed into the tubing using a silicone-based adhesive. The copolymer tubing was supported by an adaptation of a standard procedure[7] for supporting regenerated cellulose tubing in a coil haemodialysis apparatus. The technique consisted of fixing parts of the tubing to a poly(vinyl chloride) mesh by heat sealing and winding the mesh and the tubing to form a coil 5 cm in diameter. To reduce the possibility of stagnant areas occurring within the coil, passages were created in the tubing by heat sealing along parallel lines.

Chemical Modification. The modification of AN–DMAEMA and AN–AA copolymers was achieved by contacting films with pure ethylene oxide at a slightly reduced pressure and at a concentration in excess of 1.4 g/l. for 3 hr at 30°C. Modification was carried out after the films had been cut into strips or assembled into a coil with the poly(vinyl chloride) mesh.

In Vitro Rumen System. The apparatus used was the "Rumenstat" developed by Ewart[8] to simulate a microbiological environment and the physiological conditions prevailing in the rumen. The natural rumen contains a dense microbial population which utilizes the host animal's ingesta to produce, under anaerobic conditions, the C_2, C_3, and C_4 fatty acids from carbohydrate dietary components. Other substances are formed by degradation of the substrates offered in the host's diet. For evaluating the membranes, a homogenate of silage with a dry matter content of 4% was the experimental "feed." Cultures were started with an inoculum from fistulated wether sheep and allowed to stabilize over 72 hr. The "Rumenstat" apparatus allowed the temperature, pH, and turnover times of the in vitro rumen system to be controlled at values close to those generally encountered in vivo. These values were 39°C, 6.5 and 18–28 hr, respectively. The chemical composition and osmolarity of the in vitro culture were maintained by the automatic addition of artificial saliva buffer solution.

Infrared Spectroscopy. The infrared spectra of films were obtained by using a Perkin–Elmer 125 spectrometer.

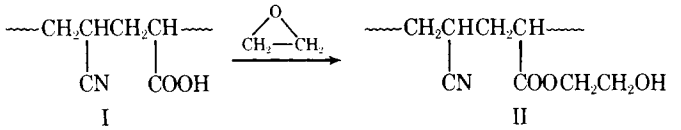
DISCUSSION

The behavior of the AN–DMAEMA and AN–AA films in the in vitro rumen system is summarized in Table I. The AN–DMAEMA films underwent progressive discoloration through the sequence yellow, red, brown, and black. The discoloration was accompanied by embrittlement and insolubility in DMF. Infrared spectroscopy showed the appearance of a peak at 1590 cm^{-1}. Therefore, the behavior of the AN–DMAEMA copolymer in the in vitro rumen system was similar to the behavior of AN and its copolymers during thermal degradation.[5,9]

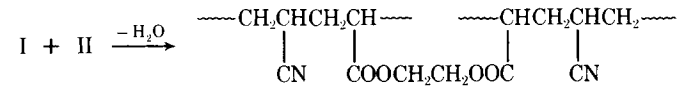
Modification of the AN–DMAEMA copolymer films by reaction with ethylene oxide made no apparent difference to the performance in the in vitro rumen system. Discoloration and embrittlement again took place. The infrared spectra were also similar except that prior to the evaluation the modified AN–DMAEMA had the peaks at 1590 and 3300 cm^{-1} associated with the ethylene oxide reaction.[1]

The AN–AA films disintegrated in the in vitro rumen system. The films displayed no apparent tendency to undergo C=N conjugation and cyclization.

After the reaction with ethylene oxide gas, AN–AA films remained clear but were insoluble in DMF. Infrared spectroscopy confirmed that there was no C=N conjugation. Previous work with *n*-butyl methacrylate–AA films as dialysis membranes[10] and biological fuel cell membranes[11] has indicated modification with ethylene oxide gas leads to ring opening by the carboxylic acid groups and crosslinking by esterification. It is suggested that AN–AA copolymers behave similarly and that the following reactions occur:



(1)



(2)

The modified AN–AA films were apparently unaltered by the in vitro rumen environment. There was no discoloration or embrittlement and no pronounced changes in the infrared spectra.

The difference in behavior between the AN–DMAEMA and AN–AA copolymers on reaction with ethylene oxide gas has interesting implications. Modification of the AN–DMAEMA copolymers offers a means of producing hydrophilic

TABLE I

Film	Behavior in rumen environment
AN–DMAEMA	progressive discoloration and embrittlement
AN–DMAEMA modified by reaction with ethylene oxide	progressive discoloration and embrittlement
AN–AA	disintegration
AN–AA modified by reaction with ethylene oxide	no apparent alteration

ladder polymers, while modification of the AN–AA copolymers offers a means of achieving low-temperature crosslinking. The promising performance of the modified AN–AA films in the in vitro rumen environment would appear to be due to the fact that such films have a reduced tendency to undergo C=N conjugation. However, crosslinking of the AN–AA films by reaction with ethylene oxide does not guarantee a satisfactory membrane. If the membrane is going to permit the transport of solutes by dialysis or water by ultrafiltration, a degree of water sensitivity is essential. This could be achieved by controlling the modification reaction to ensure that CH_2CH_2OH groups remain after crosslinking. Such control would depend on a successful selection of monomer proportions and appropriate values for the reaction parameters of time, temperature, and relative humidity.

The present study has shown that it is possible to alter the structure of an AN copolymer to improve the resistance to degradation in particular applications.

The authors wish to acknowledge the guidance of Professor R. M. Kenedi, Director of the Bioengineering Unit, University of Strathclyde.

References

1. J. M. Courtney and T. Gilchrist, *J. Appl. Polym. Sci.*, **19,** 1503 (1975).
2. J. M. Courtney, T. Gilchrist, and W. M. Muir, Brit. Pat. 1,411,843 (Oct. 19, 1975).
3. J. M. Courtney, J. D. S. Gaylor, I. Martin, and R. M. Lindsay, in *Technical Aspects of Renal Dialysis,* T. H. Frost, Ed., Pitman Medical, Tunbridge Wells, 1978, p. 126.
4. J. M. Courtney, G. B. Park, I. A. Fairweather, and R. M. Lindsay, *Biomaterials, Med. Dev. Artificial Organs,* **4,** 263 (1976).
5. N. Grassie and J. N. Hay, *J. Polym. Sci.*, **56,** 189 (1962).
6. British Standard Specification 1133: Section 21, 1964.
7. J. M. Courtney, J. D. S. Gaylor, and T. Gilchrist, in *Physical Techniques in Medicine,* Vol. 1, J. T. McMullan, Ed., Wiley, New York, 1977, p. 195.
8. M. Ewart, *Proc. Nutr. Soc.*, **33,** 125 (1974).
9. W. J. Burlant and J. L. Parsons, *J. Polym. Sci.*, **22,** 249 (1956).
10. W. M. Muir, R. A. Gray, J. M. Courtney, and P.D. Ritchie, *J. Biomed. Mater. Res.*, **7,** 3 (1973).
11. S. Affrossman, J. M. Courtney, T. Gilchrist, and I. Martin, *Med. Biol. Eng.*, **13,** 539 (1975).

Received January 25, 1978
Revised February 24, 1978