NOTES

Accelerated Degradation of Poly(ester urethane) by Adenosine Triphosphate

INTRODUCTION

The ability to withstand the harsh biological milieu is perhaps the most desirable qualification of any polymeric implant. The investigations accumulated over the years identify water, oxygen, enzymes, etc., as factors that destabilize a polymeric implant.[1-3] Among these, the role played by enzymes has been subjected to extensive studies.[4-8] However, the role of other biological molecules, like adenosine triphosphate (ATP), in destabilizing a polymer in a biological environment has not been understood well. Our effort here is to understand the hydrolytic degradation of a ester polyurethane in the presence of ATP, the energy supplier of the living system.

EXPERIMENTAL

The ester polyurethane used in this study was based on 2,4-toluene diisocyanate, polyethylene adipate, and 1,4-butanediol. Sodium salt of ATP (Sigma) was used as received. ATP solution having a concentration of 3 mg/mL was prepared in triple distilled water. Sodium azide was added as antibacterial agent. The polymer strips were kept in control (water and sodium azide) and ATP solution at 37°C for varied duration.

For estimating the molecular weight parameters of the polymer strips kept in control medium and solution, a Waters HPLC system consisting of model 6000A solvent delivery pump, U6K injector, and model 440 absorbance detector was used. A bank of 3 μ-styragel columns having pore sizes of 10^5, 10^4, and 10^3 Å in conjunction with dimethylacetamide (DMAC) as elutant at a flow rate of 1 mL/min was used for the estimation. Lithium bromide, 0.05%, was added to the mobile phase to prevent the aggregation of polymeric species.

Pieces of polymer strips, placed in water and ATP solution, were dissolved in DMAC, and 50 μL each of the solution was injected onto the columns. The column effluents were monitored at 280 nm, and the chromatograms were obtained on an ominescribe recorder (Houston Instruments, Austin, TX U.S.A.). The molecular weight averages were estimated from the chromatograms as reported elsewhere.[9] For analyzing the ATP solution, a μ-bondapak C18 column was used. The separation was effected by water : methanol (80 : 20 v/v) at a flow rate of 1 mL/min.

RESULTS AND DISCUSSION

It is well known that poly(ester urethane) undergoes hydrolytic degradation at a faster rate in comparison to

Table I Effect of ATP on the Molecular Weight of Poly(Ester Urethane) (M_n = 99,136; M_w = 202,660; D = 2.04)

Time (h)	Water			ATP Solution		
	M_w	M_n	D	M_w	M_n	D
66	181,970 ± 9928	81,590 ± 3000	2.04 ± .02	157,460 ± 7200	67,870 ± 5070	2.32 ± 0.08
120	150,314 ± 7266	73,420 ± 2150	2.10 ± .04	122,470 ± 4720	57,090 ± 2650	2.15 ± 0.09
240	137,870 ± 9299	61,829 ± 3100	2.25 ± .08	82,860 ± 9340	31,870 ± 4716	2.6 ± 0.05

Journal of Applied Polymer Science, Vol. 43, 825–827 (1991)
 CCC 0021-8995/91/040825-03$04.00

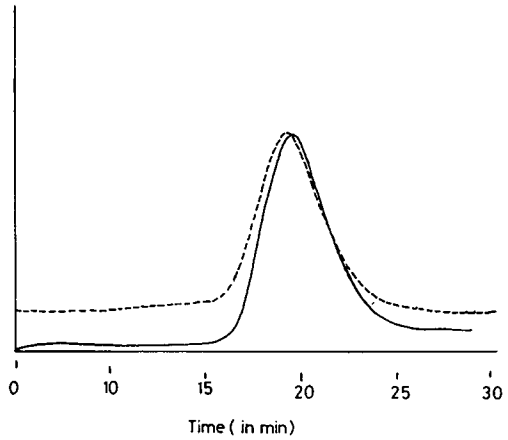

Figure 1 Representative GPC traces of poly(ester urethane) from water (- - -) and ATP solution (——). Duration of exposure = 120 h.

poly(ether urethane). Accelerated degradation in the presence of ATP therefore can be assessed in a shorter period of time.

Figure 1 shows typical GPC traces of the samples from water and the test solution. A reduction in molecular weight of the polymer in the presence of ATP is apparent from the chromatograms in the form of a shift to the higher time scale.

Table I provides the molecular weight averages of the virgin polymer, kept in the control and in the test solution for varied periods of time. The influence of ATP in the hydrolytic degradation is remarkable. The number average molecular weight of the polymer kept for 240 h is more or less than half of the value of the strips kept in water for the same period, indicating an accelerated effect of ATP on the hydrolytic degradation.

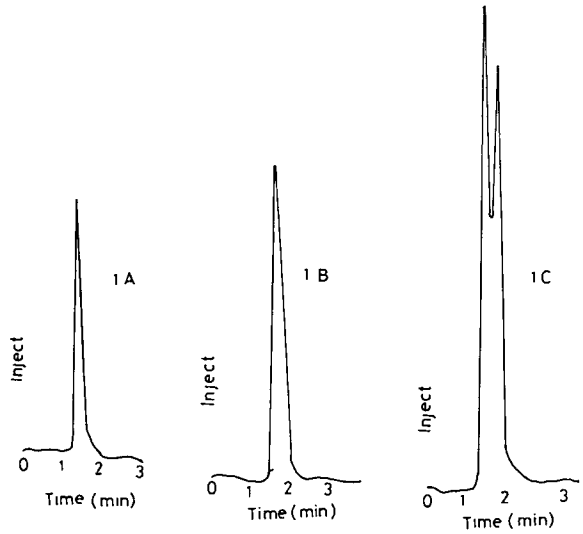

Figure 2 High-performance liquid chromatograms of (A) ATP, (B) ADP, and (C) ATP solution after 240 h.

Table II Variation in pH of the Control and Solution With Time

Time (h)	Control (water)	ATP Solution
66	7.1	6.6
240	6.9	5.4

It is well known that ATP releases 7.3 kcal/mol of energy when hydrolyzed to adenosine diphosphate (ADP),[10] and this energy is used for biosynthesis and biological functions in the bioprocess ATP function through coupled reaction.[11] A coupling reaction, and thus the effective use of liberated energy for breaking the bond of the polymeric chains, is most unlikely here.

ATP slowly hydrolyzes to form ADP and energy. The ATP solution after 240 h was subjected to HPLC analysis. The HPLC traces illustrated in Figure 2 indicate the conversion of ATP to ADP with time. The hydrolysis of ATP also provides H^+ ions through the reaction.[12]

$ATP + H_2O \rightarrow ADP + HPO_4^{2-}$ + energy. It may be relevant to point out that poly(ester urethane) hydrolysis is accelerated by H^+.[13] The H^+ ions formed by the reaction could catalyze the polymer hydrolysis. The pH values summarized in Table II indirectly favor this possibility.

The observation made here is inadequate to highlight the influence of ATP in the *in vivo* degradation of polyurethane. However, the report indicates the possible involvement of small molecules like ATP, apart from enzymes, in the complex phenomenon of biodegradation.

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K. SREENIVASAN
M. JAYABALAN

Biomedical Technology Wing
Sree Chitra Tirunal Institute
for Medical Sciences and Technology
Poojapura, Trivandrum 695 012, India

K. V. C. RAO

Vikram Sarabhai Space Centre
Thumba, Trivandrum 695 022, India

Received May 9, 1989
Accepted November 30, 1990