Degradation of a poly(ether urethane urea) elastomer: infra-red and XPS studies

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The potential for a poly(ether urethane urea) (PEUU) elastomer to undergo degradation, under the conditions prevalent in the biological environment, was investigated using an *in vitro* model system. The effect of exposing an unstabilized PEUU to an aqueous environment containing the proteolytic enzyme, papain, for one month was examined by Fourier transform infra-red spectroscopy, X-ray photoelectron spectroscopy and chromatographic methods. Evidence of degradation was observed in both enzyme- and water-treated PEUU, but was restricted to the surface regions of the polymer. Analysis of methanol extracts from polymer samples revealed evidence for the degradation of ether linkages, which was independent of the enzyme, whereas the degradation of urethane and urea groups, indicated by the detection of a primary aromatic amine degradation product, depended on the presence of the proteolytic enzyme.

(Keywords: poly(ether urethane urea); degradation; infra-red spectroscopy; X-ray photoelectron spectroscopy; papain; proteolytic enzyme)

INTRODUCTION

In recent years, the use of segmented poly(ether urethanes) (PEU) for long term cardiovascular and soft tissue applications has increased considerably. In spite of this wide interest in PEUs as biomedical elastomers, little specific information is available regarding the degradation behaviour or potential for long term biodegradation.

PEUs are a diverse family of polymers and their significance as biomaterials is derived from a wide range of useful properties which can be incorporated into the polymers by adjusting the molecular composition. These linear elastomers consist of moderately flexible, long linear polyether segments and relatively hard, glassy short segments usually comprising urethane linkages and aromatic groups. If diamine chain extenders are used, rather than diols, then urea linkages will also be incorporated into the hard segment. The soft and hard segments are usually incompatible at the temperature of use, consequently the material undergoes microphase separation, with resultant formation of hard and soft domains. Many of the thermal and mechanical properties can be understood in terms of this domain structure[1-3].

For many biomedical applications, materials are required to be biologically resistant for long periods and consequently, the possibility of biodegradation has to be considered. In general, any disruption to the chemical structure of the backbone macromolecular chains, or to the chemical or physical crosslinks that maintain the macroscopic integrity of polymers, can result in a dramatic decrease in the performance properties of the material. Thus despite the excellent mechanical properties of poly(ester urethanes) in air, these were found to undergo hydrolytic degradation with an associated loss of properties when implanted[4]. The poly(ether urethanes) have thus gained prominence as biomaterials for long term applications.

The degradation of synthetic biomaterials not under stress but exposed to the many interactions that result from implantation is now well documented. The reasons for the *in vivo* degradation remain controversial however[5,6]. The involvement of proteolytic and hydrolytic enzymes capable of either direct reaction with the polymer or indirectly through catalytic action, has been a popular, but often unsubstantiated, hypothesis as a degradation mechanism for several polymers[7-11]. Significant reductions in tensile strength or fatigue properties have been a common finding of previous studies. A satisfactory explanation for this behaviour in poly(ether urethane urea) has yet to be resolved.

Stabilizers such as radical chain terminators and u.v. absorbers are normally present in commercial biomedical elastomers, the rationale being to increase shelf life and to inhibit u.v. initiation of degradation prior to implantation. It is normally supposed that biodegradation, if it occurs, will follow a hydrolytic mechanism rather than an oxidative process. Thus, the presence of stabilizers, such as substituted benzotriazoles and hindered bisphenols are not specifically designed to provide protection from potential biodegradation mechanisms. However, in a recent study[12] it was established that an unstabilized poly(ether urethane urea) (PEUU) will undergo significant loss of tensile strength and a dramatic decrease in fatigue lifetime, when exposed to an *in vitro* medium containing the proteolytic enzyme, papain. The presence of stabilizers in the same polymer markedly reduced these effects, which suggested a degradation phenomenon was responsible. The work presented here was carried out in order to obtain some understanding of the deterioration in mechanical properties of the unstabilized polymer. In this study, an unstabilized PEUU, similar in composition to the commercially available elastomers, was analysed for evidence of chemical degradation following a one month immersion in papain solution. Untreated and treated

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PEUU samples were characterized by Fourier transform infra-red spectroscopy (*FT*i.r.), X-ray photoelectron spectroscopy (XPS), and chromatographic methods.

EXPERIMENTAL

Materials

Films of unstabilized poly(ether urethane urea) (PEUU), the structure of which is shown in *Figure 1*, were synthesized and prepared by Mercor, Inc., Berkeley, CA, USA. Poly(tetramethylene glycol) (PTMG) ($\bar{M}_n = 2000$) was reacted with diphenylmethane-4,4′-diisocyanate (MDI), and then chain extended using ethylene diamine in dimethylacetamide (DMAC). The molar ratio of PTMG, MDI and ethylene diamine was 2.5:3.5:1.0. Films (3 mm thick) were prepared from PEUU/dimethylformamide solutions which were filtered and web-coated on clear Mylar. The film was water extracted at 60°C for 24 h to remove any residual solvent. The complete removal of residual solvent was confirmed by infra-red analysis.

In vitro *treatment*

Test samples ($70 \times 60\,mm^2$) were cut from the PEUU film, sonicated in distilled water for 15 min and then suspended in a treatment medium for one month at 25°C. Treatment media included papain solution, and a control medium of distilled water. Papain, a plant thiol endopeptidase which has similar specificity to the lysosomal enzyme Cathepsin B, was obtained from Boehringer Mannheim. The enzyme activating agent solution consisted of 0.05M cysteine and 0.02M EDTA with a pH adjusted to 7.5 using NaOH. The amidase activity of the papain solution (6.0 mg/ml) was measured using a colorimetric assay[13], which involves enzymic hydrolysis of *N*-benzoyl-D,L-arginine-*p*-nitroaniline into benzoyl arginine and *p*-nitroaniline. The absorbance of the *p*-nitroaniline product was measured at 410 nm. A unit of papain activity is defined as that amount of enzyme activity that will liberate 1 μmole of *p*-nitroaniline in one min at 25°C at pH 7.5. The specific activity is expressed as the number of units of activity per microgram of protein.

The specific activity of the enzyme was found to decrease linearly with time at a rate of 6.4%/day. To provide a relatively constant enzyme activity, treatment media were changed once every two days. In this way, the papain activity was maintained in the range $12.5 \pm 0.9\ U/\mu g$ throughout the treatment period. Sodium azide (0.02% w/v) was added to all treatment media to inhibit bacterial growth and thus any interference from bacterial enzymes.

After the treatment period, untreated as well as treated samples were cleaned and dried before analysis. The cleaning procedure has been previously described[11] and is used to remove any adherent particulate contamination. Briefly, this procedure involves placing samples in 0.1M Tris-HCl buffer at pH 8.5, containing Triton X-100 (1% v/v) and sonicating for 15 min. This is repeated using an Ivory soap solution (1% v/v). The samples are then sprayed with distilled water and sonicated in distilled water for 15 min. Samples were air-dried for 1 day, at 60°C for 15 min and then stored in a vacuum desiccator before analysis. Treated and untreated samples were analysed by Fourier transform infra-red spectroscopy (*FT*i.r.), X-ray photoelectron spectroscopy (XPS) and chromatographic methods.

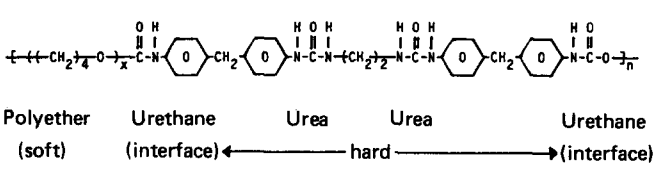

Figure 1 Structure of PEUU

Infra-red spectroscopy

Small specimens from each of the treated and untreated samples were dissolved in dimethylformamide and solution cast directly onto KBr salt plates. Films were air-dried and then vacuum-dried at 60°C and then ambient temperature to remove residual solvent. Film thicknesses were estimated at 10 μm and controlled by monitoring the absorbance of selected bands (e.g. ν(C–H) at $2938\,cm^{-1}$). Films were recast until the desired approximate thickness was achieved. Accurately weighed specimens of untreated, water-treated and papain-treated samples were extracted in methanol (spectroscopic grade, Sigma Chem. Co.) at ambient temperature for 3 days. Methanol extracts were slowly evaporated, dried under vacuum to constant weight and then redissolved in DMF. Extract solutions were then recast on KBr salt plates as described above and analysed.

A Digilab FTS-14 Fourier Transform infra-red spectrometer (Digilabs Inc., Cambridge, MA, USA) was used to obtain transmission spectra of the thin polymer films over the $3800–600\,cm^{-1}$ wavenumber region. Two hundred sample scans and reference scans were averaged and subtracted and provided spectra with a resolution of $4\,cm^{-1}$. Baseline correction routines, but no smoothing procedures, were used when plotting the spectra.

X-ray photoelectron spectroscopy

XPS analysis of the treated and untreated samples was performed using a Surface Science model SSX-100 ESCA spectrometer (Surface Science Laboratories Inc., Mountain View, CA, USA), which employs a monochromatized Al Kα X-ray source. The X-ray gun was operated at 10 kV and 12 mA with the sample chamber at a pressure of approximately 10^{-9} torr. With this instrument, irradiation of the sample surface with monochromatized X-rays is limited to a 600 μm diameter circle. No visible damage (at 50×) to the samples was observed during the exposure time. Surface charging that can occur due to the non-conductive nature of the samples was neutralized with 1–10 eV low energy electrons from an electron flood gun.

All data were processed using the standard software provided with the instrument. The sensitivity factors used with the software to calculate the atomic percentage composition of the 4 elements present in the samples were: C_{1s} (1.000), N_{1s} (1.678), O_{1s} (2.494) and Si_{2p} (0.903). The sensitivity factors take into account the Scofield photoelectron cross-sections, the kinetic energy dependence of the inelastic mean free path of emitted electrons and the electron kinetic energy dependence of the transmission function[14–16]. C_{1s} spectra were resolved using the assumption of Gaussian peak shapes. The value of 285.0 eV was used for the binding energy of the C_{1s} core level photoemission of all peaks equivalent to saturated hydrocarbon. Binding energy data were reproducible to within ±0.2 eV.

Chromatography

Gel permeation chromatography (g.p.c.) of the untreated and treated samples was performed using a Waters Model 244 liquid chromatograph equipped with two E-linear and one 60A Microbondgel columns connected in series and operated with a dimethyl acetamide (DMAC)/0.05 M LiBr mobile phase at 0.5 ml/min. G.p.c. of the methanol extracts, which had been evaporated to dryness and redissolved in tetrahydrofuran (THF), were performed using a Perkin Elmer Series 10 liquid chromatograph and a Sigma 15 Chromatography Data Station. PL-gel column packing was used with the THF mobile phase operated at 1.0 ml/min, a temperature of 40°C and the u.v. detector set at 254 nm. Calibration of each system was achieved using monodisperse polystyrene standards. Weight-average ($\bar{M}_w$) and number-average ($\bar{M}_n$) molecular weights were obtained from the computer analysis of the elution volumes and peak shapes.

H.p.l.c. spectra of the methanol extracts and methylene dianiline (MDA) reference compound were obtained using an ISCO Model HPLC equipped with a UA-5 dual beam absorbance detector set at 254 nm and sensitivity at 0.05 AUFS. The standard h.p.l.c.column was packed with a slurry of C_{18}, 5 μm spheres, and used with a methanol mobile phase at an elution rate of 1.0 ml/min at ambient temperature.

Separation of components within the respective extracts was carried out by using an ion exchanger and based on the method of Mulder[17]. Extract samples in methanol were passed through a column of Dowex 50-X12 in the H^+ form, after which the column was rinsed with a mixture of equal volumes of methanol and water. Using this procedure, the eluate contains, primarily, the polyether component of the PEUU. Any aromatic amine degradation product in the extract remains strongly bound to the cation exchanger and is only slowly eluted by using an equal volume mixture of methanol and concentrated hydrochloric acid. This second eluate will therefore contain any aromatic amine in its acid salt form. Each eluate was evaporated using a rotovap and subsequently analysed using *FT*i.r.

RESULTS AND DISCUSSION

PEUU:Bulk characteristics—g.p.c. and i.r.

Table 1 shows very clearly that the enzymic treatment had little effect on the molecular weight averages of the PEUU. Within experimental error, the molecular weights are identical.

Figure 2 shows the transmission i.r. spectra of the untreated (A), H_2O-treated (B) and papain-treated (C) PEUU samples. Important peak assignments, based on previous studies, are presented in *Table 2*. The presence of a single N–H absorption at 3320 cm^{-1}, and the absence of an N–H band at 3450 cm^{-1} in the PEUU indicates that the urethane and urea N–H are essentially all hydrogen bonded[18,19]. The amide I urea carbonyl absorbed at 1639 cm^{-1} as a single symmetric band indicative of complete hydrogen bonding, and thus associates the urea group with the completely phase-separated hard segment domain. The results showed that both hydrogen bonded (1709 cm^{-1}) and non-hydrogen bonded (1734 cm^{-1}) urethane carbonyls were present in the PEUU. The urethane linkage is present at the interface between the hard segment domain and the polyether soft segment phase. The sharpness of the interfacial region improves with decreasing hydrogen bonding of the urethane carbonyls.

The urea and urethane C–N stretching and N–H bending amide II modes absorb in the 1535 cm^{-1} region

Table 1 Molecular weight g.p.c. analysis of PEUU

Polymer	Molecular weight		
	$\bar{M}_w$	$\bar{M}_n$	$\bar{M}_w/\bar{M}_n$
Untreated PEUU	154 000	83 000	1.85
Untreated PEUU (cleaned)	155 000	82 000	1.86
Papain-treated PEUU	155 000	83 000	1.87

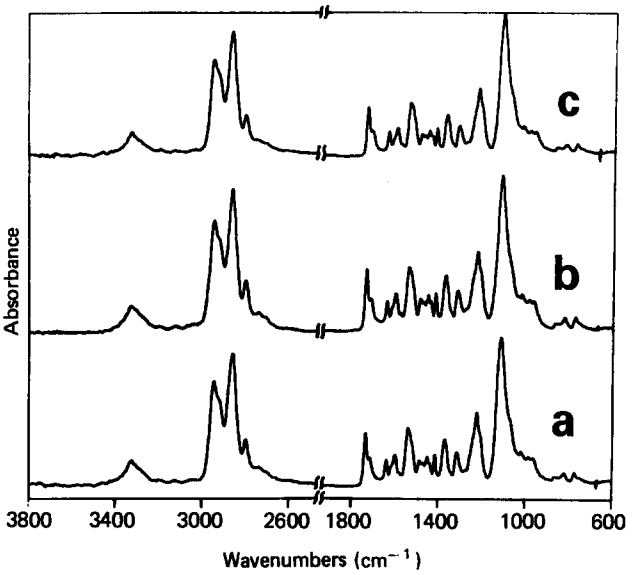

Figure 2 *FT*i.r. spectra, 3800–600 cm^{-1} region: (A) untreated PEUU, (B) water-treated PEUU and (C) papain-treated PEUU

Table 2 *FT*i.r. band assignments for PEUU

Wavenumber (cm^{-1})	Relative intensity[a]	Assignments[b]
3320	M	ν(N–H), H-bonded
3035	W	ν(C–H) aromatic ring
2938	VS	ν_a(C–H) in CH_2
2852	VS	ν_s(C–H) in CH_2
2795	M	ν_s(C–H) in CH_2–O
1733	S	ν(C=O) urethane amide I, nonbonded
1709	M	ν(C=O) urethane amide I, H-bonded
1639	W–M	ν(C=O) urea amide I, H-bonded
1615	W, sh	ν(C=C) aromatic ring
1595	M	ν(C=C) aromatic ring
1540–1525	S	ν(C–N)+δ(N–H) amide II
1480–1430	M	δ(C–H) in CH_2
1370	M	w(C–H) in CH_2
1310	M	ν(C–N)
1225	S	ν(C–N)+δ(N–H) amide III
1110	VS	ν_a(C–O–C) aliphatic ether
1070	M, sh	ν_s(O=C–O)
1020	W	δ(C–H) in plane, aromatic ring+ν_s(C–O–C)
980	W	δ(C–H) out-of-plane, aromatic ring
960	W	δ(C–H) out-of-plane, aromatic ring
830–750	W	ν(C–H) in CH_2, δ(O=C–O) out-of-plane

[a] Relative intensity: VS=very strong, S=strong, M=medium, W=weak, sh=shoulder

[b] ν=stretching mode, ν_a=asymmetric stretching, ν_s=symmetric stretching, γ=bending mode, w=wagging mode, r=rocking mode

as overlapping bands. Similarly, the amide III bands overlap in the 1200–1250 cm^{-1} spectral region. Aromatic rings are adjacent to urethane and urea linkages and are associated with the interfacial and hard segment regions of the polymer. The aromatic C–C stretching vibrations absorb in the 1600 and 1410 cm^{-1} regions. The C–O–C etheral asymmetric stretching vibration derived from the polyether soft segment absorbs at 1110 cm^{-1} and represents the most intense band of the PEUU spectrum.

In comparing spectra of treated and untreated samples, the analysis included qualitative inspection; spectral subtraction using a least-squares analysis programme[20]; and calculation of indices of relative concentration of characteristic groups using the peak height method with the ν(C–H) band at 2852 cm^{-1} as the normalizing denominator. The analyses did not reveal any significant differences between treated (papain or H_2O) and untreated samples and no new bands or significant peak shifts were observed. A product of degradation of PEUUs invariably includes aromatic amines[17,21,22]. This appears to be the case whether the mechanism is through hydrolysis or some form of oxidative degradation. However, the i.r. analysis showed virtually no perturbation to the amide II band. The absence of O–H or new N–H peaks in the 3300–3600 region further suggested the absence of degradation under the test conditions. The initial i.r. and g.p.c. results gave clear indication that if biodegradation was occurring at all, it was limited to the PEUU surface.

PEUU: Surface characteristics—XPS

Low-resolution wide scanning provides a determination of which elements were present in PEUU. High resolution spectra were then obtained from the C_{1s}, O_{1s}, N_{1s} and Si_{2p} peaks. All samples analysed contained small amounts of silicone contaminant. Four C_{1s} peaks were identified at 285.0 eV, 286.5 eV and two small shoulders at 288.2 and 289.3 eV. The major C_{1s} peak located at 285.0 eV corresponds to the aliphatic carbon, while the peak at 286.5 eV corresponds to the ether carbon of the polyether soft segment. The small peaks at 288.2 eV and 289.3 eV correspond to the carbonyl carbon derived from the urea and urethane linkages. A N_{1s} peak at 397.8 eV was observed and corresponds to the nitrogen in the urea and urethane groups and is often used as an index of hard segment concentration. The O_{1s} peak observed at 532.5 eV is derived mostly from the etheral oxygen with contribution from the carbonyl oxygens.

Table 3 shows the surface composition analysis for the untreated and treated samples. It should be noted that the low concentration of the hard segment phase in the surface limited accurate quantification of the nitrogen content. However, *Table 3* shows that one month treated samples were slightly higher in carbon (C_{1s}) and lower in oxygen (O_{1s}) content compared with the treated materials. Thus, all one month treated samples gave

Table 3 XPS of unstabilized PEUU: surface composition (atomic %)

Sample	C_{1s}	N_{1s}	O_{1s}	Si_{2p}	C_{1s}/O_{1s}
Untreated PEUU	73.3	2.2	22.6	1.9	3.2
Water-treated PEUU	77.6	1.4	18.7	2.3	4.1
Papain-treated PEUU	76.1	1.8	19.2	2.9	4.0

0° take-off angle
Approximate experimental error = 10%

Table 4 XPS of unstabilized PEUU:carbon 1s analysis

Sample	C–C	C–O	C=O	C–C/C–O
Untreated PEUU	56.1	41.2	2.7	1.36
Water-treated PEUU	60.2	36.7	3.1	1.64
Papain-treated PEUU	64.1	32.9	3.0	1.95

0° take-off angle
C_{1s} peak resolved using Gaussian fit
Approximate experimental error = 10%

increases in the C/O atomic ratio, which appears to be primarily caused by a loss in surface oxygen content.

The sensitive C_{1s} peak can be accurately resolved into contributions from C–C (hydrocarbon), C–O (ether) and C=O (urea, urethane). This analysis, shown in *Table 4*, gave consistent relative increases in C–C and decreases in C–O for the treated samples. This was particularly evident for the enzyme-treated samples which demonstrated significant reductions in the relative amount of C–O content. This change is illustrated in *Figure 3* which compares the untreated with the enzyme-treated samples.

The XPS results suggest a loss in surface ether linkage content for the treated samples. This may have been caused by a surface degradation phenomenon which affected the ether linkage. With PEUU elastomers, the possibility of chain rearrangement in the polymer surface contributing to this change cannot be ignored. However, PEUU interaction with an aqueous environment would tend to promote a relative decrease in the nonpolar hydrocarbon contribution (e.g. see ref. 23) and not increase it as shown here.

Methanol extracts: Chromatography and i.r.

Methanol extraction of untreated, water-treated and papain-treated PEUU removed $1.5 \pm 1.0\%$ by wt, $4.1 \pm 1.3\%$ by wt and $3.9 \pm 1.7\%$ by wt, respectively. Previous studies by Ratner[23,24] on polyurethane elastomers intended for use in biomedical applications have indicated that low molecular weight polymers and oligomers are readily extracted by methanol. The g.p.c. chromatographs for the extracts of untreated and treated polymers, shown in *Figure 4*, support Ratner's work. All extracts contain similar peaks estimated to be in the 17 000 and 700 molecular weight ranges. The higher value suggests the presence of extractable low molecular weight polymer, while the 700 molecular weight peak is more likely to be oligomer or a polymer component such as the polyether. For the treated polymer extracts, however, additional peaks in the 200 molecular weight range were observed, which suggested the presence of degradation products.

The h.p.l.c. results of the methanol extracts are shown in *Figure 5*. For the extract of the untreated polymer (A), two distinct peaks were observed at 3.10 and 3.44 ml elution volume. For the extract of the enzyme-treated polymer (B), an additional small peak at 2.8 min was observed. The possibility of this additional peak being a degradation product was examined by comparing its retention time with that of a probable degradation product[25], methylene dianiline (MDA, M wt = 198). Exact correspondence in retention times was obtained between MDA and the unknown peak. This provided preliminary evidence that the degradation product includes aromatic amine.

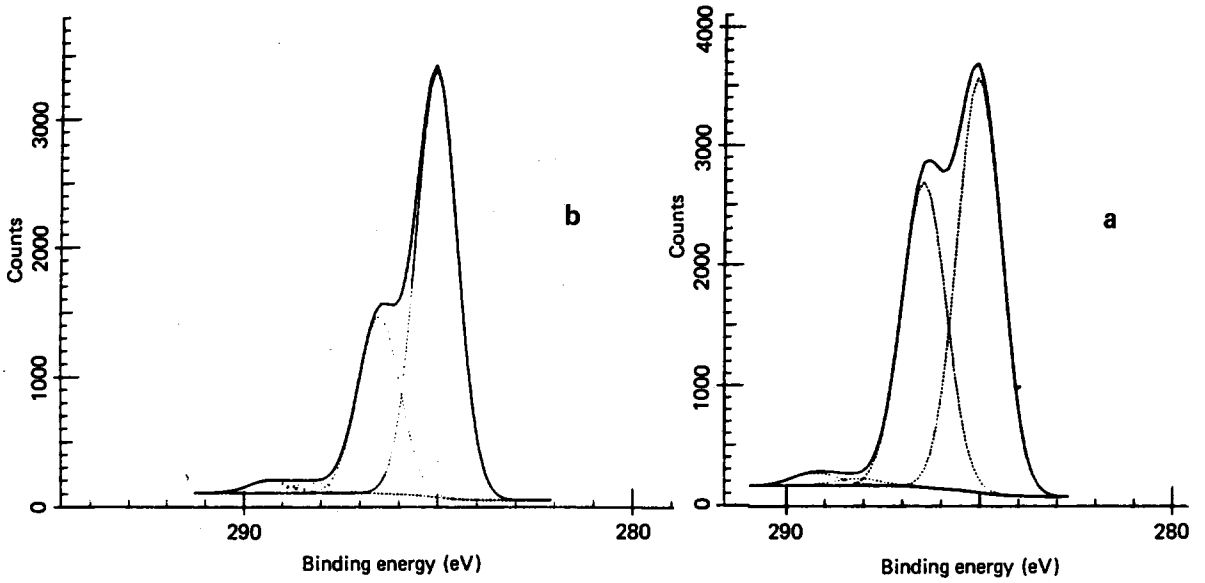

Figure 3 XPS spectra, C_{1s} region: (A) untreated PEUU; (B) papain-treated PEUU. (———)=C_{1s} spectrum (- - - -)=deconvoluted spectra using gaussian fit into C–C at 285.0 eV, C–O (ether) at 286.4 eV, C=O (carbonyl) at 288.2 eV, and N–C=O (urea, urethane) at 289.3 eV

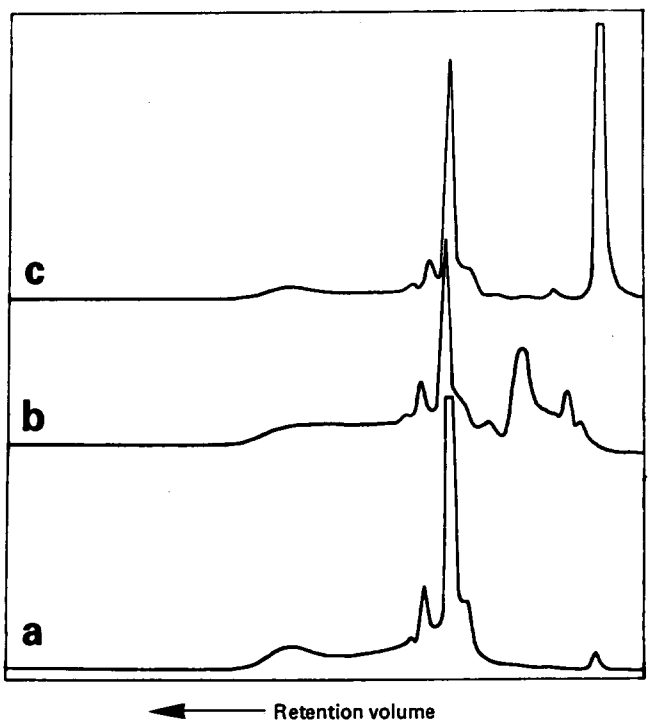

Figure 4 G.p.c. chromatographs: (A) extract of untreated PEUU, (B) extract of water-treated PEUU and (C) extract of papain-treated PEUU

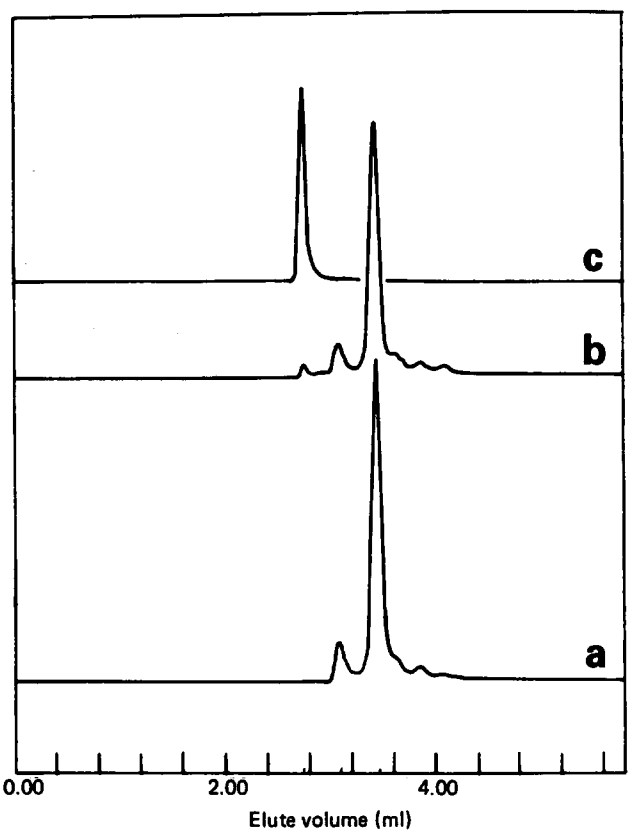

Figure 5 H.p.l.c. spectra: (A) extract of untreated PEUU; (B) extract of papain-treated PEUU and (C) ethylene dianiline reference component. Flow rate: methanol at 1 ml/min; sensitivity = 0.05 AUFS

Figure 6 compares the *FT*i.r. spectra of the extracts with the spectrum of the untreated polymer. As with the high molecular weight PEUU, the spectra of the extracts are complicated by perturbations derived from intermolecular and intramolecular interactions. Nevertheless, the spectra of the extract from the untreated PEUU and the parent polymer are remarkably similar. This reflects the dominance in the spectrum of the higher molecular weight extractable fraction. Some disruption in the H-bonded, N–H stretching absorption at 3320 cm^{-1} and in the urea carbonyl at 1640 cm^{-1} were the only significant differences. Assuming that degradation of the untreated polymer is negligible, then the splitting and broadening of the urea carbonyl may be due to hydrogen bond dissociation in the extract. This would lead to a reduction in intensity, and splitting of the ν(N–H) band, since non-bonded N–H groups absorb at higher frequency and have a significantly lower molar extinction coefficient compared with H-bonded N–H groups[26]. Thus, the total absorption area for bonded and non-bonded N–H will decrease with increasing H-bond dissociation. Consequently, the extract appears less ordered, and the hard segment urea phase disrupted, compared with its parent polymer. No quantitative assessment of this effect was attempted, because of the relatively low urea content in the original PEUU.

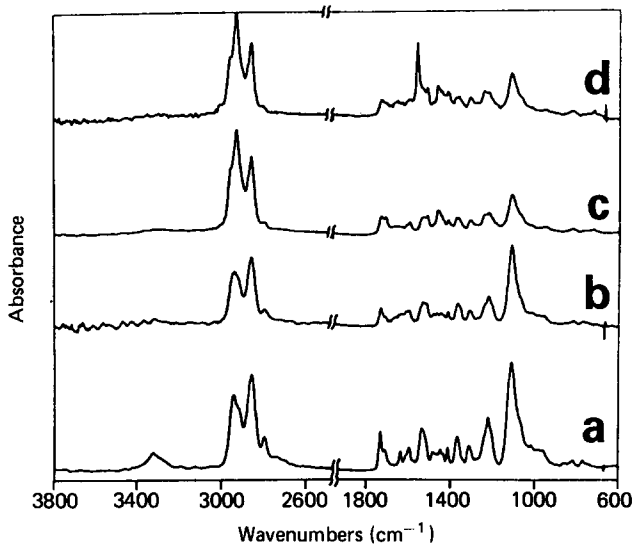

Figure 6 *FT*i.r. spectra, 3800–600 cm^{-1} region: (A) untreated PEUU, (B) extract of untreated PEUU, (C) extract of water-treated PEUU and (D) extract of papain-treated PEUU

In contrast with the untreated-polymer extract, the extracts from the papain- and water-treated polymers showed marked spectral deviations from the original PEUU, particularly in contributions derived from the polyether soft segment phase. The ν(C–H) absorption derived from the CH_2–O group of the polyether at 2795 cm^{-1} virtually disappeared and the contribution from the principal polyether band, C–O–C at 1110 cm^{-1} was disproportionally diminished compared with the ν(C–H) region at 2850–2940 cm^{-1}. This decrease in the ether linkage content correlates well with the observed decrease in the parent polymer surface as shown by the XPS results.

Polyethers are well known to be highly resistant to hydrolysis, which is why polyethers rather than polyesters are incorporated into biomedical polyurethane elastomers. Polyethers are, however, susceptible to light and free radical initiated oxidative degradation processes[27–29]. Free radical formation can be achieved in a variety of ways, e.g. thermal, u.v. or mechanical stress, the latter being of considerable importance in view of the intended biomedical application of PEUU elastomers. Based on the strong evidence of previous studies, it is suggested that degradation of the ether linkages in the PEUU occurs primarily by a free radical initiated mechanism, which is believed to involve hydrogen abstraction reactions from the α-carbon to the ether linkage[28]. This view is supported by the fact that the observed deterioration in mechanical properties was significantly retarded when stabilizers were incorporated into the same PEUU[12].

Figure 7 shows expanded spectra of the 1800–1400 cm^{-1} region, which amplifies some additional spectral differences. Most apparent was the disrupted amide **II** peak at approximately 1530 cm^{-1}. In both spectra A and B, the amide **II** band has undergone some splitting of the contributing δ(N–H) and ν(C–N) overlapping bands and a reduction in intensity suggesting a degradation effect. For the enzyme-treated polymer extract (C), a new peak (or shifted peak) at 1561 cm^{-1} appeared, tentatively assigned to δ(N–H) of a primary amine. In this respect the extracts from the enzyme-treated and water-treated polymers differed, otherwise the two spectra were very similar. Both spectra showed an increased central band in the δ(C–H) fingerprint region at 1468 cm^{-1}. This perturbation may have been caused by the loss of etheral oxygen with the concomitant shift in the δ(C–H) frequency of the αCH_2. Disruption in the urethane and urea carbonyls (1640–1730 cm^{-1}) was also a common feature. The reduced intensity and peak broadening of the urea carbonyl occurred in all three extract spectra to varying degrees. Degradation products from the polyether may partially account for this and for the increased relative concentration of the H-bonded (1703 cm^{-1}) to non-bonded (1730 cm^{-1}) urethane carbonyl groups. In repeating this work, the same changes were consistently found, although the degree of change was variable.

If the new 1561 cm^{-1} amide **II** peak is derived from δ(N–H) of an amine degradation product, rather than from the amide function of the polymer, then passage through the ion exchanger, using the method of Mulder, should facilitate separation and therefore elimination of the 1561 cm^{-1} peak from the spectrum. Comparison of the original and purified extract spectra, shown in *Figure 8*, demonstrates that the separation was achieved.

The spectra (1800–700 cm^{-1} region) of the eluates derived from the ion exchanger after acid washing are shown in *Figure 9*. Spectra are shown for extracts of papain-treated (B) and untreated (A) PEUU and for

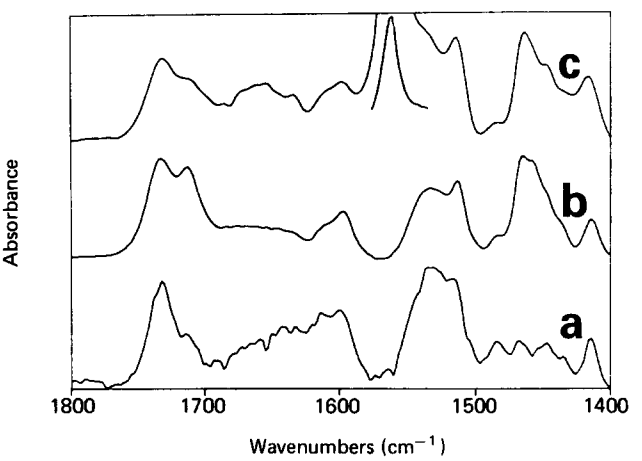

Figure 7 *FT*i.r. spectra, 1800–1400 cm^{-1} region: (A) extract of untreated PEUU, (B) extract of water-treated PEUU and (C) extract of papain-treated PEUU

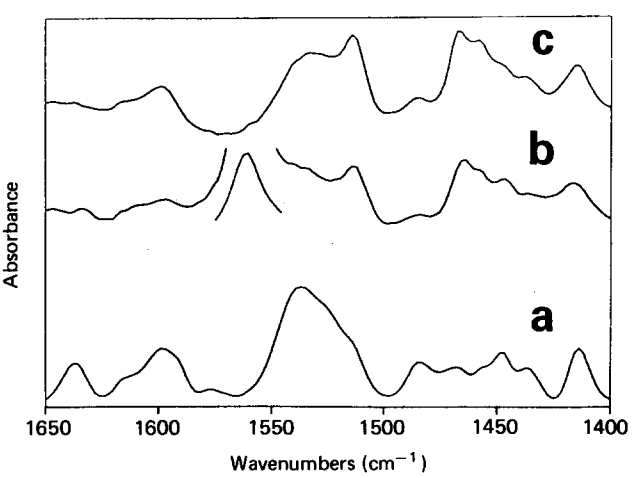

Figure 8 *FT*i.r. spectra, 1650–1400 cm^{-1} region: (A) papain-treated PEUU, (B) extract from papain-treated PEUU and (C) first eluate from ion exchanger of extract from papain-treated PEUU

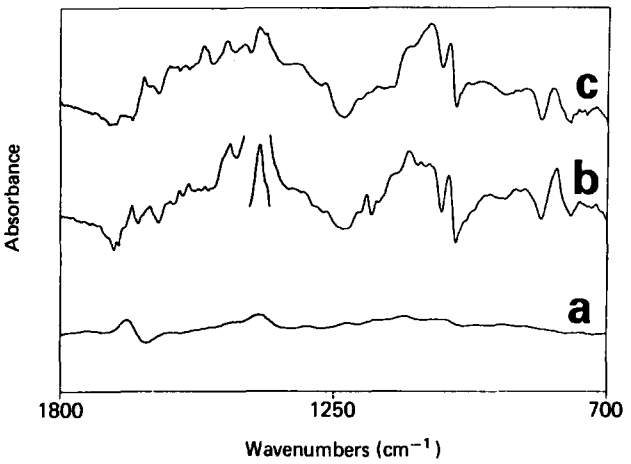

Figure 9 *FT*i.r. spectra of eluates after acid washing, 1800–700 cm^{-1} region: (A) from extract of untreated PEUU, (B) from extract of papain-treated PEUU and (C) acid salt of methylene dianiline

MDA hydrogen chloride model compound (C). Any degradation reaction is very likely to produce a mixture of products resulting in some i.r. peak broadening and loss of resolution. Nevertheless, correspondence between the 'degradation product' with the spectra of MDA HCl reference is remarkably good, suggesting that the MDA degradation product was generated by the *in vitro* enzyme treatment.

Degradation of the PEUU should, using *FT*i.r., lead to a relative decrease in CH_2–O, C–O–C, C–N and possibly C=O absorptions, accompanied by a conversion of the amide N–H absorption to primary amine absorptions. This pattern was generally observed for the enzyme-treated samples and, except for the formation of primary amine, for the water-treated samples. This difference may account for the evidence that enzyme-treated samples undergo a greater loss in mechanical properties compared with water-treated samples and that the use of stabilizers affords less protection for the enzyme-treated samples[12]. The presence of the enzyme papain accelerates the degradation of urethane and urea groups, leading to the formation of primary amine degradation products, which include methylene dianiline. Unlike the poly-ether reaction, the mechanism of urethane and urea degradation may be hydrolytic. However, no evidence for the formation of hydroxyl-terminated degradation products was observed to support this possibility.

CONCLUSIONS

*FT*i.r., XPS and chromatographic methods were used to investigate the chemical stability of an unstabilized poly(ether urethane urea) (PEUU) based on poly(tetramethylene oxide), diphenylmethane-4,4′-diisocyanate and ethylene diamine. The analyses were performed before and after the samples were immersed in an aqueous *in vitro* media containing the proteolytic enzyme, papain and compared with water-treated and untreated control samples. It can be concluded from the results of this study that chemical degradation occurs in both the enzyme- and water-treated samples. However, evidence for degradation was restricted to the surface regions of the PEUU. No evidence of bulk degradation, as determined by g.p.c. and *FT*i.r., was observed, although XPS analysis revealed a loss of etheral oxygen from the treated polymer surfaces. Analysis of methanol extracts from the polymer samples revealed evidence of degradation in treated samples, which involved cleavage of both the soft (polyether) and hard (urethane and urea) segments of the PEUU. Evidence for degradation of ether linkages was observed in both enzyme- and water-treated samples, whereas evidence for the formation of primary aromatic amine degradation products, derived from urethane or urea groups, was found only with the enzyme-treated samples.

The value of PEUU elastomers for use in long-term biomedical applications depends on their resistance to biodegradation. Further detailed studies are needed to elucidate the exact nature of the degradation mechanism(s) which accompany the deterioration in mechanical properties.

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