Oxidative Degradation Study of L-tyrosine based Polyurethanes

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Statement of Purpose: The degradation of polyurethanes in physiological environment is caused by several factors including oxidative attack from the immune system via macrophages, phagocytes, foreign body giant cells etc[1]. Several studies have been done to investigate the mechanism of oxidation by reproducing the physical and chemical environment in vitro. Studies on biostability of polyurethanes under such conditions have been completed for polyether, polyester and polycarbonate urethanes[1]. An oxidative solution of 0.1 M $CoCl_2$(Cobalt chloride) in 20% (W/V) H_2O_2(Hydrogen peroxide) at 37°C is believed to mimic the in vivo oxidative environment[2].

Tissue engineering polymeric scaffolds are also subjected to oxidative degradation. Amino acid based polyurethanes have been developed in our lab for tissue engineering purposes. Two L-tyrosine based polyurethanes are developed: (i) poly(ether)urethane with polyethylene glycol (PEG) and (ii) poly(ester)urethane with polycaprolactone diol (PCL) as the soft segment. The hard segment is from hexamethylene diisocyanate (HDI) and desaminotyrosyl hexyl ester (DTH), a diphenolic chain extender synthesized from L-tyrosine. In this work, the oxidative degradation behavior of the two L-tyrosine based polyurethanes is reported.

Materials, Method and Analytical Procedures

- **Materials.** DTH was synthesized according to literature from L-tyrosine and desaminotyrosine[2]. PEG (M_w 1000), PCL (M_w 1250), HDI, Stannous Octoate ($Sn(Oct)_2$), Dimethyl formamide (99%), Chloroform (99%), Sodium chloride (NaCl), $CoCl_2$, H_2O_2(30% W/V) were used.

- **Method.** The polyurethanes were synthesized by standard two step method under inert N_2 atmosphere. In the first step, the diol is reacted with diisocyanate in DMF (solvent) in 1:2 molar ratios at 110°C for 3 hours with $Sn(Oct)_2$ as catalyst. After this step, the reaction was cooled down to room temperature and the DTH was as the proportion of the diol and the temperature was raised to 80°C. After 12 hours, the reaction was quenched in cold saturated NaCl solution. The polymer precipitated out was either filtered or centrifuged depending on the physical characteristics of the polymer and dried in vacuum.

- **Characterization and Analytical Procedures.**

Solvent (chloroform) cast polyurethanes films were cut approximately into 1cm × 1cm×~1 mm. 0.1 M $CoCl_2$ solution of 20% H_2O_2 solutions were prepared from 30% H_2O_2 solution by proper dilution with distilled water. The polymer films were added to these solutions at 37 °C. Two samples from each of these solutions were taken out at 3, 5, 7, 15, and 22 days interval and dried in vacuum oven at 40 °C for two days prior to characterization. The test solutions were changed every 7 days to maintain the ionic concentration relatively constant. The films were characterized by FT-IR in Nexus 870-FTIR fitted with ATR attachment with germanium crystal. Spectra were collected at a resolution of 2 cm^{-1} with a sampling area of 3mm[2]. The results presented here are the average of the three spectrums recorded for each sample, i.e. a total of six spectrums, each with 32 scans.

Results/Discussion:

o *Polyether urethanes (PEG based)*: Comparison of spectra of degradation after 7 and 21 days against the non-degraded polyurethane shows increased intensity at 1618 cm[-1](normalized to peak 1658cm^{-1} as assigned for the amide I bond of DTH which is assumed to be non degraded) due to formation of vinylic C=C in between the ether linkage due to α-hydrogen abstraction. The degradation of the polyurethanes is represented as percent change in the peak ratio (1618 cm^{-1}/1658cm^{-1}) with respect to non degraded sample, as in Figure 1.
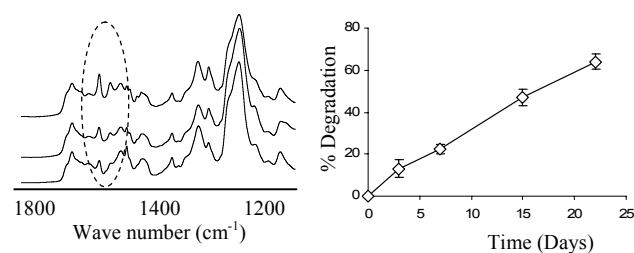

Figure 1. Oxidative degradation of polyether urethane 0, 7, and 21 days stacked from bottom

o *Polyester urethane (PCL based)*: Comparison of spectra of degradation after 7 and 21 against the non-degraded polyurethane shows decreased intensity at 1533 cm^{-1} (normalized to peak 1167cm^{-1} as assigned for the C-C-O of PCL which is assumed to be non degraded) due to degradation of urethane linkage at the interphasic region of the polyurethanes. The degradation of the polyurethanes is represented as percent change in the peak ratio (1533 cm^{-1}/1167cm^{-1}) with respect to non degraded sample, as in Figure 2.
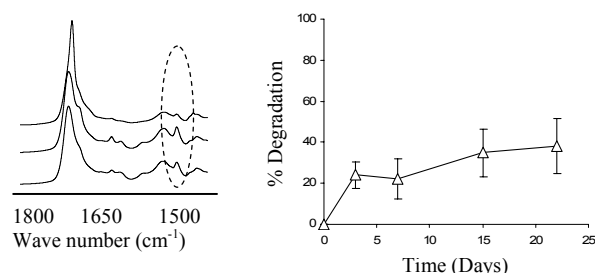

Figure 2. Oxidative degradation of polyester urethane 0, 7, and 21 days stacked from bottom

Conclusions: L-tyrosine based polyether and polyester urethanes undergoes oxidative degradation but by different mechanism. Polyether urethanes are degraded in the soft segment but polyester urethanes are degraded at the inter phase of the two segments.

References:
1. Santerre, J.P.; et. al. Biomaterials, 26, 7457-7470, 2005
2. Christenson, E. M.;et. al. J. Biomed. Mater. Res. 70A, 245-255, 2004