# Comparative Analysis of *In Vitro* Oxidative Degradation of Poly(carbonate urethanes) for Biostability Prediction

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**Statement of Purpose:** Poly(carbonate urethanes) (PCUs) have generated significant interest as a potential replacement of poly(ether urethanes) (PEUs) in medical devices due to their resistance to oxidation and environmental stress cracking. Several *in vitro* models have been developed to predict the oxidative stability of segmented polyurethanes (SPUs) *in vivo*; however, a comparative analysis which evaluates the predictive capabilities of these test methods has yet to be completed. High concentrations of reactive oxygen intermediates produced by a combination of hydrogen peroxide and dissolved cobalt ions have frequently been used as an accelerated testing method to predict long term *in vivo* stability. Alternatively, the ISO 10993-13 suggests a method utilizing 3% $H_2O_2$ concentration without metal ions. To evaluate these methods, we have utilized both systems to test the oxidative stability of three commercially available polyurethanes: Bionate® PCU (80A and 75D), Bionate® II PCU (80A and 75D), and CarboSil® TSPCU (20 80A and 20 55D) polymers. The soft-segment content of PCUs may also influence the degradation rate; therefore, materials representing the range of commercially relevant hardness grades (80A – 75D) were evaluated.

**Methods: *In Vitro* Biodegradation*:*** Unstrained PCU films were tested at 37°C in two different oxidative solutions. An oxidative solution comprised of 0.1 M $CoCl_2$ and 20% $H_2O_2$ in deionized water was used to treat the PCUs at an accelerated rate for 36 days, with solution changes every three days to maintain a relatively constant concentration of radicals. PCU specimens treated according to ISO standard 10993-13 were subjected to a 3% $H_2O_2$ solution with weekly media changes for 12 months. The 3% $H_2O_2$ method did not include any concentration of metal ions to catalyze hydrogen peroxide decomposition. Percent hydrogen peroxide decomposition of both solutions was calculated using a basic iodometric titration process. Following degradation, the films were rinsed with reverse osmosis water and vacuum dried overnight at ambient temperature before characterization.

**Material Characterization:** Changes in surface chemistry were monitored using attenuated total reflectance-Fourier transform infrared spectroscopy (ATR)-FTIR. Soft segment loss was quantified by monitoring differences in the 1256 $cm^{-1}$ peak height (C-O of soft segment carbonate) relative to the internal reference peak at 1600 $cm^{-1}$. Scanning electron microscopy was used to examine the surfaces of PCU films before and after *in vitro* treatment. Degraded samples were strained to failure, and the susceptibility of the material to environmental stress cracking (ESC) was evaluated according to a method developed by Christenson et al.[1] Changes in bulk mechanical properties were characterized by uniaxial tensile testing. Tensile strength, 2% secant modulus, and ultimate elongation were all calculated from the resultant stress vs. strain plots. Changes in molecular weight and molecular weight distribution were monitored using gel permeation chromatography (GPC).

**Results:** All materials exhibited signs of surface degradation when exposed to the accelerated oxidative environment. Loss of surface soft segment content and evidence of surface damage on all of the PCUs were comparable to previous *in vitro* and *in vivo* data[1]. Bulk properties of all PCUs were found to remain intact, with only small changes in molecular weight and tensile properties after 36 days. Samples exposed to 3% $H_2O_2$ exhibited no changes in surface or bulk properties after 12 months of treatment. In addition, no significant hydrogen peroxide decomposition to reactive oxygen intermediates (ROI) was detected in the 3% $H_2O_2$ solution. **Table 1** shows a comparison PCU soft segment loss when exposed to the two methods over the course of the study**.**

**Table 1:** Surface soft segment loss of PCUs after 12 months *in vitro* treatment (3% $H_2O_2$ at 37°C) and accelerated *in vitro* treatment (0.1 M $CoCl_2$/20% $H_2O_2$ at 37°C)

| | | 12 Months 3% $H_2O_2$ Percent Change | 36 Days Accelerated Percent Change |
|---|---|---|---|
| Bionate® PCU | 80A | -7 ± 2% | -27 ± 10% |
| | 75D | -1 ± 1% | -16 ± 1% |
| Bionate® II PCU | 80A | +18 ± 5% | -34 ± 3% |
| | 75D | -2 ± 1% | -21 ± 2% |
| CarboSil® TSPCU | 20 80A | +1 ± 3% | -27 ± 9% |
| | 20 55D | +2 ± 1% | -20 ± 6% |

**Conclusions:** Minor changes in PCU molecular weight and mechanical properties indicate bulk properties were retained for all materials in both treatments. Furthermore, the absence of surface cracking in degraded and strained-to-failure specimens suggests that the PCUs are resistant to ESC. Thus, these materials are all likely to outlast conventional poly(ether urethanes) *in vivo* and should be considered as strong candidates for biostable medical devices. The absence of changes to the surface of materials exposed to 3% $H_2O_2$ for 12 months does not correlate with previous *in vivo* results, which suggests the test method does not simulate physiological conditions.[1] The lack of ROI production over the incubation period raises concern as to the efficacy of the 3% $H_2O_2$ test method. Oxidation of PCUs is not expected without the presence of oxygen radicals. Therefore, the 3% $H_2O_2$ method does not represent an oxidative environment previously demonstrated in other *in vitro* tests but does effectively demonstrate the hydrolytic stability of these materials after 12 months. Based on a comparison between the two test methods with previous *in vivo* results, the accelerated metal ion-catalyzed method should remain the recommended choice for predicting polyurethane biostability.

**References:** [1]Christenson et al. *J Biomed Mater Res A* 2004:70A2, 245-255.