

# High Temperature Aging of Polyurethanes in the Prediction of *In Vivo* Biostability

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**Statement of Purpose:** Dissatisfaction with the performance of poly(ether urethane) (PEU) pacemaker leads in the 1980s prompted a strong research effort to develop methods to predict polyurethane biostability. Although numerous accelerated *in vitro* testing methods have been developed as screening tools, validation that *in vitro* methods reproduce *in vivo* degradation is critical to the selection of appropriate tests. High temperature aging of polyurethanes has recently been proposed as a method to accelerate hydrolytic degradation and the principle of time temperature superposition (TTS) used to predict long term changes at body temperature using shorter time, higher temperature results.<sup>1,2</sup> These reports predicted significant loss in molecular weight and tensile properties of a polydimethylsiloxane-based polyurethane (E2A) and a PEU (E80A) over time that was attributed to hydrolysis of the polymer backbone. However, correlation of this prediction to *in vivo* performance of explanted pacemaker leads was poor.<sup>3</sup> Water uptake and microstructural changes that were shown to occur at these elevated temperatures invalidate key assumptions in the application of the TTS principle. In the current work, the discrepancy between *in vivo* and the accelerated *in vitro* data was explored in more detail by reproducing the high temperature aging experiment on extruded films in an effort to identify the relevance of hydrolysis on *in vivo* performance.

**Methods:** Microtensile films of E2A and E80A were aged at 37, 55, 70 and 85°C in deoxygenated phosphate buffered saline (PBS) at pH 7.4 for 26 weeks. Molecular weight of E2A and E80A was monitored using gel permeation chromatography (GPC). Activation energy was calculated by using a linear regression of plots depicting initial number average molecular weight over the number average molecular weight at each time point and temperature, and an Arrhenius plot was generated from the natural logarithm of the linear slopes. Predictive hydrolysis curves were constructed using an acceleration factor based on the calculated activation energy.<sup>1</sup>

**Results:** Specimens aged at 37°C did not present any significant loss in molecular weight (MW) or tensile properties after 26 weeks. In contrast, MW loss was observed for both polymers aged at temperatures above 37°C with higher temperatures resulting in significantly higher losses, Figure 1.

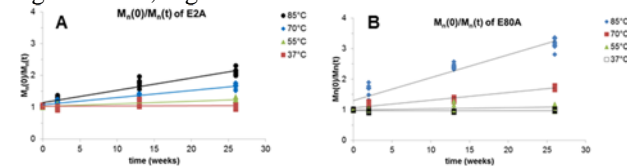


Figure 1: Molar mass loss over time of E2A (A) and E80A (B).

The activation energy for hydrolysis of E2A was determined to be ~84 kJ/mol, which differed significantly from the previous study report of ~36 kJ/mol. The

predicted time to reduce the molar mass by 50% also increased to from 6.7 years to 32 years. Similarly, the calculated activation energy for E80A was ~171 kJ/mol, nearly twice the previously reported ~90 kJ/mol.<sup>3</sup> This data was based on polyurethane MW measurements relative to polystyrene standards. Absolute MW data yielded significantly different Ea from the relative MW data, Figure 2.

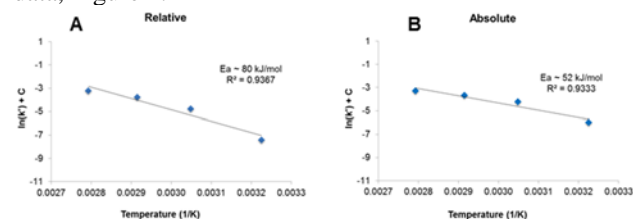


Figure 2: Arrhenius plots of E2A using (A) relative MW and (B) absolute MW

The linear fit of the master plot using the absolute MW data was also poor with an  $r^2$  value of ~0.5. Absolute MW measurements provide more reliable estimations of polyurethane MW given the known over-estimation that occurs with polyurethanes when using polystyrene standards. Finally, the calculation of activation energy from this data or previous reports is based on the assumption that the concentration of water and the labile bonds stay constant over the temperature range studied. However, water uptake increased for both materials with temperature and incubation time, Figure 3.

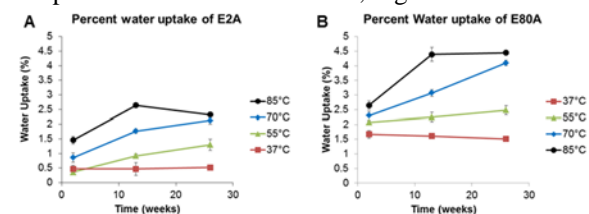


Figure 3: Water uptake over time of E2A (A) and E80A (B).

**Conclusions:** No changes in tensile strength or MW were observed in E2A or E80A after 37°C hydrolytic aging for 26 weeks. Although molecular weight losses were observed at higher aging temperatures, the observed losses did not yield activation energies that correlated with previously reported studies.<sup>1,2</sup> Notably, the activation energy from the current aging study predicted a 5 fold increase in E2A molar mass half life. Furthermore, the calculation of activation energy deviated significantly when using absolute MW measurements as compared to relative MW measurements. Overall, high temperature aging can be used to accelerate polyurethane degradation but the relevance of predictions made from this data on long term *in vivo* performance remains questionable.

## References:

- <sup>1</sup>Chaffin, et al. *Macromolecules* 2012; 45: 9110-9120.
- <sup>2</sup>Chaffin, et al. *Macromolecules*, 2014, 47 (15), 5220–5226
- <sup>3</sup>Padsalgikar et al. *J Biomed Mater Res Part B: Appl Biomater.*, 2014; 00B:000–000.