

## Alternative Methods to Determine Extractable Monomer Content of Polydioxanone (PDO)

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**Statement of Purpose:** Polymers typically do not reach full conversion of monomer when polymerization reactions occur. The concern when forming medical devices is that some monomers, when above certain concentrations, can negatively affect the toxicity of a material<sup>1</sup>. Testing of polymers for monomer content, especially extractable monomer content, has been a growing field in medical device manufacturing. Standard testing methods usually call for gas chromatography (GC) testing of polymers or extraction eluents to determine relevant monomer levels in a sample. When a GC is unavailable or a sample cannot be tested by GC, the question of how else to test for monomer content is raised. In addition to GC, material characterization testing often includes testing by ultra violet and visible light absorption (UV/Vis) or gel permeation chromatography with a refractive index detector (GPC). Because of solubility difficulties with PDO, a sample of the polymer could not be tested as a bulk material. Testing for low percentage components presented signaling problems as well. The larger percentage components decreased the ability to accurately detect the signal produced by the low percentage component materials. In order to allow testing to proceed and obtain a reliable response for < 1% components in the material, the samples were subjected to a standardized extraction process so the monomer alone could be confidently analyzed. Success of these methods would provide faster, readily available and economical testing methods for sample screening before other testing or determining the safety and processing control of materials intended for further processing and biomedical end products. The scope and goal of the study was to quantitatively determine the concentration of 1,4-dioxan-2-one monomer in the bulk polymer.

**Methods:** The extraction was performed in Dichloromethane (DCM) for 16.75 hours at 37°C with one gram of polymer exposed to a 10 mL of solvent in a glass vial. Other solvents such as water, minimum enriched medium (MEM), and hexafluoro-2-propanol (HFIP) were also attempted to determine solvent feasibility. DCM was chosen for the resolution and repeatability of the analysis observed. Standard curves for both methods were created using stock dilutions of 1,4-dioxan-2-one monomer in DCM. By determining the concentration of monomer in the extraction eluent based on the standard curves, an extractable monomer content value for the polymer sample was calculated. Though the standard curves were made with solutions of 1,4-dioxan-4-one in DCM, it was unknown if oligomers would also be extracted and detected in the same signal by either method.

**Results:** Standard curves were successfully created using the intensity of signal for stock dilutions of monomer in DCM for both GPC and UV/Vis analysis methods. Only very small concentrations could produce linear standard curves using UV/Vis due to absorbance restrictions

described by the Beer-Lambert Law. Each sample extracted was tested using both analytical techniques.

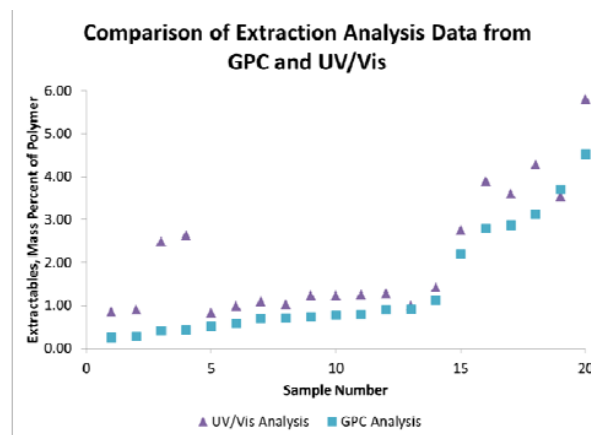


Figure 1. GPC and UV/Vis Measurements of Extractable Monomer Content, Expressed as Mass Percent of the Polymer Sample

Within each testing method, very consistent values were observed. The standard deviations for a given sample were never above 6.2% of the reported value and averaged 2.7% of the reported value. Excluding outliers, the UV/Vis technique yielded values an average 30% higher than the values determined by GPC. Though the samples compared were tested from the same lot, the granule size did show an inverse correlation to the amount of monomer detected in the eluent. The UV/Vis method was believed to be detecting oligomers. The GPC method detected oligomer peaks that were resolved from the monomer peak used for calculation.

**Conclusions:** Repeatable extractable monomer content values were measured for a highly varied set of polymer samples. A consistent difference was often observed between the two methods, but outliers prevented any confidence in a direct correlation between the analysis methods. The UV/Vis method typically measured higher values than the GPC method. It is hypothesized that the UV/Vis method was able to detect but not differentiate extractable oligomers in the samples. The GPC method also detected oligomers, but was able to differentiate them from the monomer. Both methods were shown to be effective methods of quickly screening samples before further testing was implemented. Future recommendations would include investigation into testing the same samples using GC in addition to UV/Vis and GPC to correlate to GC. Other future work should include investigation of how the polymer's granule size affects the extraction.

### References:

1. ASTM D4827 - 03(2009) Standard Test Method for Determining the Unreacted Monomer Content of Latexes Using Capillary Column Gas Chromatography