Rheologically Modified Methoxypropyl-Based Cyanoacrylate Tissue Adhesives:

A Preliminary Study <u>K.J. Garcia^{1,2}</u>, K.J.L. Burg^{2,3}, J.T. Corbett^{1,2}

¹Poly-Med, Inc., 52 Technology Dr., Anderson, SC 29625; ²Dept of Bioengineering, Clemson University, Clemson, SC 29634; ³Dept of Chemical Engineering, Kansas State University, Manhattan, KS 66506

Statement of Purpose:

Uncontrolled hemorrhage can occur without warning, with potentially fatal consequences, in a clinical or trauma setting. Currently, medical professionals rely on commercially available hemostatic products such as Tisseel[®] and BioGlue[®] to seal the wound in these events; however, these products fail to create a full seal for venous and/or arterial bleeding, thereby failing to stop the loss of blood.^{1,2} Excessive bleeding renders the products incapable of ceasing blood flow to allow wound approximation and clotting of blood to occur.

A potentially effective solution to these challenges is absorbable cyanoacrylate tissue adhesives and pastes (sealants). The proposed cyanoacrylates would have modulated rheology and mechanical properties (adhesive joint strength & flexibility) to better facilitate thrombogenesis & wound approximation over currently marketed sealants (such as Tisseel® and BioGlue®) and adhesives (such as Dermabond[®] and Histoacryl[®]). Previous research has shown that the addition of novel absorbable polymers results in a rheologically modified adhesive with potentially improved clinical handling and use in hemorrhagic conditions.³⁻⁶ These cyanoacrylate adhesives form superior unions through the creation of interpenetrating tissue networks (IPTN) between the cured adhesive and the target tissue.³⁻⁶ These networks in turn create a tight seal, thereby closing off wounds and stopping blood flow. This research examined the interrelationship between novel polymeric rheological modifiers and the resulting cyanoacrylate adhesive rheology, as well as mechanical properties to facilitate wound approximation. The goal of this work was to identify candidate materials for commercial use, in both current external and future internal applications. Methods:

In the preliminary study, absorbable poly(e-caprolactoneco-glycolide) polymers were synthesized at variable molar percentages of e-caprolactone (Cap.) to glycolide (Gly.), and mixed with methoxypropyl cyanoacrylate (MPC) to create tissue adhesives & sealants of variable weight percentage polymer. These adhesives, along with Histoacryl[®] (n-butyl cyanoacrylate based, used as a benchmark), were then tested to determine their rheologies, and adhesive t-peel strengths (using a test method based on ASTM D1876 – 08).

Results:

The preliminary results from the viscosity testing are found in Figure 1.

Figure 1 compares the polymeric weight percentages and resulting adhesive viscosity.

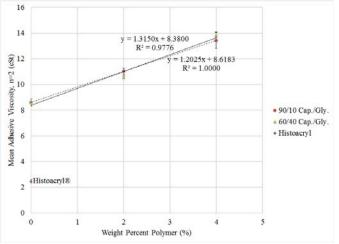


Figure 1: Relationship between adhesive viscosity and polymeric rheological modifier

The t-peel strength results showed a grand mean for all the adhesives tested of 5.64 ± 0.75 MPa.

Conclusion:

The preliminary results show that there is a positive, linear relationship between polymer weight percentage and adhesive viscosity. The results also indicate that there is no observable relationship between the tested polymer weight percentages (2% & 4%) and adhesive t-peel strength based on the low standard deviation for the grand mean. These results (pending statistical studies) indicate that mixing the polymer into the cyanoacrylate successfully rheologically modified the cyanoacrylate, but did not significantly affect the adhesive's t-peel strength. This conclusion provides strong evidence that the novel adhesives will likely maintain their position on the applied tissue and appropriately function once applied in an appropriate clinical application.

References:

1.Kheirabadi, B. S. et al., Determination of Efficacy of New Hemostatic Dressings in a Model of Extremity Arterial Hemorrhage in Swine, *J. Trauma*, <u>67</u>, 450-460 (2009).

2.Arnaud, F. et al., Comparison of 10 Hemostatic Dressings in a Groin Puncture Model in Swine, *J. Vasc. Surg.*, <u>50</u>, 632-639 (2009).

3. Shalaby, S. W. Stabilized polyester/cyanoacrylate tissue adhesive composition. 2006. USPTO 7083634.

4. Shalaby, S. W. Stabilized polyester/cyanoacrylate tissue adhesive composition. 2006. USPTO 7083634.

5. Linden Jr., C. L., & Shalaby, S. W., Performance of a Modified Cyanoacrylate Composite as Tissue Adhesives for Soft and Hard Tissues. J. Biomed. Biomater. Res., Appl. Biomater., 38(4) (1997).

6. Shalaby, S. W. (2009). Absorbable adhesive paste (U.S. Patent Application Serial No. 61/276,130 ed.)