Drug Eluting Cements for Hard Tissue Repair: Evaluating efficacy against *S. aureus*.

A.W. Wren[1], T.M. Eidem[2], A. Coughlan[1], P.M. Dunman[2], M.R. Towler[3].

[1]Inamori School of Engineering, Alfred University, NY.
[2]University of Rochester Medical Center, Rochester, NY, USA
[3]Department of Mechanical and Industrial Engineering, Ryerson University, Toronto, Canada.

Introduction: Glass ionomer cements (GICs) have been widely used in the past, predominantly in dental applications such as luting and restorative applications. However, the ability to easily manipulate their chemistry and properties has resulted in a highly versatile material that has attracted interest in orthopaedics. These materials consist of a glass phase (SiO_2-Al_2O-CaO), a polymer phase (Polyacrylic acid – PAA) and water. Upon mixing, ions leach from the glass and crosslink COO^- groups on the acid chains which results in a hard set cement[1]. These materials versatility stems from the ability to manipulate the chemistry of the glass phase to be more suitable for orthopaedic applications. Additionally, the molecular weight and the concentration of PAA used can also be used to tailor the setting characteristics and mechanical properties. This study was conducted to develop a drug-eluting cement to release RNPA1000, a *S. aureus* RnpA inhibitor. This compound was developed as it possesses the potential to reduce the prevalence of *S. aureus* related infections if applied to orthopaedic applications[2].

Methods: A glass $0.43SiO_2$-$0.05TiO_2$-0.36ZnO-0.12CaO-0.04SrO was fired (1500ºC, 1 h) in a platinum crucible and shock quenched in water. The resulting frit was dried, ground, and sieved to retrieve a glass powder with a maximum particle size of 45 μm. Cements were formulated from a range of (Powder:Liquid) P:L ratios (comp A 2:1.25, comp B 2:1.5, comp C 2:1.75) with 40, 50, and 60 wt% additions of PAA. Complete mixing was completed within 20 seconds. 20 wt% Vancomycin (F.W.1485.73, Fisher Scientific, Pittsburgh, PA) and 20 wt% RNPA1000 (F.W. 464, TimTec, Newark, DE) were substituted for both the PAA and the water in order to determine the best cement formulation. Working (T_w) and Setting times (T_s) were conducted in accordance with relevant standards and antibacterial testing was conducted using *S. aureus* by the agar diffusion method where the inhibition zones (IZ) were calculated as follows:.

$$\text{Inhibition Zone } (mm) = \frac{Halo\ \phi - Disc\phi}{2}$$

Results: T_w and T_s are presented in figure 1. GICs produced with 40wt% formed T_w of 182s (comp A), 203s (comp B) and 258s (comp C). Increasing the P:L ratio in addition to using the lowest concentration of PAA resulted in longer T_w. GICs containing 40wt% PAA produced T_s of 223s (comp A), 250s (comp B) and 272s (comp C). GICs containing 40wt% PAA and a P:L ratio of 2:1.75 was selected for antibacterial testing. Figures 2 and 3 present antibacterial testing in *S. aureus*, where the Control cements did not present any IZ. Van./PAA and Van./H_2O substituted cements produced IZ of 9.1mm and 9.8mm, while the RNPA/PAA and RNPA/H_2O produced IZ of 1.9 and 2.2mm respectively.

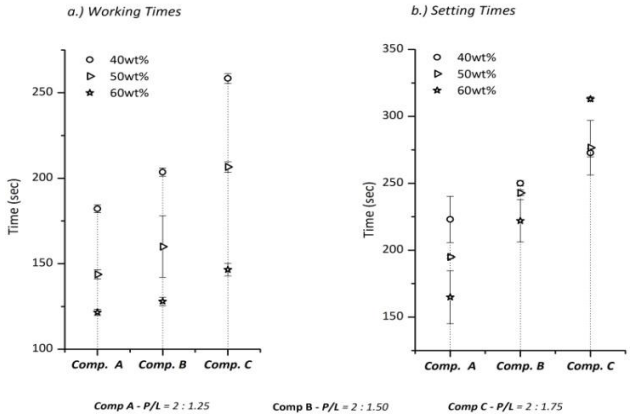

Figure 1. Rheological characteristics of GICs.

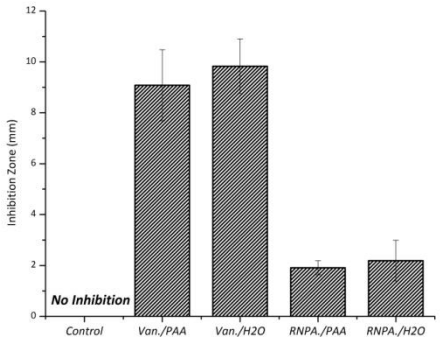

Figure 2. GIC doped with Van and RNPA in *S. aureus*.

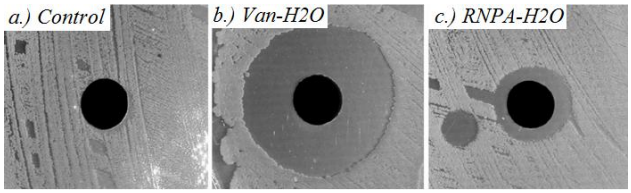

Figure 3. a.) Control b.) Van & c.) RNPA containing GIC.

Conclusion: A novel GIC was formulated with suitable handling characteristics. Also, RNPA1000 did exhibit antibacterial properties when tested against *S. aureus*, suggesting it may potentially be a substitute for current antibiotics. Further studies will be needed to determine RNPA1000 efficacy levels in *S. aureus*.

References:

1. Boyd, D., Towler, M.R. *J Mat Sci: Mat Med*, 16, 843, 2005.

2. Eidem, T.M., Coughlan, A., Towler, M.R., Dunman, P.M., Wren, A.W. *J Biomat App*. DOI: 10.1177/0885328213503388