Zinc and Silver Glass Polyalkenoate Cements: An Evaluation of their Antibacterial Nature.

A. Coughlan[1,2], K. Scanlon[3], B.P. Mahon[3] & M.R. Towler[1,2]
[1]Inamori School of Engineering, Alfred University, Alfred, NY, USA.
[2]Materials & Surface Science Institute, University of Limerick, National Technological Park, Limerick, Ireland.
[3]Institute of Immunology, National University of Ireland, Maynooth, Co. Kildare, Ireland.

Introduction: Methicillin resistant *Staphylococcus aureus* (MRSA) is the most commonly identified antibiotic-resistant pathogen in the developed world [1]. Glass polyalkenoate cements (GPCs), formed by the reaction between an ion-leachable glass and an aqueous solution of polyacrylic acid (PAA) [2], have proven to be both antibacterial and cariostatic [2]; properties related to their ability to release beneficial amounts of therapeutic ions [3]. We have previously shown that silver and zinc- containing glass polyalkenoate cements (GPCs) eliminated *S. aureus* bacteria *in vitro* [4].

The larvae of *Galleria mellonella* (G. *mellonella*) have been used as non-mammalian hosts to study the virulence of bacterial and fungal pathogens [5]. *G. mellonella* provides a screening method that is cost-effective and more ethically acceptable. The objective of this research is to compare the antibacterial efficacy of novel silver- and zinc- containing GPCs against published research using six different strains of Vancomycin (the most commonly used antibiotic against *S. aureus*) in eliminating MRSA *in vivo* [6].

Materials & Methods: 0.5g of glass ($56.04SiO_2$, $32.76ZnO$, $0.33Ag_2O$ and $10.87Na_2O$, mol.%), was ground down to <25µm particles and mixed with 0.2g PAA (Mw:210,000) and 0.25ml distilled water to form GPC coatings. These were applied onto Ti6Al4V discs (25mmØ, 2mm th.) and placed in distilled water (~65ml, 24h) to make up the elutes. Two dilutions of elutes were undertaken (5% and 10%). 50µl or 100µl of elute was added to replicate bacterial cultures in a final volume of 1ml PPB. *G. mellonella* in final larval stage were infected with $1x10^6$ CFU/larvae of (MRSA). Delivery was by injection into the last proleg. After 20min recovery, a second injection of either 20µl 1mM PPB or 20µl elute was administered. The larvae were stored in an incubator (30°C) and assessed for viability at 48h & 72h. Six *G. mellonella* were used per treatment. Larvae were assessed for responsiveness and colour.

Results & Discussion:

Antibacterial efficacy is independent of pH (pH 7 was recorded for all solutions at all time frames), inferring that metal ion release alone is responsible for the coatings' antibacterial efficacy. Larvae that were not infected remained 100% viable both in terms of movement and colouration. *G. Mellonella* that received the control 1mM PPB post infection were all non-viable (immobile and discoloured) at 48hr. Viability was rescued with the addition of GPC elutes, but demonstrated reduced efficacy over time in the *G. Mellonella* that received day 7 elutes compared to day 1. GPC elutes from day 30 demonstrated no beneficial effects when administered, resulting in 100% mortality at 48h. Comparing with the literature, when Vancomycin was injected into *G. Mellonella* infected with strains of MRSA (figure 1), the 1 day GPC solutions after 72h performed better than two and poorer than four strains of Vancomycin.

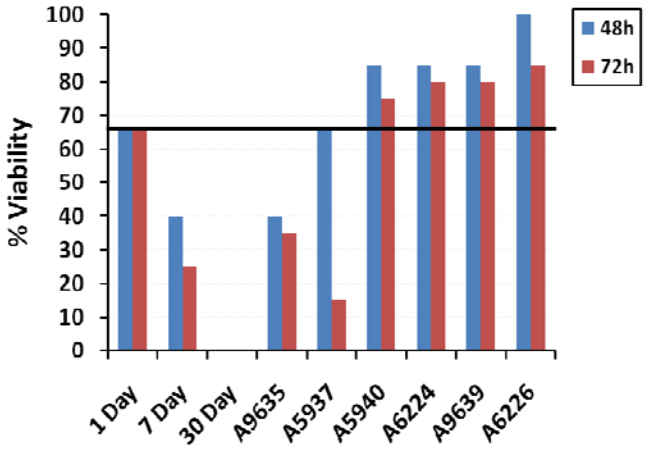

Figure 1: 1, 7 & 30 day GPC elutes % survival at 48h and 72h compared to Vancomycin using different strains of *S. aureus*

Conclusion

The objective of this work was to compare, using a novel *in vivo* test modality, the ability of zinc and silver ion released from novel GPCs, to inhibit or retard the colonisation of MRSA compared to Vancomycin. The GPC solutions showed comparable results against different strains of MRSA. As bacteria can readily build up resistance to antibiotics, these novel Zn-Ag GPC solution can provide a new solution to rid bacteria from hospitals.

Reference

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