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| **Investigation of copper and zinc ions as antibacterial candidates for prevention of capsular contracture** |
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| **Background:** Capsular contracture (CC) is one of the most common clinical complications following breast augmentation or reconstruction surgery using implants. While the pathogenesis of CC is still uncertain and likely multifactorial, it results in an excessive fibrotic **foreign** **body** **reaction (FBR)** that occurs after implantation; the adherence of bacteria to the highly hydrophobic surface of the implant is probably a major contributing factor. While the use of implants with textured surfaces has led to reduced incidence of fibrous capsule formation around implants, this strategy is also associated with anaphylactic large cell lymphomas. Therefore, new strategies are needed to reduce rates of CC. Copper and zinc ions (Cu2+ and Zn2+) have been reported as effective antibacterial agents against gram-positive *S. aureus* and gram-negative *E. coli* strains, bacteria widely implicated in implant colonization and infection. The incorporation and release of Cu2+ and Zn2+ ions from breast implants have not previously been studied. Their incorporation into the silicone shell of the implants could offer an inorganic-based pharmacological alternative strategy to reduce the risks of CC and implant associated infection. |
| **Methods:** Silicone elastomer films (0.3 cm thick) containing 1–30% w/w copper nanoparticles, zinc nanoparticles, anhydrous copper sulfate or anhydrous zinc acetate were prepared from medical grade addition-cure silicone elastomer dispersions (MED 6400 and MED 6600, NuSil). Briefly, silicone parts A and B (1:1) were mixed with agent (1 min, 3000 rpm), left overnight for solvent evaporation, and then post-cured (3 hr, 90oC). Changes in the tensile strength of the materials were measured by elongating films until break. Films were incubated at 37oC, 60 rpm in a phosphate buffer (PBS), sampled every 24 hr over three weeks, and the samples analysed using ICP-OES to quantify Cu2+ and Zn2+ release. Antibacterial capacities of the materials against *S. aureus* (ATCC 6538) were assessed by incubating films with the bacteria in Mueller Hinton Broth (MHB) over 5, 24 and 48 hr, and biofilm formation and planktonic concentrations were measured using the Miles and Mesra method. |
| **Results:** Silicone elastomer films were successfully prepared containing up to 30% w/w of each of the four candidates. While physical properties, such as tensile strength, remained unaffected by the presence of the NPs, they were significantly decreased (by up to 5 MPa) with incorporation of copper sulfate and zinc acetate. NPs provided limited ion release irrespective of loading, and therefore exhibited no antibacterial effects. In comparison, the salt forms released sufficient quantities of copper/zinc ions to reach the minimum inhibitory and bactericidal concentrations (MIC and MBC) for *S. aureus*.  |
| **Conclusions:** Incorporation of copper/zinc anhydrous salts – but not nanoparticles – into implant-grade silicone elastomers provided sufficient release of antibacterial copper/zinc to warrant further investigation as a strategy to reduce the incidence of CC. However, careful consideration of the salt loading is required so as not to impact the mechanical strength and integrity of the implant. In further studies, we will evaluate the antibacterial activity on *E. coli.*  |