# The Application of High-Throughput Methods to the Research and Development of Polysiloxane-Based Antimicrobial Surface Coatings

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**Statement of Purpose:** A unique combinatorial/high-throughput workflow has been constructed for the research and development of antimicrobial polymers and surface coatings. This workflow was used to develop detailed structure-antimicrobial relationships for novel polysiloxane coatings containing covalently-bound ("tethered") quaternary ammonium salt (QAS) moieties. QASs are well known antimicrobial agents that function by disrupting the cell wall of microorganisms. The general compositional space that was investigated is shown in Figure 1. The compositional variables investigated included the molecular weight of the silanol-terminated poly(dimethylsiloxane) ("n" in Figure 1), length of the alkyl chain associated with the QAS ($R_1$ in Figure 1), length of the alkyl chain between the nitrogen and silicon atoms of the QAS ($R_2$ in Figure 1), and the composition of the halide anion associated with the QAS (X in Figure 1). Approximately 160 unique coating compositions were produced and characterized for the study. The results showed that the chemical composition of the reactive QASs as well as other coating compositional variables had a strong effect on antimicrobial activity. From the study, coating compositions were identified that showed broad spectrum antimicrobial activity. These coatings could be very useful for preventing device associated infection such as sometimes occurs with the use of urinary catheters.

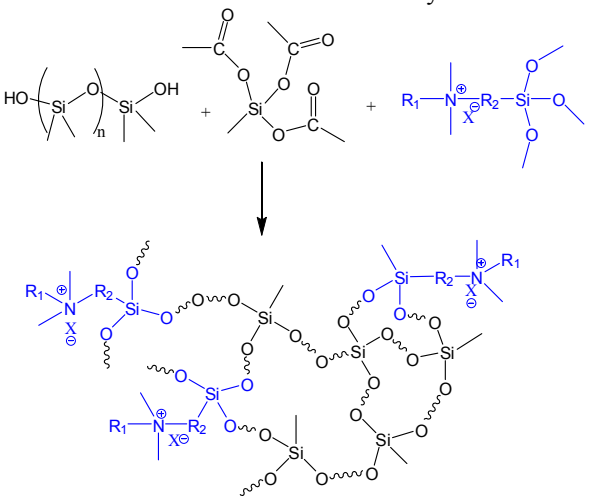

Figure 1. Schematic illustrating the production of polysiloxane coatings containing tethered QAS moieties.

**Methods:** The combinatorial/high-throughput workflow used for the study has been described in detail elsewhere.[1] In addition, the high-throughput methods for determining antimicrobial activity have been previously described.[2] Antimicrobial activity was determined toward three different microorganisms, namely, *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*. Prior to determining the antimicrobial properties of the coatings, the coatings were preconditioned by immersion in a circulating, sterilized water tank for 21 days to remove leachable, potentially toxic components from the coatings. After this preconditioning, coating leachates were collected and tested for toxicity.[3]

**Results:** Prior to testing the antimicrobial properties of the coatings produced, a high-throughput leachate toxicity assay was conducted. The results of the leachate toxicity assays showed that none of the coatings were leaching toxic components from the coatings. Thus, the observation of antimicrobial activity for a given coating could be attributed to a surface associated phenomenon. The results of the study showed that antimicrobial activity ranged widely as a function of coating composition. A statistical analysis of the antimicrobial results showed that coating compositions derived from a QAS possessing an alkyl chain length greater than 14, short spacer length between the nitrogen and silicon atom ($R_2$ = 3 in Figure 1), and bromine counterion provided broad spectrum antimicrobial activity. Characterization of coating surface morphology using atomic force microscopy indicated that the generation of a heterogenous coating surface morphology consisting of micron-size surface protrusions was critical for obtained antimicrobial activity. Thus, the variation in antimicrobial properties observed as a function of coating compositional variables may have been driven more by the effect of these variables on coating surface morphology than the nature of the interaction of the surface bound QAS moieties with the cell wall of the microorganism.

**Conclusions:** Detailed structure-antimicrobial relationships were developed for polysiloxane coatings containing tethered QAS moieties. Compositional variables associated with the chemical structure of the trimethoxysilane-functional QAS were found to strongly affect antimicrobial activity. Characterization of coating surface morphology resulted in the observation of a strong correlation between compositional variables, surface morphology, and antimicrobial properties. Compositions that resulted in a heterogeneous surface morphology were found to exhibit the highest antimicrobial activity. Compositions were identified that provided broad spectrum antimicrobial activity. These coatings may have utility for inhibiting infection associated with implantable devices such as urinary catheters.

**References:**

1. Chisholm BJ. JCT Res. 2007; 4(1):1-12.
2. Webster DC. Biofouling. 2007; 23:179-192.
3. Stafslien S. Biofouling. 2007; 23:37-44.