

Terminally functionalized urethane oligomers containing Quaternary Ammonium groups for antimicrobial efficacy

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Introduction: Implant infections are increasing due to an aging population and the rapid increase of antimicrobial resistance (AMR). There is a direct clinical need to develop biocompatible implant coatings that 1) adhere to metal, 2) prevent bacterial adhesion and biofilm formation, and 3) provide a strong antimicrobial response. The aim of this study was to determine if terminally functionalized urethane oligomers containing quaternary ammonium groups could demonstrate all these user needs using an iterative technology design process.

Materials and methods

Polyurethanes (PUs)

- Cardiovascular, orthopaedic, urology and neurology applications
- PUs are made antimicrobial by incorporation of antimicrobial groups or antimicrobial agents¹
- Target: Develop a non-eluting antimicrobial (AM) polyurethane

Oligomer structure: TDI-C12: C12-QAC-TDI-Polyether-TDI-QAC-C12

TDI-C16: C16-QAC-TDI-Polyether-TDI-QAC-C16

LDI-C16: C16-QAC-LDI-Polyether-LDI-QAC-C16

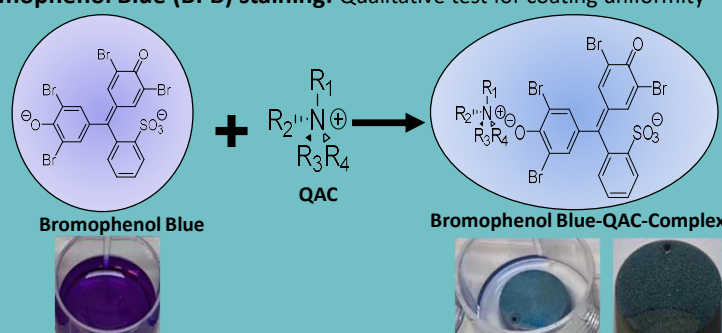
Quaternary ammonium compounds (QACs)

- Negatively charged bacteria adsorb to positively charged QACs^{2,4}
- Alkyl group of the QACs penetrates the cell membrane to kill bacteria^{2,3}

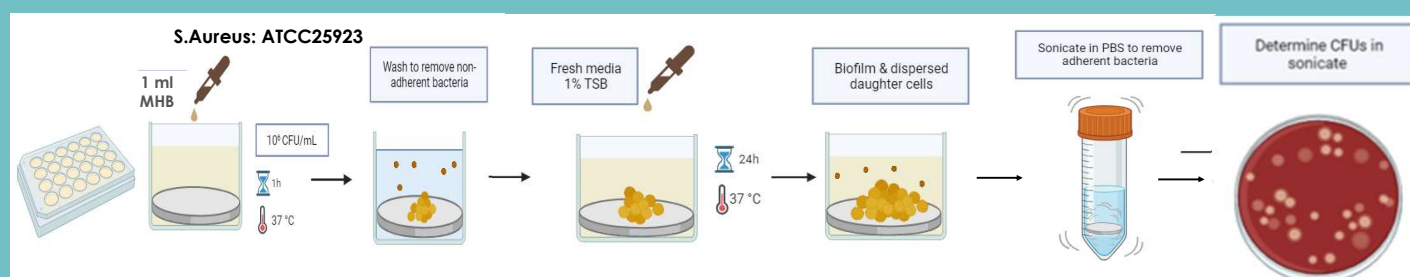
Changes in the structure to meet the user needs

- QAC alkyl group penetrates bacterial cell wall and was varied (C12 and C16)
- Variation in diisocyanate used: aliphatic, aromatic
- Adhesion and stability of coating on different substrates with different primers

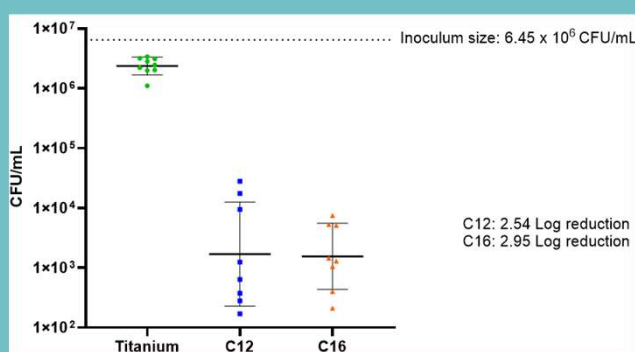
Bromophenol Blue (BPB) staining: Qualitative test for coating uniformity



Results

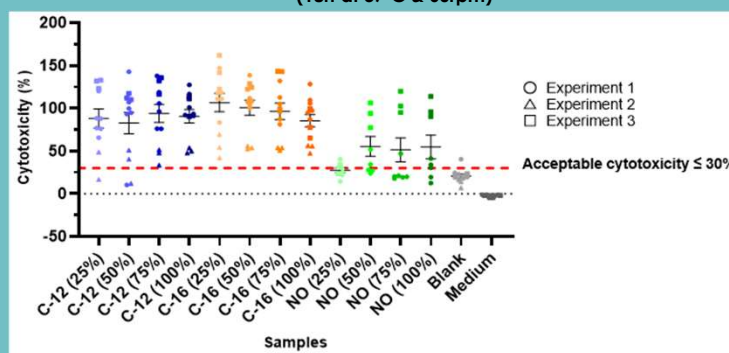


Static biofilm assay



Cytotoxicity assay

- WST/LDH-assay based on ISO 10993-5
- Macrophage seeded 1.5 x 10⁴ / well
- Extracts of coatings prepared in cell medium (18h at 37°C & 60rpm)



Conclusions:

- QAC-urethane oligomer coatings were successfully synthesized and demonstrated very good antimicrobial properties up to almost 3-log reduction in CFU.
- Cytotoxicity testing revealed toxicity above the accepted threshold of 30%, most likely due to low MW extractable compounds. The polyether urethane backbone effectively drives physical adhesion to titanium (tested with BPB staining) while maintaining a high quaternary ammonium density for robust antibacterial performance against *S. Aureus*. Future refinement will focus on synthesis and work up optimization to reduce low MW extractables and mitigate cytotoxicity.

References

- 1) Xu L.-C., et al. (2016), Woodhead Publishing, 247-284; 2) Yao, C., et al. (2008), Journal of Membrane Science, 320 (1-2), 259-267. 3) Bakshi, H., et al. (2013), Mater Sci Eng C Mater Biol Appl, 33 (1), 153-64.; 4) Bakshi, H., et al. (2013), J Biomed Mater Res A, 101 (6), 1599-611.

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