



## Preparation and Investigation of Antibacterial Protein-based Surfaces

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### ABSTRACT

*Surfaces bearing protein units (wool, silk) have been modified in a two step process to incorporate at the free side-chain hydroxyl groups functionalities (lipophilic with polycationic units) that bear antibacterial activity. The approach has involved tosylation of the hydroxyl groups followed by displacement with a tertiary amine bearing cationic and lipophilic components. The effectiveness of these modified surfaces for antibacterial action against a series of Gram + and Gram - bacteria is reported. Structural factors maximizing the activity against all species tested have been studied and appropriate surfaces have been generated. Preparative procedures along with methods of investigation of the antimicrobial activity are included along with a discussion of mode of activity.*

*Keywords: antibacterial, surfaces, antimicrobial*

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### INTRODUCTION

It has for some time been recognized that cationic surfactants bear antibacterial activity.<sup>1-5</sup> Investigations of structure-activity relationships have demonstrated that in addition to a cationic site, a significant lipophilic component of the surfactant is involved in optimization of activity. With simple alkylbenzyltrimethylammonium chlorides in their action against *Pseudomonas aeruginosa*, the optimal length of the alkyl chain has been noted to be twelve carbon atoms.<sup>3</sup> Optimal activity toward a variety of bacterial species for numerous structural variations of the water soluble cationic surfactants appears to occur when an alkyl chain of between ten and fourteen carbon atoms is present.<sup>6-10</sup>

The mechanism of action of such cationic surfactants on bacteria is understood to be one of electrostatic interaction and physical disruption, as opposed to interference with a metabolic pathway, as is commonly the situation with antibiotic species.<sup>11</sup> After the cationic site of the agent attached to a significant lipophilic component binds to anionic sites of the cell wall surface it is then able to diffuse through the cell

wall and bind to the membrane. Acting as a surfactant, it is able to disrupt the membrane and permit the release of electrolytes and nucleic materials, leading to cell death.

While the construction of antibacterial agents that express their activity in such a manner has been well investigated, the remaining challenge has been to impart such activity to a surface from which the active agent is not released and will be able to maintain activity indefinitely. The binding of quaternary ammonium sites to glass surfaces through the use of silyl-ether linkages was found to impart antibacterial activity to such surfaces.<sup>12</sup> Several polymeric surfaces have also been investigated, including polystyrene<sup>13,14</sup> and poly(propylene imine).<sup>15</sup>

In this light, it appeared a reasonable possibility that other types of surfaces could be rendered antibacterial by the covalent attachment of polycationic units having lipophilic adjuncts. Prior efforts of our laboratory had demonstrated the facility with which such polyammonium units having lipophilic adjuncts could be prepared,<sup>16,17</sup> as well as the manner in which