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Salicylic acid-releasing polyurethane acrylate polymers as anti-biofilm urological catheter coatings

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ABSTRACT

Biofilm-associated infections are a major complication of implanted and indwelling medical devices like urological and venous catheters. They commonly persist even in the presence of an oral or intravenous antibiotic regimen, often resulting in chronic illness. We have developed a new approach to inhibiting biofilm growth on synthetic materials through controlled release of salicylic acid from a polymeric coating. Herein we report the synthesis and testing of a ultraviolet-cured polyurethane acrylate polymer composed, in part, of salicyl acrylate, which hydrolyzes upon exposure to aqueous conditions, releasing salicylic acid while leaving the polymer backbone intact. The salicylic acid release rate was tuned by adjusting the polymer composition. Anti-biofilm performance of the coatings was assessed under several biofilm forming conditions using a novel combination of the MBEC Assay™ biofilm multi-peg growth system and bioluminescence monitoring for live cell quantification. Films of the salicylic acid-releasing polymers were found to inhibit biofilm formation, as shown by bioluminescent and GFP reporter strains of *Pseudomonas aeruginosa* and *Escherichia coli*. Urinary catheters coated on their inner lumens with the salicylic acid-releasing polymer significantly reduced biofilm formation by *E. coli* for up to 5 days under conditions that simulated physiological urine flow.

1. Introduction

Catheter-associated urinary tract infection (CAUTI) is a particularly intransigent problem and is the most common source of hospital-acquired infections [1], with roughly 450,000 cases occurring per year in the USA alone [2]. When Foley urinary drainage catheters are used for a few days or less, infections are rare, but many patients are catheterized for weeks or months – in some cases indefinitely. Bacterial colonization of an indwelling urological catheter is universal after 2 weeks [3] and symptomatic infection becomes increasingly likely with time [4]. Despite considerable effort to address infection rates, the past 30 years have yielded little benefit from either modified clinical practice or new products [4,5]. Several "antimicrobial" Foley catheters are available commercially, including a successful silver-releasing product, but careful reviews are equivocal about the magnitude of benefit [6], and the CDC recently stopped short of recommending their general use [1]. Since October 2008, the US Centers for Medicare and Medicaid Services has denied reimbursement for treatment of hospital-acquired catheter associated urinary tract and vascular infections, which it considers preventable [7]. Better anti-infective Foley catheters are direly needed. Direct treatment costs of CAUTIs in US hospitals are over $350 million [2]; when extended care facilities and international cases are included, the direct costs amount to over a billion dollars, to say nothing of the immense patient suffering associated with these infections.

The main reason device-associated infections are so recalcitrant is the formation of bacterial biofilms on the surfaces of the devices [8,9]. The organisms that commonly cause CAUTIs are diverse – *Escherichia coli*, *Candida* spp., *Enterococcus* spp., *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Enterobacter* spp. – and include both Gram-positive and Gram-negative bacteria, as well as yeast [1,4]; each is capable of adhering to surfaces and forming biofilms. Planktonic, or free-floating, cells migrate both up the inner lumen

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