Studies of polymeric quaternary ammonium salts with biomimetic catechol terminal end: synthesis and its application for surface modification of various biomaterials

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Statement of Purpose:

Healthcare-associated infections (HAIs) are infections acquired by patients while receiving health care in hospitals, such as central line-associated bloodstream infections, ventilator-associated pneumonia, surgical site infections, and catheter-associated urinary tract infections. Most infections are caused by bacteria attached to the surface of medical equipment such as catheters and surgical instruments and then entering the human body. To reduce this occurrence, researchers have attempted to deposit an antibacterial coating on the surface of medical equipment to prevent the spread of bacteria.

Inspired by the mussel's attachment onto various substrates, such as rock on the seashore, and metal and plastic parts of the boat, the development of surface binding chemistry that mimics the dopamine/catechol chemical configuration noted in mussel adhesive protein has been attempted.

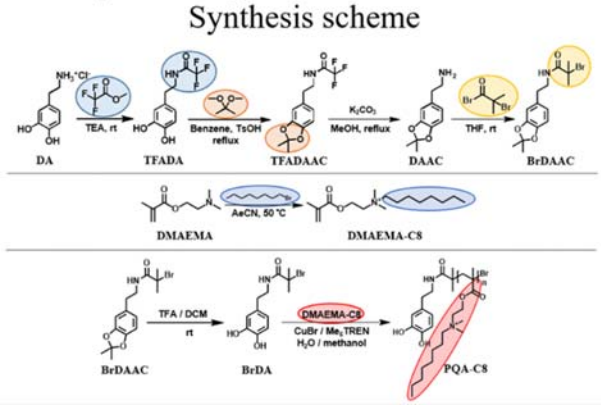
Previous studies have noted that the surface with cationic functionality, such as the one with the quaternary ammonium group, can reduce the number of bacteria attached through the contact-killing mechanism, in which the microbial membrane was disrupted by the surface cationic functionalities.

Given the ease of surface attachment capability by the mussel-inspired biomimetic chemistry, a novel polymeric compound carrying the cationic quaternary ammonium functionality and mussel's mimic catechol group; PQA-C8, was synthesized in this investigation. Its application on surface modification of various biomedical grade titanium and medical polypropylene and polydimethylsiloxane was explored.

Methods:

Synthesis of PQA-C8

The synthesis scheme for PQA-C8 is shown below. The purity of each intermediate and final compound was verified by the NMR spectra.



Substrate preparation and surface modification

The titanium, PP, and PDMS were used as substrates for surface modification. All substrates were cleaned by various solvent ultrasonication methods. Following the surface cleaning, different substrates were modified by the (1) one-step surface modification scheme using solutions with various ratios of PQA-C8 and dopamine, with or without the oxidants ($CuSO_4/H_2O_2$) added, (2) two-step modification scheme, in which the substrate was modified by the dopamine solution first, followed by the PQA-C8 solution.

Surface property characterization, antibacterial activity evaluation, and cytotoxicity assessment

The surface properties of different substrates were assessed using the static contact angle method and ESCA. The antibacterial activity was assessed against *S. aureus* and *E. coli*. The cytotoxicity was determined using the eluent from the different substrates following the modified ISO 10993-5 protocol.

Results:

The NMR spectrum of the final product, PQA-C8, has revealed that the synthesis was successful with high purity.

Contact angle analyses revealed the surface hydrophilicity varied with the treatment scheme employed as well as the substrate used. ESCA analyses have shown success in the surface modification of titanium substrates. For the two medical plastics, PP and PDMS, studied, the PP was easier to be modified by the one-step scheme than PDMS. Nevertheless, these two plastics were surface modified by the two-step scheme.

Antibacterial activity assessment against the *S. aureus* and *E. coli* indicated that the titanium modified using the solution with ($CuSO_4/H_2O_2$) oxidant added had greater than 98% antibacterial activity. For the titanium substrate modified without the oxidant added, the antibacterial activity against *S. aureus* ranged from 46% to 98% depending upon the ratio of PQA-C8 to dopamine, in which the highest antibacterial activity (98%) was noted upon the one modified with PQA-C8 only. For this substrate, the *E. coli* antibacterial activity was only 72.3%. This might be related to the exterior LPS-based membrane noted in Gram-negative *E. coli*.

The antibacterial activity of the modified PP and PDMS varied significantly depending on the substrate used. The one-step modified PDMS didn't exhibit any antibacterial activity against *S. aureus* (<10%). For the PP modified by the one-step scheme with the ($CuSO_4/H_2O_2$) oxidant solution added, the antibacterial activity was much better, 80-98%, dependent upon the amount of dopamine added. Nevertheless, for those modified PP with 95% antibacterial activity against *S. aureus*, the antibacterial activity against E. coli was only <30%. In contrast, the two-step modified PP and PDMS substrates showed 99.9% and 91.2% antibacterial activity against *S. aureus*, respectively. For the two-step modified PP and PDMS, the antibacterial activity against *E. coli* was 96.17% and <30%, respectively.

The cytotoxicity assay demonstrated all modified titanium, PP and PDMS showed good antibacterial activity against *S. aureus* and/or *E. coli* were nontoxic using the L929 as the testing cell line.