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Antimicrobial films obtained from latex particles functionalized with quaternized block copolymers

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ABSTRACT

New amphiphilic block copolymers with antimicrobial properties were obtained by atom transfer radical polymerization (ATRP) and copper catalyzed cycloaddition following two approaches, a simultaneous strategy or a two-step synthesis, which were proven to be very effective methods. These copolymers were subsequently quaternized using two alkyl chains, methyl and butyl, to amplify their antimicrobial properties and to investigate the effect of alkyl length. Antimicrobial experiments in solution were performed with three types of bacteria, two gram-positive and one gram-negative, and a fungus. Those copolymers quaternized with methyl iodide showed better selectivities on gram-positive bacteria, *Staphylococcus aureus* and *Staphylococcus epidermidis*, against red blood cells, demonstrating the importance of the quaternizing agent chosen. Once the solution studies were performed, we prepared poly(butyl methacrylate) latex particles functionalized with the antimicrobial copolymers by emulsion polymerization of butyl methacrylate using such copolymers as surfactants. The characterization by various techniques served to test their effectiveness as surfactants. Finally, films were prepared from these emulsions, and their antimicrobial activity was studied against the gram-positive bacteria. The results indicate that the antimicrobial efficiency of the films depends not only on the copolymer activity but also on other factors such as the surface segregation of the antimicrobial agent to the interface.

1. Introduction

Antimicrobial polymeric coatings are emerging as very versatile alternative to meet the need in many materials, in particular in medical surfaces preventing biofilm formation and reducing microbial infections. Especially nowadays, multi-resistant bacteria such as *Staphylococcus aureus* (typically acquired in hospitals) [1], suppose an important risk that limits the ability to treat common infections and minor injuries. Infections by resistant bacteria in hospitals are increasing; particularly patients with implants and catheters have a high risk of infection, and long-term treatments suppose an elevated associated cost per patient. Therefore, the development of antibiotic resistant bacteria has become a threatening issue worldwide that requires urgent actions. In this sense, the incorporation of antimicrobial properties to the surface of medical devices or even of common products could help to solve this demand, at least partially, because they can reduce biofilm formation and contagion. There are numerous antimicrobial polymeric surface coatings described in literature, mainly based on bacterial adhesion resistant or surfaces with bactericidal action. Most antifouling biomaterials consist on slippery [2,3] and hydrophilic surfaces [4,5]. However, once the microorganisms are irreversibly attached to the surface, the surface is not able to kill them. On the other hand, the bactericidal approaches allow them to kill the bacteria in a very efficient manner. Many of these strategies are focused in the incorporation of biocidal agents into the polymeric matrix to allow their slow release into the near surrounding. Nevertheless, these kinds of strategies have normally short-term

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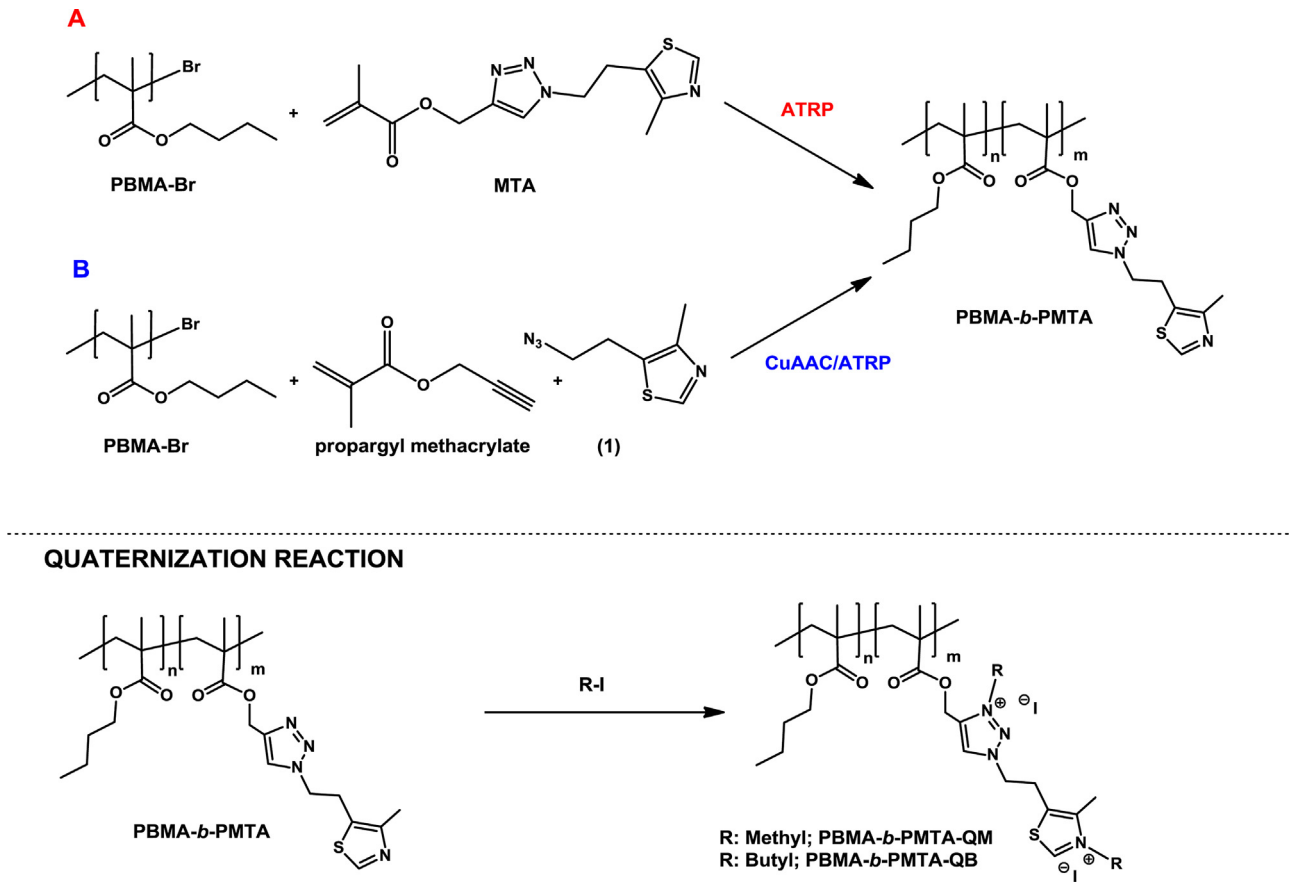

Scheme 1. Synthetic pathways for the preparation of quaternized PBMA-*b*-PMTA block copolymers following two strategies: (A) ATRP polymerization of MTA from the PBMA macroinitiator and (B) one-pot reactions by simultaneous CuAAC click reaction and ATRP.

effect and present toxicity due to the leaching of the agent, thus do not solve the problem of generating resistant [6,7]. Alternatively, antimicrobial activity can be obtained by covalent attachment of the antimicrobial agent onto the surface of the polymeric coating [8–12], but multiple chemical steps are generally needed, which might limit the scale-up processing. The physical incorporation of antimicrobial polymers into the coating may settle the inconveniences of these two above described approaches. On one hand, this strategy does not require chemical reactions and modification steps, and on the other hand, the leaching of the antimicrobial polymer is limited because of their low diffusion coefficient due to their high molecular weight. Even if the diffusion of the antimicrobial polymers occurs, the mechanisms of action against the microorganism are in general different in comparison with low molecular weight antibiotics, and the development of resistance is significantly limited. In particular, in cationic polymers most of the proposed mechanisms are based on their electrostatic interactions with the negatively charged phospholipids within the bacterial membrane, which disrupt the cell membrane, provoke leakage of intracellular components and finally bacterial death [13,14].

In the current work, we describe a one-step strategy to prepare antimicrobial polymeric surfaces with block copolymers based on quaternized 1,3-thiazole and 1,2,3-triazole side chain groups as antimicrobial additive. This approach consists in the preparation of latex particles by emulsion polymerization in the presence of the antimicrobial block copolymers, which act as surfactants. By this way, the emulsion polymerization is carried out without the addition of low molecular weight emulsifiers, normally toxic, while at the same time, these antimicrobial polymeric surfactants are presented at the latex nanoparticle surfaces, thereby conferring their activity to the final films formed from the latexes. As commented this emulsion polymerization approach has been previously used to obtain contact active antimicrobial coatings using antimicrobial polymer surfactants [15,16] but also inorganic nanoparticles such as TiO_2 for Pickering stabilization [17]. In the last example, however, UV-light irradiation is necessary to induce bacterial inactivation. In those examples with polymeric surfactants, alkylated polymer derivatives from commercial monomers such as vinyl pyridine and 2-(dimethylaminoethyl) methacrylate were employed simultaneously as stabilizers and antimicrobial agents. Herein, novel block copolymers containing two pendant azole groups per monomer unit, both suitable for alkylation, were employed to provide polycationic antimicrobial agent that are expected to be very active. This monomer, (1-(2-(4-methylthiazol-5-yl) ethyl)-1*H*-1,2,3-triazol-4-yl) methyl methacrylate (MTA) was previously developed by our group and homopolymerized and copolymerized by conventional radical polymerization [18–20]. The resulting polymers showed very outstanding antimicrobial properties and low toxicity in solution. Besides, it has been demonstrated that the incorporation of both of the pendant azole groups in the monomeric unit enhances the antimicrobial activity in comparison with similar polymers containing only thiazole groups in their structures [18]. In this work, this monomer, MTA, will be polymerized in a controlled manner for the first time and we go one step further investigating their antimicrobial activity as a component of a polymeric surface. As explained above, this used strategy requires antimicrobial polymers with good stabilizing properties. Thereby, well-defined block copolymers were synthesized with poly(butyl methacrylate) as hydrophobic segment and PMTA as cationic block, varying the length of the PMTA segment and using a combination of