Self-Assembled Brush Polymers Bearing Glycine Derivatives and Their Biocompatibility

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Introduction

Most conventional biomedical materials have drawbacks that vary according to their purpose and mode of action. One of the key requirements of biomaterials irrespective of their application is biocompatibility. The successful development of biomaterials having good biocompatibility could be achieved through the proper and in depth understanding of the interactions associated with biocompatibility phenomena. In this study, we synthesized brush polymers with various glycine derivatives conjugated to the parent ethylene oxide backbones via alkyl chain spacers, and evaluated their physicochemical and biological characteristics with respect to their use as biomaterials. The glycine was chosen as an amino acid because of its structural simplicity and, more importantly, isoelectric point of pH 6.06, hence remaining almost neutral at physiological pH. Furthermore, the incorporation of glycine derivatives into a polymer can facilitate self-assembled monolayer (SAM) formation, as they can impart least steric hindrance during the SAM formation process by their hydrogen bonding ability. The glycine derivatives used in this study were methylglycine, dimethylglycine, and acetylglycine.

Results and Discussion

In this study, we designed polymers containing the glycine derivatives methylglycine, dimethylglycine, and acetylglycine, which form films with significant biocompatibility. These functional groups were incorporated onto the ends of the long alkyl bristles of a PECH-based brush polymer to form the polymers: PMUTE, PDUTE, and PAUTE (Figure 1). The thin films of each of these brush polymers were investigated to determine their morphological structure, hydrophilicity, hydrophobicity, water sorption, blood compatibility, bacterial adherence, cell adhesion, and biocompatibility in mice. The thin films of all three brush polymers were found to contain a multibilayer structure supported by the laterally ordered bristles as well as hydrogen bonding of the glycine derivatives at the bristle ends, which can provide surfaces enriched with functional groups. Due to the enrichment of the film surfaces with functional groups, these films all exhibit hydrophilic characteristics. However, their multibilayer structures do vary, depending on the glycine derivatives at the bristle end; a multibilayer structure with no bristle interdigitation is formed in the PMUTE polymer film, whereas a multibilayer structure with partially interdigitated bristles is formed in both the PDUTE and PAUTE polymer films. These structural differences result in different water sorption behaviors of the films of the brush polymers. The multibilayer structure without bristle interdigitation permits more water sorption than those with partial bristle interdigitation. The films of the brush polymers with such multibilayer structures exhibit excellent resistance to fibrinogen adsorption (Figure 2), platelet adhesion, and bacterial adherence (Figure 3). Moreover, these polymer films promote the adhesion, growth and proliferation of HEp-2 cells on the surfaces. The brush polymer films also exhibit excellent biocompatibility in mice. These results confirm that these brush polymer films are very suitable for use in biomedical applications, including in medical devices and biosensors that require biocompatibility and offer the possibility of reduced post-operative infection.

Acknowledgments

This study was supported by the National Research Foundation (NRF) of Korea (Basic Research Grant No. 2010-0023396) and the Ministry of Education, Science and Technology (MEST) (Korea Brain 21 Program and World Class University Program (R31-2008-000-10059-0)).

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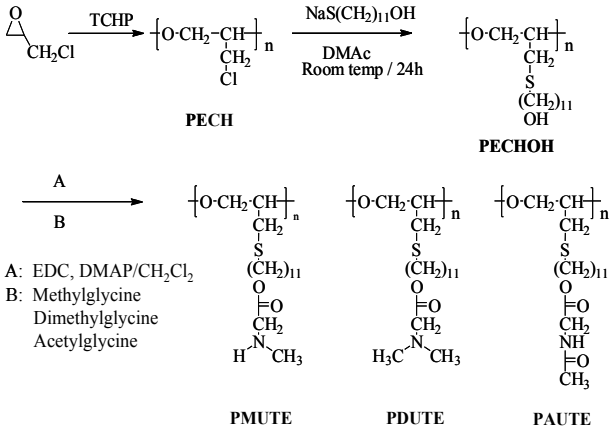

Figure 1. Synthetic scheme of brush polymers with glycine derivatives: (a) poly[oxy(methylamino-n-undecylesterthiomethyl)ethylene] (PMUTE), (b) poly[oxy(dimethylamino-n-undecylesterthiomethyl)-ethylene] (PDUTE), and (c) poly[oxy(acetylamino-n-undecylesterthiomethyl)ethylene] (PAUTE).

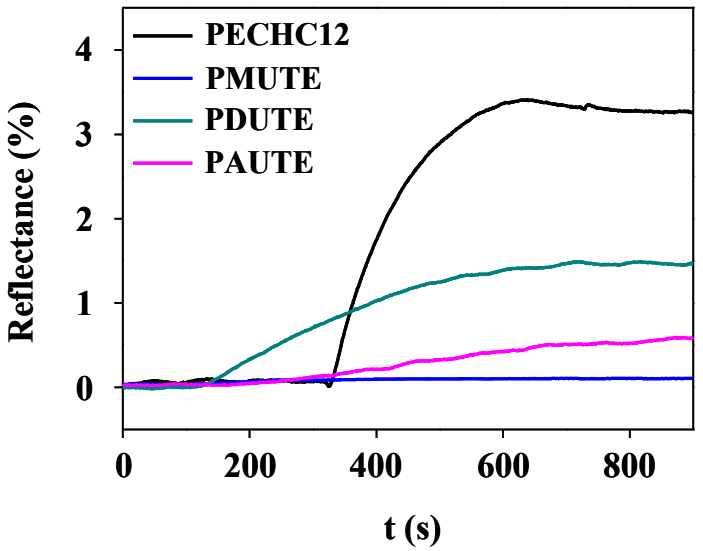

Figure 2. Reflectance variations of the brush polymer films measured during the adsorption of fibrinogen in PBS (1 mg/mL) at 25 °C by SPR spectroscopy at a fixed angle at which the film reveals the minimum light reflectance. The flow rate of the fibrinogen solution was 7.5 μL/min.

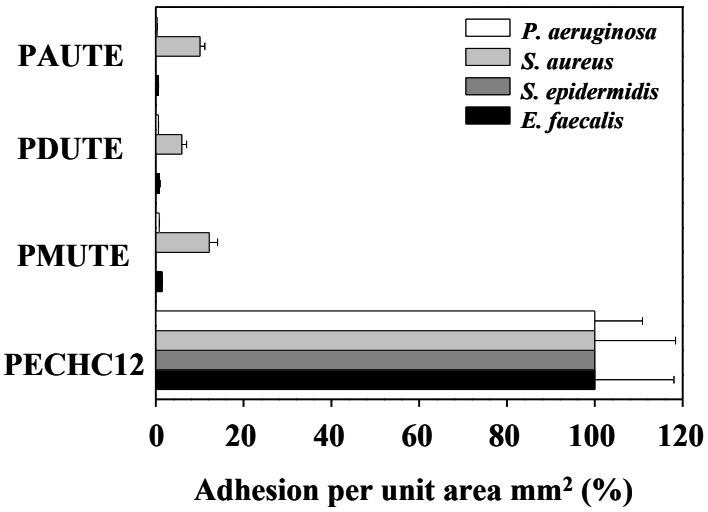

Figure 3. Bacterial adherence to the brush polymer films.