Protein-Resistant Polyurethane by Sequentially-Grafted Poly(HEMA) and Poly(Oligo(Ethylene Glycol) Methacrylate (OEGMA)) via Surface-Initiated ATRP

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Introduction

Nonspecific protein adsorption is believed to be the initiating event in tissue-material interactions and is strongly detrimental to biocompatibility.[1] Surfaces modified by grafting with hydrophilic polymers such as polyethylene oxide have been shown to be protein resistant to varying degrees.[2] It has been found that increased surface density of the grafted polymers resulted in increased protein resistance.[2,3] However, it has also been found[4] that there is an optimum chain density above which resistance decreases. In this study, we examine the hypothesis that the key parameter is not chain density itself but rather the surface density of monomer units, specifically ethylene oxide (EO) units. To achieve high EO density we used a sequential grafting approach whereby the surface was grafted first with poly(2-hydroxyethyl methacrylate) (HEMA) by surface-initiated atom transfer radical polymerization (si-ATRP). Grafts of oligo(ethylene glycol) methyl ether methacrylate (OEGMA) were then grown from the hydroxyl groups on the HEMA chains by a second ATRP. The protein resistant properties of the surfaces were evaluated by adsorption experiments with fibrinogen (Fg) and lactalbumin (Lac).

Materials and Methods

The surfaces were prepared in five steps. (1) Polyurethane (PU) film was treated in an oxygen plasma to introduce reactive sites (-O• and -OO•). (2) The PU film was immersed in 2-bromoisobutyryl bromide (BIBB)/toluene solution to form a layer of ATRP initiator. (3) si-ATRP of HEMA was carried out with Cu(I)Br/2bpy complex as catalyst. Ethyl 2-bromoisobutyrate (EBIB) was added to the solution to form free polymer (molar ratio of HEMA:EBIB = 50:1). (4) The poly(HEMA)-grafted PU (referred to as PU/PH50) surface was treated with BIBB/toluene solution again to form initiator sites on the HEMA chains. (5) OEGMA was grafted from the PU/PH/initiator by ATRP. The OEGMA chain length was varied by varying the molar ratio of OEGMA:EBIB (5:1, 50:1, 100:1). The final surfaces are referred to as PU/PH/PO5, PU/PH/PO50, PU/PH/PO100. The adsorption of fibrinogen (MW 340 kDa) and lactalbumin (MW 14.1 kDa) was investigated in single protein and binary protein experiments using radio-iodinated proteins.[2]

Results and Discussion

The grafted surfaces were characterized by water contact angle and X-ray photoelectron spectroscopy (XPS). The data were consistent with successful grafting of poly(HEMA) and poly(OEGMA). XPS data showed that the oxygen content was higher for PU surfaces with "double-grafted" HEMA-OEGMA than for those with single-grafted OEGMA, and increased with the OEGMA chain length for both kinds of surface.

Fg adsorption data for the single-grafted and double-grafted surfaces are shown in Fig. 1. For each type of surface, Fg adsorption decreased with increasing OEGMA chain length. Adsorption was inhibited more on double-grafted (high EO density) than on single-grafted surfaces.

The effect of protein size was also investigated. For each of the proteins, adsorption was very low. For example, at a protein concentration of 0.05 mg/ml, adsorbed amounts of both Fg and Lac ≤ 5 ng/cm^2 were observed on the PU/PH/PO100 surface. Fig. 1(b) shows data for binary solutions of Fg and Lac presented as molar ratio on the surface. It is seen that for all of the surfaces the ratio on the surface is greater than in the solution indicating a preference for the smaller protein. However, the grafted (protein resistant) surfaces show ratios much closer to the solution ratio than do the controls. The ratio on the grafted surfaces may reflect the relative ability of the proteins of different size to penetrate the grafted polymer layers.

Conclusions

Highly protein-resistant PU surfaces were prepared by sequential ATRP grafting of poly(HEMA) and poly(OEGMA) with variable OEGMA chain lengths. The highest resistance was observed on PU/PH/PO100 surface with a reduction of ≥ 99% for both fibrinogen and lactalbumin.

References

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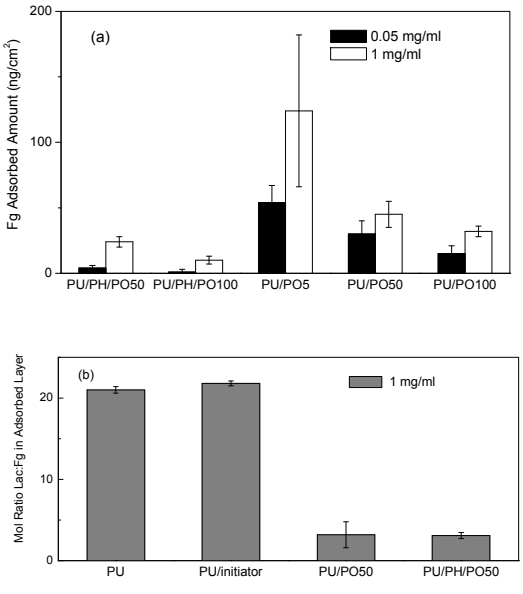

Fig. 1. (a) Fibrinogen adsorption. (b) Adsorption from binary solutions of Lac and Fg, molar ratio Lac:Fg 1:1 in solution. TBS, pH 7.4, 2 h.