Biofunctional Coatings By Surface-Initiated ATRP

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BIOFUNCTIONAL COATINGS BY SURFACE-INITIATED ATRP

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Introduction

The storage and administration of protein drugs are imperative in modern society. Glass is conventionally used for storage of drugs; however, glass is fragile and does not provide the desirable design freedom for products in mass production. The use of polymers will especially be suitable for devices with demands for greater dose accuracy and minimum waste of precious drugs. In addition to the normal attractive polymer properties a number of other polymer material challenges like compatibility between the polymer and the protein, low level of non-toxic leachables, and inhibition of protein adsorption exist. An initial obstacle is the fact that most commercially available thermoplastic polymers are hydrophobic that is known to be a disadvantage with respect to protein adsorption. The initial task then becomes firmly anchoring of a hydrophilic, protein compatible polymer layer onto the base thermoplastic polymer surface achieved in a *grafting* from strategy by Surface-Initiated Atom Transfer Radical Polymerization (SI-ATRP).[1,2]

Result and Discussion

Initially SI-ATRP has been exploited to hydrophilize PEEK.[3] The ketone groups on the PEEK surface were reduced to hydroxyl groups which were converted to bromoisobutyrate initiating sites for SI-ATRP as illustrated in Figure 1.

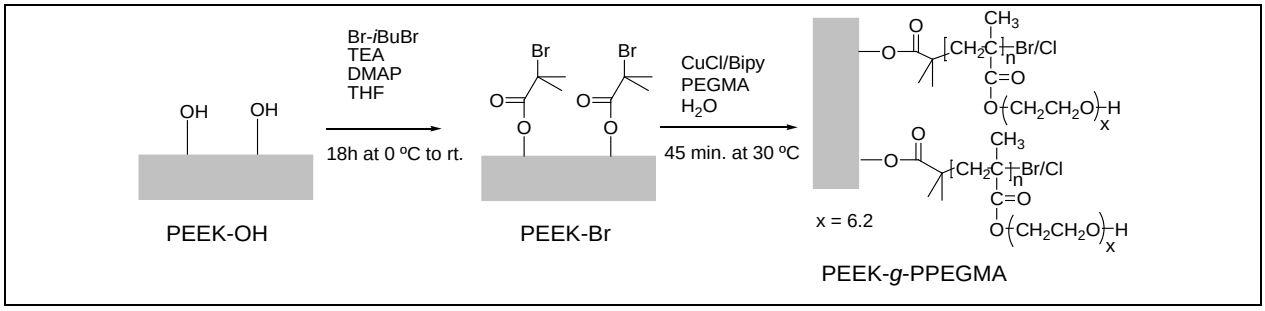

Figure 1. (1) Anchoring the initiating groups on the hydroxyl-functionalized PEEK surface. (2) Grafting PPEGMA brushes from the PEEK films employing SI-ATRP.

The modification steps were followed by contact angle measurements and XPS. Moreover, ATR FTIR has successfully been used to confirm the formation of initiating groups on PEEK as opposed to unsuccessful attempts with many other substrates. Grafting of poly(ethylene glycol) methacrylate (PEGMA) from PEEK was performed in aqueous solution. The presence of the PPEGMA grafts on PEEK was revealed by the thermograms from TGA whereas investigations with AFM rejected changes in the surface topography. Two possible applications arose from the hydrophilization of PEEK, metal deposition and protein repellency. The performed modification allowed for successful electroless deposition and good adhesion of nickel as well as copper.

In the continuous efforts it is noted that polypropylene (PP) is a substrate of interest for pharmaceutical packaging and delivery systems due to its resistance to most chemicals, high fatigue strength and good processability. The inherent hydrophobic surface, however, needs a hydrophilic coating in order to

improve the protein drug compatibility. Grafting of PEGMA and *N*,*N*-dimethylacrylamide (DMAAm) from UV-initiator modified polypropylene (PP) was performed by SI-ATRP as illustrated in Figure 2.

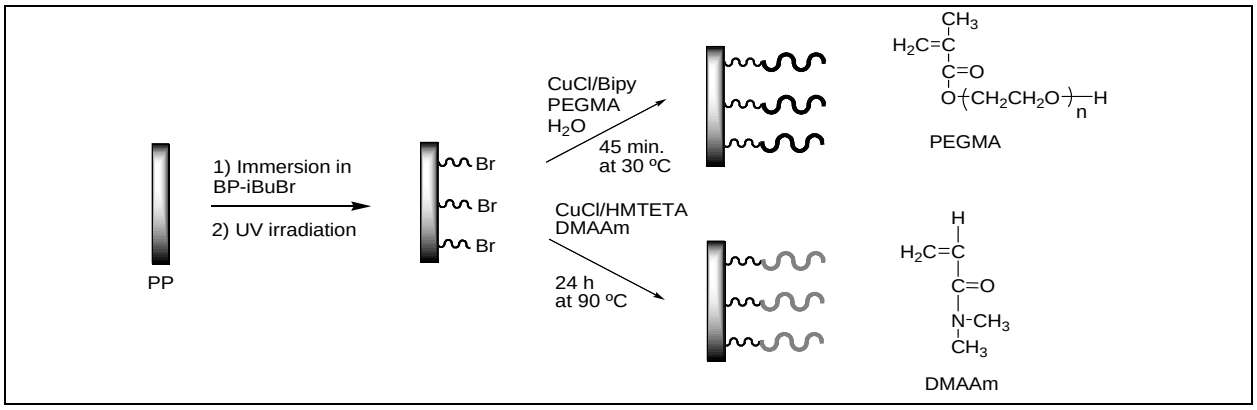

Figure 2. The SI-ATRP strategy when grafting poly(PEGMA) and poly(DMMAm) from a PP surface.

The modification and hydrophilization of the PP substrates were confirmed with ATR FTIR and Water contact angle (WCA) measurements. Confocal fluorescence microscopy of modified and unmodified substrates immersed in labeled insulin aspart (Asp^{B28}) showed superior repulsion of this protein for the poly(PEGMA) grafts due to the achieved architecture. The influence of surface modification on the chemical and physical stability of Asp^{B28} insulin was evaluated by two chromatographic methods (SEC and RP-HPLC) and the Thioflavin T test. PP coated with poly(DMAAm) resulted in a poor chemical stability and a significantly improved physical stability compared with unmodified PP. Increased physical stability was determined as a lower tendency to form fibrils. In addition to this, observations like higher content of Asp^{B28} insulin related impurities, lower phenol concentration, and presence of copper were made for the poly(DMAAm) coating. The results from the poly(PEGMA) coating looked auspicious with respect to the stability of Asp^{B28} insulin in comparison with the data from unmodified PP.

Conclusions

Hydrophobic, thermoplastic polymers like PEEK and PP have been successfully provided with hydrophilic coatings through SI-ATRP. Among the attractive new material properties the poly(PEGMA) coated PP has gained is promising insulin aspart compatibility potentially paving the way for replacement of glass for storage of drug product formulations.

Acknowledgements

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