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Preparation and characterization of nonfouling polymer brushes on poly(ethylene terephthalate) film surfaces

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ABSTRACT

In this study, a surface grafting of nonfouling poly(ethylene glycol) methyl ether acrylate (PEGMA) on poly(ethylene terephthalate) (PET) was carried out via surface-initiated atom-transfer radical polymerization (SI-ATRP) to improve hemocompatibility of polymer based biomaterials. To do this, the coupling agent with hydroxyl groups for the ATRP initiator was first anchored on the surface of PET films using photochemical method, and then these hydroxyl groups were esterified by bromoisobutyryl bromide, from which PET with various main chain lengths of PEGMA was prepared. The structures and properties of modified PET surfaces were investigated using water contact angle (WAC), ATR-FTIR, X-ray photoelectron spectroscopy (XPS) and Atomic force microscopy (AFM). The molecular weights of the free polymer from solution were determined by gel permeation chromatography (GPC). These results indicated that grafting of PEGMA on PET film is a simple way to change its surface properties. The protein adsorption resistance on the surfaces of PET was primarily evaluated by an enzyme-linked immunosorbent assay (ELISA). The result demonstrated that the protein adsorption could be well suppressed by poly(PEGMA) brush structure on the surface of PET. This work provides a new approach for polymers to enhance their biocompatibility.

1. Introduction

It is well-known that numbers of synthetic polymers have been widely used for blood-contacting devices, exemplifying hemodialysis membranes, artificial blood vessels, heart valves, stents and biosensors. Especially, microporous polyurethanes, expanded poly(tetrafluoroethylene) (ePTFE) and Dacron [poly(ethylene terephthalate)], have been successfully used to fabricate large-diameter (>6 mm) vascular substitutes in wide clinical applications [1,2]. However, these materials for small-diameter (≤6 mm) applications such as coronary artery bypass grafting have been extensively unsuccessful mainly due to early graft occlusion [3,4]. Clearly, the surface structure and properties play a major role in the in vivo biological performance of materials and devices [5], because many biological reactions are triggered by chemical structure, topography, and molecular flexibility of the materials near the surface, such as protein adsorption, blood coagulation, complement activation, inflammation, and biodegradation [6–8]. To enhance hemocompatibility of biomaterials, surface modification without affecting their bulk properties is a promising approach for traditional biomaterials [9,10]. Thus, numerous strategies have been developed for surface modification of poly(ethylene terephthalate) (PET), which is one of the most widely used materials in synthetic vascular grafts. Generally, the coupling agents for PET surface modification were introduced to produce hydroxyl, carboxyl or amino group using oxidative hydrolysis [11,12], reduction [13], aminolysis [14,15], photochemical modification [16,17] and plasma deposition [18]. Then, PEG and its derivatives [19,20], bioactive molecules [15,21], P(NIPAM-co-AAc-co-PEGDA) microgel particles [22] and poly(2-methacryloyloxyethyl phosphorylcholine) (polyMPC) [23] were covalently coupled onto the surfaces of the above-mentioned PETs. Biocompatibilities of these modified PETs surfaces, which were mainly related to grafted polymer chain length and density, were investigated [20].

Recently, several types of polymer brushes, such as, poly(ethylene glycol) methacrylate (PEGMA) [24–26], poly(oligo(ethylene glycol)acrylamide) [27] polyMPC [28–30], poly(sulfobetaine methacrylate) (polySBMA) and poly(carboxybetaine methacrylate) (poly-CBMA) [31,32] have been shown to have enhanced biocompatibility based on silicon, glass and gold substrates. These polymer brushes were immobilized onto various materials surfaces using surface-initiated atom-transfer radical polymerization (SI-ATRP), which has played a significant role in the modification of surface properties [33–35]. Among the above-mentioned polymer brushes, PPEGMAs have been the most commonly employed antifouling materials to suppress protein adsorption and platelet adhesion, because of outstanding properties of PEG and its derivatives, such as non-toxicity, non-

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immunogenesis, non-antigenicity, excellent biocompatibility, and solubility [36]. Particularly, much attention has been paid to the grafting of polymer brushes by SI-ATRP on polymer surfaces in the last two years [37–40]. However it is difficult to introduce ATRP surface initiator on most polymer substrates owing to the inert surfaces. Some research groups employed benzophenone as the photoactive crosslinker for surface modification of biomaterials [41,42]. The benzophenone crosslinker is advantageous over aryl azides in biomedical field due to its inability to react with water, and a key competitor of the photoaffinity labeling reaction and preferentially reacting with fairly unreactive C–H bonds [43,44]. Another example using benzophenonyl 2-bromoisobutyrate as surface initiator in antibacterial polypropylene preparation was reported by Huang et al. [45].

To further improve hemocompatibility of PET film, in this work, poly(ethylene glycol) methyl ether acrylate (PEGMA) brushes were grafted on the surfaces of poly(ethylene terephthalate) (PET) via SI-ATRP. The structures and properties of modified PET surface were investigated. The relationship between chain length (monomer units) of PEGMA brushes grafted on PET surfaces and protein adsorption resistance on the surfaces was primarily evaluated as well. To obtain a facile method for anchoring surface initiator of ATRP on biomaterial surfaces, we prepared hydroxyl-group-bearing polymer surfaces using photochemical method. The hydroxyl groups were esterified by bromoisobutyryl bromide to obtain ATRP surface initiator, which can be applied on surfaces of all hydrocarbon polymers.

2. Materials and methods

2.1. Materials

PET films (about 0.15 mm thickness) were cut into small pieces (1.0 cm × 1.0 cm) for the experiments. Poly(ethylene glycol) methyl ether acrylate (PEGMA average Mn: 454) was provided by SHIN-NAKAMURA CHEMICAL CO. LTD, and purified by passing through an activated basic alumina column to remove the inhibitor. Copper (I) bromide (CuBr 98%) and 4-benzoylbenzoic acid (BBA, 99%), 2,2-bipyridine (bpy, 99%), bromoisobutyryl bromide (BIBB 98%) and ethyl 2-bromoisobutyrate (EBriBu, 98+%) were purchased from Aldrich, ACROS and Alfa, respectively. Fibrinogen (Fg) and goat anti-human fibrinogen/HRP, bovine serum albumin (BSA, 98%), *O*-phenylenediamine (OPD, 98%) were obtained from Beijing BIOS Biotechnology Co. LTD, Sanland and Solarbio, respectively. Tris(hydroxymethyl) amino methane, N-hydroxysuccinimide (HOSu), 4-(N,N-dimethylamino)pyridine (DMAP) and dicyclohexylcarbodiimide (DCC) were used as received.

2.2. Synthesis of 4-benzoyl-N-(2-hydroxy-1,1-bishydroxymethyl-ethyl)-benzamide (BHAM)

1.13 g (5 mmol) of 4-benzoylbenzoic acid (BBA) and 0.60 g (5.25 mmol) of N-hydroxysuccinimide (HOSu) were dissolved in 50 ml of acetonitrile. And then, 1.13 g (5.5 mmol) of dicyclohexylcarbodiimide (DCC) was added into the solution at room temperature. After stirring for 15 h at room temperature, the solution was filtered, the solvent was evaporated under vacuum, and the residue was recrystallized from ethyl acetate to obtain 4-benzoylbenzoic acid-N-hydroxysuccinimide-1-yl ester (BBM). Then, 20 ml of 1,4-dioxan solution of BBM (1.16 g) were added into 5 ml tris(hydroxymethyl) amino methane (THAM) (0.48 g) water solution and stirred for 24 h at room temperature. The solution was evaporated under vacuum, and the residual was recrystallized from ethyl acetate to obtain a white crystal, which was washed twice with ethyl ether, and dried under vacuum at room temperature to yield 49.3% of BHAM. The synthesis route is shown in Fig. 1. APCIms (positive) *m*/*z* theoretical 329 g/mol, observed 330 g/mol; ^{1}H NMR (DMSO, TMS, 400 MHz) δ ppm: 3.72 (6H, –CH_2–OH), 4.65 (3H, –OH), 7.45 (1H, –NH–), 7.56–7.96 (9H, benzene).

2.3. Immobilization of atom-transfer radical polymerization (ATRP) initiators on the PET films

PET films were washed with alcohol to remove the organic residues on the surface. BHAM solution (10 mg/mL, CH_3OH/CH_2Cl_2, 1/1, v/v) were deposited on the PET surface via spin coating. Then PET films were UV irradiated for 5 min with power 400 W

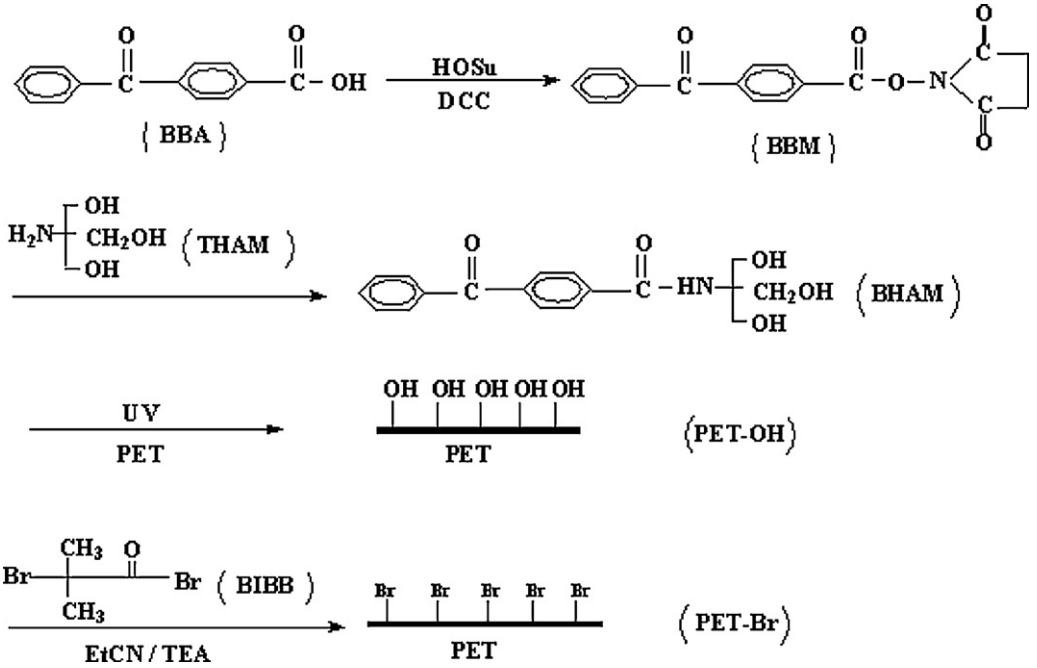

Fig. 1. The synthesis route of 4-benzoyl-N-(2-hydroxy-1,1-bishydroxymethyl-ethyl)-benzamide (BHAM) and immobilization of ATRP initiators on the PET films.