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Reducing diffusion limitations in Ion exchange grafted membranes using high surface area nonwovens

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ABSTRACT

Polybutylene terephthalate (PBT) nonwovens can be readily grafted with glycidyl methacrylate (GMA) via UV induced radical polymerization to create uniform and conformal polymer brush networks around each fiber that can be chemically modified to function as anion or cation exchangers. Protein binding capacities achieved by these grafted materials are many times larger than monolayer coverage around the fibers, but require very long residence times to reach equilibrium due to diffusional limitations within the grafted layers. The rates of adsorption of proteins by ion exchange were measured in an islands-in-the-sea (I/S) PBT nonwoven with average fiber diameter of approximately 1 μm and in a commercially available PBT nonwoven with average fiber diameter of approximately 3 μm. Both nonwovens were grafted successfully with poly(glycidyl methacrylate) (PGMA) and they showed almost identical ion exchange equilibrium protein binding capacities at similar weight % grafting. However, the grafted I/S nonwoven membrane exhibited a substantially higher amount of protein binding at short times and it was able to reach equilibrium in a fraction of the time required by the grafted commercial nonwoven with larger fiber diameters. The faster rate of protein adsorption observed with the I/S PBT nonwoven is the result of the thinner PGMA graft layer thicknesses around the fibers compared to those in the commercial PBT with the same weight % grafting. The data for the rate of adsorption of protein through the functionalized PGMA grafted layers was analyzed using a shrinking core model.

1. Introduction

Membrane chromatography offers several potential advantages over traditional packed bed chromatography as a platform for bioseparations. The interconnected pores of membranes permit high rates of volumetric throughput without substantial pressure drops when compared to packed beds [1–5]. Protein binding to membranes is largely limited to the surface area created by the pores that are available for both flow and adsorption [1,2,4,5]. This eliminates all diffusional limitations to adsorption, but it also reduces the binding capacity of membranes compared to chromatographic resins. Commercial nonwovens have a fraction of the surface area of chromatographic resins, resulting in low binding capacities for most target protein capture applications [6]. By tethering polymer brushes to the surface of the fibers of nonwoven membranes, 3-dimensional binding domains are created that can substantially increase the overall protein binding capacity [2,7–10]. Polymer brush grafting has been known to increase protein adsorption capacity by several times that of monolayer coverage in traditional chromatography resins, hollow fiber membranes, cast membranes, and nonwoven membranes [2,11–13].

Nonwovens grafted with poly(glycidyl methacrylate) (PGMA) offer a convenient platform for the development of effective ion exchange membranes with enhanced binding capacities. Saito et al. [14] successfully grafted PGMA brushes to polypropylene fabrics and polyethylene hollow fibers. These grafted materials were functionalized with phosphoric acid groups to develop strong cation exchange membranes to capture divalent metal cations. Sartorius AG has developed the Sartobind Ion Exchange Membrane Adsorbers which are made by grafting methacrylate based polymers to regenerated cellulose membranes. These membranes are commercially available in a wide range of

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configurations and have achieved protein binding capacities as high as 50 mg/ml [15,16]. In a study by Zheng et al. [11] PGMA was grafted to polypropylene nonwoven and functionalized with diethyl amine (DEA) to develop a weak anion exchanger. This material achieved equilibrium binding capacities for bovine serum albumin (BSA) of 120 mg/g of membrane. Liu et al. [17] investigated the effects of various degrees of PGMA grafting on nonwoven PBT for the capture of BSA by anion exchange. In that study, PGMA grafts were converted to weak anion exchangers with DEA and challenged with BSA. It was determined that the overall protein binding capacity increased with the degree of grafting (% weight gain). The largest equilibrium binding capacity of 800 mg/g (144 mg/ml) was observed at a 12% PGMA weight gain. This investigation also showed that residence times of several hours to a full day were required to reach maximum binding, and that these binding times increased with increased grafting (% weight gain). These long residence times preclude the use of these PGMA grafted nonwoven PBT membranes for the development of high throughput, high capacity protein capture devices for downstream processing. These long residence times resulted from diffusional limitations for protein transport through the grafted polymer layer. It was suspected that the diffusional limitations could be mitigated using nonwoven PBT membranes with smaller fiber diameters, and thus higher specific surface areas, that would result in correspondingly thinner PGMA grafted layers for a given % weight gain of grafting.

There are some nonwoven technologies capable of producing fabrics with submicron sized fiber diameters that can yield a significant increase in specific surface area however, many of them suffer from slow rates of production [18]. Islands in the Sea (I/S) nonwoven technology utilizes bicomponent filaments that can be extruded using rapid commercial production techniques such as spunbonding that deposits the filaments into a nonwoven mat with a high degree of mechanical integrity [18,19]. This type of nonwoven has many permanent polymer cores within the fiber known as “islands” embedded in a sacrificial polymer sheath known as the “sea”. I/S nonwovens are capable of achieving smaller fiber diameters and therefore, higher specific surface areas compared to commercially available nonwovens made by melt blown or spunbonding technologies [19].

In this paper, we investigate the properties of anion and cation exchange membranes generated by grafting PGMA layers onto I/S PBT nonwovens with 1 μm average fiber diameters and commercial melt blown PBT nonwoven fabrics with 3 μm fiber diameters. The grafted nonwovens were functionalized to create both weak anion exchange and strong cation exchange membranes and tested for their ability to capture the target proteins BSA and human immunoglobulin G (hIgG) respectively. The effects of the PGMA grafting levels on the equilibrium binding capacities for protein adsorption were determined and compared. The rates of protein adsorption were also measured to determine the extent of protein diffusion limitations within the PGMA grafted layers in these two nonwoven systems and the results were analyzed using a shrinking core diffusion model. This paper focuses on the chemistry and synthesis of the ion exchange membranes and the role that the polymer grafting chemistry has on the equilibrium protein binding of the membranes. Additional research needs to be done to increase the membrane strength and to improve flow properties before these membranes can be used in pressure driven chromatography based bioseparations.

2. Experimental

2.1. Materials and reagents

Islands-in-the-sea nonwoven PBT fabrics with a 108 island count were produced on the pilot facilities at the Nonwovens Institute (NWI, North Carolina State University, Raleigh, NC). The island count refers to the number of discrete PBT fibers that are liberated once the PLA “sea” has been removed. The novel I/S nonwoven mat was manufactured with a basis weight of 100 g/m^2 consisting of 50% PLA as the “sea” polymer and 50% PBT as the “island” polymer, the basis weight after “sea” removal is 50 g/m^2. Macopharma (Tourcoing, France) provided commercially available melt blown PBT nonwovens with a basis weight of 52 g/m^2. Glycidyl methacrylate (GMA) was purchased from Pflatz & Bauer (Waterbury, CT). Inhibitors in GMA were removed through a prepacked inhibitor removal column to remove hydroquinone and monomethyl ether hydroquinone (Sigma Aldrich, St. Louis, MO). Benzophenone (BP) was purchased from Sigma Aldrich (St. Louis, MO). Sodium hydroxide, 1-butanol, tris base, hydrochloric acid, sodium chloride and sodium acetate trihydrate were purchased from Fisher Scientific (Fairlawn, NJ). Tetrahydrofuran (THF), methanol, sulfuric acid, and acetic acid were purchased from BDH (West Chester, PA). Diethylamine (DEA) was purchased from Alfa Aesar (Ward Hill, MA). Phosphoric acid (85%) was purchased from Acros Organics (Fairlawn, NJ). Solid phase extraction tubes were purchased from Supelco (Bellefonte, PA). Albumin from bovine serum (BSA) was purchased from Sigma Aldrich (St. Louis, MO). Human immunoglobulin G (hIgG) was purchased from Equitek-Bio Inc. (Kerrville, TX).

2.2. PLA removal from I/S nonwovens

The 50% PLA “sea” of the 108 I/S nonwovens had to be removed to liberate the PBT “islands” prior to grafting. PLA was decomposed using 10% w/w sodium hydroxide in DI water at 80–90 °C. I/S nonwovens were submerged in caustic bath for 5 min with constant stirring until all of the PLA had been dissolved from the nonwovens. The PBT nonwovens were then washed extensively with DI water until a neutral pH was achieved. Samples were then allowed to air dry overnight. The remaining nonwoven mat contained intertwined bundles of approximately 108 one micron PBT fibers per bundle.

2.3. UV-induced PGMA grafting onto PBT nonwovens

The GMA grafting solution consisted of 20% v/v GMA monomer in 1-butanol as the solvent. The photoinitator benzophenone (BP) was added to the grafting solution in a BP:GMA ratio of 1:20 (mol:mol) [11]. Commercially available PBT nonwovens and 108 I/S PBT nonwovens after PLA removal were cut to 75 × 50 mm size samples and weighed prior to grafting, samples were approximately 200 mg and 180 mg for commercial PBT and 108 I/S PBT respectively. Nonwovens were saturated with grafting solution by spraying 1.5–2.0 ml of grafting solution via syringe, and placed between two borosilicate glass slides (75 × 50 mm). A UV lamp (model EN-180L, Spectronics Corporation, Westbury, NY) with a 365 nm wavelength and an intensity of 5 mW/cm^2 was used to induce free radical polymerization of the GMA onto the PBT surface [12]. The distance between the lamp and the sample was 3 mm. Samples were irradiated at various exposure times to achieve different degrees of PGMA grafting with different % weight gains. After PGMA grafting, the samples were placed in a flask containing 100 ml of THF, the flask with the THF and samples was sonicated with an ultrasonic bath (Bransonic 3510R-MT, Branson Ultrasonics Corporation, Danbury, CT) for 30 min to remove any