Composites Communications xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Composites Communications

journal homepage: www.elsevier.com/locate/coco

Electrospun nanofibrous composite materials: a versatile platform for high efficiency protein adsorption and separation

Qiuxia Fu[a], Cheng Duan[a], Zishuo Yan[a], Yang Si[a], Lifang Liu[a,*], Jianyong Yu[b], Bin Ding[a,b,**]

[a] Key Laboratory of Textile Science & Technology, Ministry of Education, College of Textiles, Donghua University, Shanghai 201620, China
[b] Innovation Center for Textile Science and Technology, Donghua University, Shanghai 200051, China

ARTICLE INFO

Keywords:
Electrospun nanofibers
Protein adsorption
Surface functionalization
Chromatography

ABSTRACT

Highly effective separation and purification of protein are extremely important for the development of pharmaceutical industry, which still remains a great challenge. As a kind of frontier new material, electrospun nanofibers show vast perspectives in fabricating high performance protein adsorption materials attributing to their competitive structure advantages involving large specific surface area, high porosity, good pore channel connectivity, easy to surface functionalization, controllable single fiber and aggregate structure. Herein, we detailedly summarize the recent progress in the design concepts, synthesis and structure control of electrospun nanofibrous composite materials with different functional interfaces for the separation and purification of proteins. Furthermore, the current challenges and future development directions in this rapidly developed field are also highlighted in this review.

1. Introduction

As an indispensable part of biomacromolecules, proteins not only play critical roles in our living activities, but also occupy important status in the development of pharmaceutical and food industries [1,2]. Generally, compared with the processes of raw materials treatment, rough extraction and finished products processing, separation and purification is considered as the most important step owing to its great influences on the quality and cost of protein products [3]. Nowadays, conventional particle gel packed column is most widely used for purifying proteins. However, several major limitations involving relatively high pressure drop and low through-put separation, seriously hinder the fast development and scale-up of the traditional chromatographic technique. Generally, these disadvantages are caused by the deformation/accumulation of particle gel beads and the intra-particle diffusion of proteins within the inner pores of beads (Fig. 1a) [4]. Therefore, novel high-performance chromatographic materials with low pressure, high adsorption capacity and rate are urgently required.

In the past decades, various materials including non-porous and rigid chromatographic beads have been developed to overcome the limitations of gel beads, because their excellent deformation resistance could reduce the penetration pressure to a certain extent [5,6]. However, the cost of these materials are generally high, and the decreased effective specific surface area (ESSA) lead to relatively low adsorption capacity. More importantly, the limitation of high flow resistance is still unresolved. As newly developed chromatographic medium, fibrous adsorbents have attracted lots of attentions owing to their advantages of convective mass transfer (Fig. 1b), thereby could greatly improve the process efficiency and liquid volume [7]. Consequently, various membranes chromatographic materials have been developed, including natural polymeric adsorbents [8,9], inorganic fibrous adsorbents [10], and synthetic polymeric adsorbents [11,12]. In spite of the improved permeation flux, fiber-based protein adsorbents still face challenges of relatively low adsorption capacity and poor cyclic performance, which are mainly resulted by their relatively large fiber diameter, low ESSA and limitations of the modified method.

With the rapid development of nano materials, nanofibrous membranes with high ESSA and porosity, unique chemical/physical and mechanical properties, ease to functionalize, have been considered as the most promising candidates for preparing high-performance protein chromatographic materials [13]. As one of the most versatile and effective methods for fabricating nanofibrous materials, electrospinning technique has obtained significant attentions in protein purification field due to its great capability in controlling the fiber assembly structure and modification [14,15]. Thus, various new types of nanofibrous protein chromatographic materials have been developed on the basis of the versatile electrospinning technique. These materials presented significant advantages as compared with traditional gel particles

* Corresponding author.
** Corresponding author at: Key Laboratory of Textile Science & Technology, Ministry of Education, College of Textiles, Donghua University, Shanghai 201620, China.
E-mail addresses: lifangliu@dhu.edu.cn (L. Liu), binding@dhu.edu.cn (B. Ding).

https://doi.org/10.1016/j.coco.2017.11.007
Received 11 October 2017; Received in revised form 21 November 2017; Accepted 24 November 2017

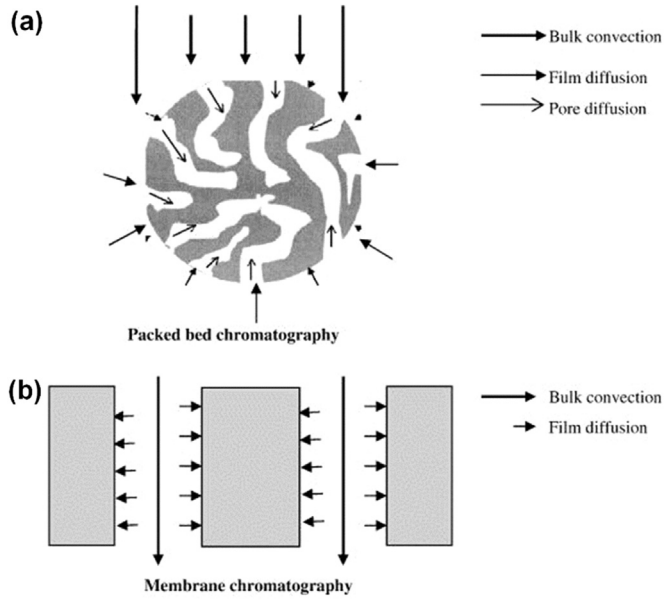

Fig. 1. Different solution transfer mode of in (a) packed gel beads and (b) membranes chromatographic materials. © 2002, Elsevier.

and fibrous membranes based protein adsorbents, which dramatically accelerated the progresses of scientific research on the fabrication of protein adsorption materials. Meanwhile, these research works also paved the way for the development of new generation commercial adsorbents with new structure and higher performance for large-scale industrial production of high purified protein products. Therefore, we summarize this review to provide a systematic overview on the structure design, fabrication and recent development of electrospun nanofibrous proteins adsorbents, which haven't been reviewed to the best of our knowledge. Based on the different adsorption mechanism between proteins and nanofibrous membranes, we will organize this review according to the following three parts: ion-exchange, affinity and hydrophobic interaction nanofibrous chromatographic membranes.

2. Nanofibrous membranes based protein adsorption materials

2.1. Ion-exchange nanofibrous chromatographic membranes

Since proteins present differential electrical properties in buffer solutions with different pH value, thus protein purification could be realized by utilizing the controllable electrostatic interactions between protein and adsorbents. Currently, ion-exchange chromatography is adopted most widely attributing to their relatively low preparation cost, mild adsorption/desorption conditions, and wide applicability [16,17]. Consequently, ion-exchange electrospun nanofibrous membranes have gained great attentions. To date, various kinds of nanofiber-based ion-exchange protein adsorbents have been developed by the combination of electrospinning method and functionalization technique, which could be divided into the following three categories: organic polymer nanofibrous membranes, organic/inorganic composite nanofiber membranes, and carbon nanofibrous membranes.

2.1.1. Organic polymer nanofibrous membranes

Organic polymer materials involving cellulose, agarose, polyacrylamide, are widely used as the base matrix to prepare commercial protein adsorption materials, owing to their rich variety, abundant availability, low cost, simple and mild manufacturing processes. Therefore, numerous efforts have been provided to research on the electrospun organic polymer ion-exchange chromatographic materials. To date, many kinds of organic polymer nanofibrous membranes have been successfully developed, mainly including functionalized cellulose fibers [18–20], PVA fibers [14,21], EVOH fibers [22] and polyacrylonitrile fibers [23].

Cellulose as a natural polymer with abundant favorable properties involving biodegradability, rich in highly reactive hydroxyls, low non-specific binding, have become the prime substrate to ion-exchange groups for protein separation and purification [24]. According to statistics, up to now, cellulose based nanofibrous protein adsorbents are responsible for over half of all the organic polymer ion-exchange protein adsorption membranes, which are including anion or cation exchange membranes. In the aspect of anion-exchange membranes, cellulose acetate (CA) electrospun nanofibers were hydrolyzed to get the regenerate cellulose (RC) membranes, and then the RC membranes were surface functionalized with weak anion-exchange ligands of diethylaminoethyl groups, the resultant anionized cellulose material presented a high water permeance flux of 801 ± 75 L min^{-1} m^{-2} 10^{-5} Pa of single layer membrane, and the adsorption capacity towards the negatively charged proteins was 40 mg g^{-1} (take BSA as the template) [18]. To further improve the performance of cellulose based anion-exchange membranes, Lan et al. selected cellulose diacetate (CDA) as raw material, and then functionalized the CDA by taking the HNO_3 and CH_2Cl_2 as nitration agent (Fig. 2a), the resultant cellulose diacetate nitrate (CDNA) was processed into uniform nanofibers with thin diameter by regulating the solvents during the electrospinning process (Fig. 2b and c). Most excitingly, the resultant strong anion-exchange membranes presented an improved adsorption capacity toward BSA with the equilibrium capacity of 300.11 mg g^{-1} (Fig. 2d) [25]. As for the cation-exchange cellulose nanofibrous materials, the RC membranes were functionalized with three dimensional nanolayers of polyacrylic acid *via* atom transfer radical polymerization technique, the functional membranes show excellent adsorption performance, the binding capacity were over 20 and 50 times larger than that of the conventional packed bed resins and commercial ion-exchange membrane, respectively. Additionally, the water permeance flux was also over 15 times higher than that of the resins packed column [20].

Polyvinyl alcohol (PVA) as a synthetic polymer with numerous hydroxyl groups on the molecule chains, presents outstanding hydrophilcity, these significant advantages make it become a wonderful candidate for preparing protein adsorptions. However, the water solubility of PVA greatly limit its practical application in protein purification field. Recently, Wang et al. gained a great progress in the preparation of PVA based ion-exchange composite nanofibrous membranes [21]. By introducing maleic anhydride into the PVA solution, and combining the electrospinning technique with in situ polymerization/functionalization method, the water-soluble PVA was not only successfully chemical crosslinked with maleic anhydride (MAH) (Fig. 3a and b), meanwhile numerous negatively charged carboxyl groups were grafted on the nanofibers (Fig. 3c). Interestingly, the obtained PVA/MAH composite ion-exchange membranes exhibit a relatively high capacity of nearly 180 mg g^{-1} toward lysozyme, excellent selectivity for positively charged template proteins, as well as good cycle performance (Fig. 3d and e).

Compared with commonly used matrix of cellulose and PVA, ethylene-vinyl alcohol copolymers (EVOH) is another extremely ideal choice for preparation of protein chromatographic materials attributing to its good hydrophilicity and water insolubility, easy to functional modification, excellent mechanical strength, biocompatibility and corrosion resistance, which are derived from the unique chemical components of hydrophilic vinyl alcohol and hydrophobic ethylene segments [26]. In previous studies, EVOH hollow-fiber and porous membranes have been fabricated as functional materials for the application of enzyme immobilizations [27,28]. Recently, Fu et al. successfully fabricated and applied the electrospun EVOH nanofibers in protein adsorption and purification for the first time [22]. Eletrospun EVOH nanofibers were fabricated by taking nontoxic isopropanol and water mixtures, and then the membranes were surface modified with edible citric acid (CCA) by dip coating technique and heat treatment, finally