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Short communication

Polydopamine meets porous membrane: A versatile platform for facile preparation of membrane adsorbers

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ABSTRACT

Polydopamine, as an intermediate layer coated on PES membrane, was applied to fabricate various membrane adsorbers. Anion-exchange, hydrophobic interaction and affinity membrane adsorbers prepared by this facile method exhibited a high selectivity in fractionation of IgG (immunoglobulin)/HSA (human serum albumin) mixture. The anion-exchange membrane adsorber containing polyethylenimine (PEI) improved the HSA purity from 17.7% to 96.7%; The hydrophobic interaction membrane adsorber with Dodecyl mercaptan (DDM) as ligand obtained an IgG purity of 94.6%; Histidine attached affinity membrane chromatography achieved nearly a 100% purity of IgG. The present work indicated that the polydopamine layer not only activated membrane surface to attach various adsorptive ligands under the mild condition, but also reduced non-specific adsorption. Due to the versatile conjunction function, this facile mussel-inspired coating is also promising for the preparation of diverse membrane adsorbers.

1. Introduction

Biopharmaceutical therapeutics such as monoclonal antibodies, recombinant proteins, viral vaccines and plasmid DNA are playing an increasingly important role in human life and their global market is growing rapidly. Considering more than 60% of the production cost is incurred during the recovery and purification in downstream process [1], the commercial manufacture requires a cost-effective separation process with high throughput and high resolution [2,3] and optimizing conditions for process development. Membrane-based separations offer a great potential in processing aqueous solutions because of their high efficiency and lower energy consumption. Adsorptive ligands could be attached to membrane surface to construct various membrane adsorbers for chromatography [4]. As the transport of solutes to their binding sites in membrane matrix takes place mainly by means of convection, membrane chromatography is endowed with a rapid separation speed [5]. In addition, this disposable chromatography product could eliminate the cost of cleaning-in-place and validation steps. Therefore, the development of membrane adsorbers for chromatography has attracted significant interest in recent years.

Membrane adsorbers are normally made by hydrophilic matrixes with less fouling potential. Among them, cellulose is widely used as base membrane since it contains a large quantity of hydroxyl groups, which could be activated for ligands immobilization. However, the mechanical strength of the cellulose based membrane is relatively low and even may deteriorate during the surface modification [6]. Meanwhile, polymer membranes with high mechanical strength are usually hydrophobic and inert. Thus, it is prone to produce membrane fouling and is hard to link ligands [7]. Previous research revealed that chemical modification and polymer grafting [3,6,8] are effective surface engineering methods for preparing membrane adsorbers. However, these approaches are relatively complex and hard to control. Meanwhile, membrane structure would be more or less damaged during surface modification [3,7]. Therefore, it is of great interest to develop a facile, universal and easy-control method for preparation of membrane adsorbers with various substrates.

Inspired by the bio-adhesion property of marine mussels, dopamine (DA) is known as a famous “bio-glue” due to its strong adhesion ability [9]. It can deposit on various substrates through the formation of strong covalent and noncovalent bonds with surfaces under alkaline condition and air atmosphere (Fig. 1a) [9–12]. The formed polydopamine (PDA) layer is bio-compatible and stable

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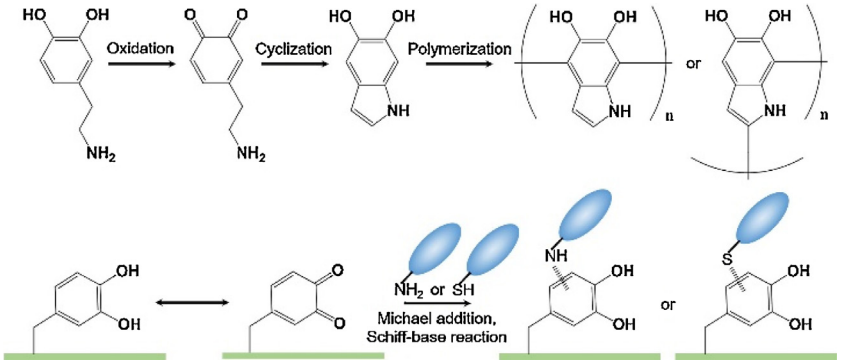

Fig. 1. (a) Possible reaction mechanism for dopamine polymerization [12] and (b) reaction mechanism of immobilization of thiol- and amino- containing compounds onto PDA coating layer.

in a relatively wide pH range. Thanks to the catechols on the PDA, the coated substrates have the versatility to link with thiol- and amino- containing compounds via Michael addition and Schiff-base reaction (Fig. 1b) [13]. Meanwhile, surface hydrophilicity and permeability could be improved by the attached catechols and amines groups from deposited PDA layer. Nowadays, this modification method has been widely used for membrane surface engineering to meet various applications such as water purification, gas separation, energy generation, hemodialysis, catalysis [12,14–17], etc. However, to the best of our knowledge, there is no report regarding preparation of membrane adsorbers based on pre-coated PDA layer. It is well known that PEI containing primary, secondary and tertiary amino groups, could be used for anion-exchange chromatography [18]; DDM with its alkyl chains could be coupled on substrates for hydrophobic modification [13]; Histidine (His) has been applied for affinity purification of IgG from human serum [19]. Based on these knowledges, in the present study, polyethersulphone (PES) microfiltration membrane (it was more hydrophobic and inert than cellulose membrane but had much stronger mechanical strength) with a PDA coating layer was employed as a versatile platform to link PEI, DDM and His molecules for preparation of anion-exchange, hydrophobic interaction and affinity membrane adsorbers (Fig. 2). The separation performance of the obtained membrane adsorbers was then evaluated by a chromatography system. Comparing with the membrane modification and non-membrane adsorber preparation by PDA coating, there are some new scientific problems in the preparation of the membrane adsorber for protein purification, such as adsorption selectivity and non-specific adsorption, which need to be clarified in the present work.

2. Materials and methods

2.1. Materials

Human serum albumin (HSA) and immunoglobulin G (IgG) were provided by Lanzhou Institute of Biological Products Co. Ltd, China. A Mustang coin units (0.35 mL) was purchased from Pall Corporation, USA. A high performance GFC column (TSKgel G3000SWXL) was purchased from Tosoh Bioscience LLC. Histidine (His), polyethylenimine (PEI, average Mn ~60,000, average Mw ~750,000), Dodecyl mercaptan (DDM) and dopamine hydrochloride were purchased from Sigma-Aldrich. Polyethersulfone (PES) membranes with a 0.45 μm pore size were bought from Millipore,

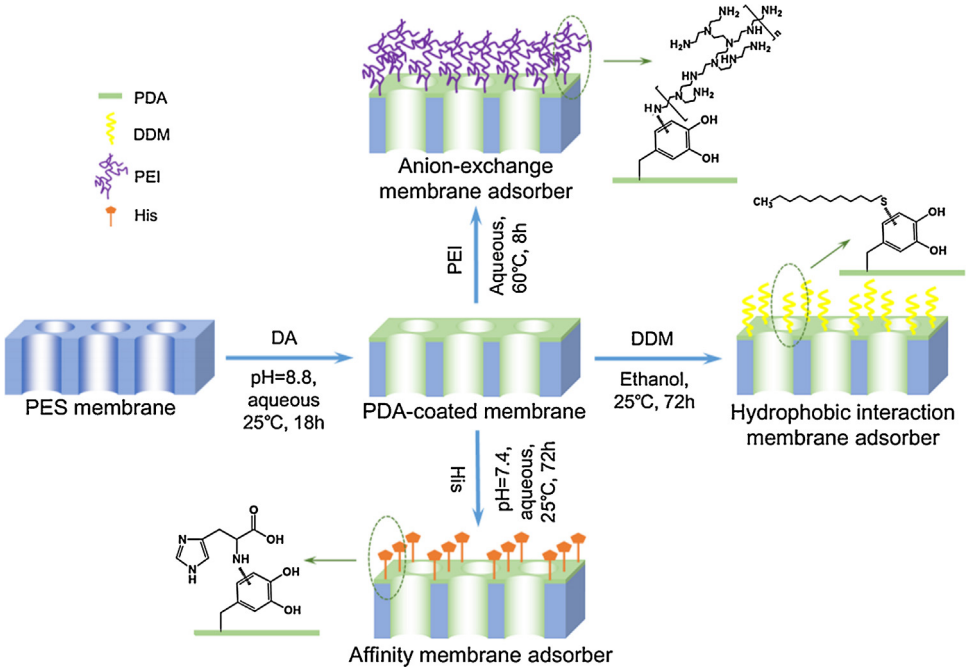

Fig. 2. Synthetic routes for anion-exchange, hydrophobic interaction and affinity membrane adsorbers via PDA-coated membrane platform.