Polymer 54 (2013) 4220–4226

Contents lists available at SciVerse ScienceDirect

Polymer

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

Layer-by-layer assembled highly adhesive microgel films

Jianfu Zhang, Dongdong Chen, Yang Li, Junqi Sun*

State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, PR China

ARTICLE INFO

Article history:
Received 7 March 2013
Received in revised form
19 May 2013
Accepted 2 June 2013
Available online 10 June 2013

Keywords:
Layer-by-layer assembly
Free-standing films
Adhesive films

ABSTRACT

Water-based adhesives which have strong adhesion and can simplify the adhesion process, endow the adhesives with desired functions are important for various applications. In this work, water-based highly adhesive films with drug delivery ability are fabricated by layer-by-layer (LbL) assembly of chemically cross-linked poly(allylamine hydrochloride)-dextran (PAH-D) microgels and hyaluronic acid (HA). Strong adhesion as high as 6.95 ± 0.92 MPa can be achieved when glass substrates deposited with LbL assembled PAH-D/HA films are slightly pressed together. Confocal laser scanning microscope (CLSM) measurements disclose that the strong adhesion originates from the intermixing of HA with PAH-D microgels at the interface of two contacted PAH-D/HA films. Free-standing PAH-D/HA films are released from substrate under assistance of a sacrificial layer for direct use as adhesives because PAH-D microgels have strong interactions with various surfaces. PAH-D/HA adhesive films can load negatively charged drugs such as ibuprofen based on electrostatic interaction between PAH-D microgels and ibuprofen molecules and release them in physiological conditions. Ibuprofen-loaded PAH-D/HA free-standing films can strongly glue periostea, promising their potential application as bioadhesives capable of accelerating the healing of damaged tissues or organs.

1. Introduction

Adhesives which can bond materials of different shapes and properties to achieve connection and package are widely used in daily life [1]. Adhesives can be either pastes or films based on their physical forms. Compared with pastes, adhesive films have the advantages of convenience in storage and handling, and conformal adhesion due to their homogenous thickness. Traditional adhesive films composed of thermoplastic polymers usually require thermal treatments or organic solvents in the adhesive process, which make the adhesion process complicated and environmentally unfriendly [2,3]. Recently, various novel adhesive films have been produced, with their functions being much better than those of traditional adhesive films. For example, gecko-inspired synthetic adhesives composed of microsized non-sticky plastic pillars with high aspect ratios of heights to radii were fabricated by mimicking the nano-topography of gecko feet [4–7]. These gecko-inspired adhesives can achieve reversible adhesion on flat surface based on van der Waals and capillary forces. More importantly, they can act as tissue adhesives when biocompatible and biodegradable elastomer is used for producing micropillar arrays [7]. Tissue adhesives are important in healing of tissues and organs where mechanical fastening using sutures might lead to unexpected damage [8]. The adhesive proteins secreted by marine mussels adhere strongly and rapidly to a variety of surfaces even in sea water. Inspired by a key composition in adhesive proteins, amino acid 3,4-dihydroxy-L-phenylalanine (DOPA) has been widely employed for the fabrication of adhesives suitable for use in aqueous environments [9–11]. As reported by Messersmith and co-workers, gecko-inspired adhesives lose most of their adhesion when immersed in water. However, when microsized pillars of gecko-inspired adhesives are coated with a DOPA-containing polymer layer, wet adhesion increases as much as 15-fold [12]. Meanwhile, substrates bearing oppositely charged polyelectrolytes, such as hydrogels [13] and polyelectrolyte brushes [14] can adhere strongly to each other based on electrostatic interaction between them. Adhesive films based on electrostatic interaction can be designed to bond/debond multiple times by an externally applied electric field [13]. With the demand to bond complex objects in a precise and controlled way, adhesive films with novel or unexplored functions are highly required. In particular, water-based adhesive films which can simplify the adhesive process, enable strong adhesion [15], and impart the adhesives with new functions are highly desirable but rarely reported.

The layer-by-layer (LbL) assembly, which involves the alternate deposition of species with complementary interactions, is currently one of the most efficient methods to fabricate composite films with

* Corresponding author. Tel.: +86 431 85168723; fax: +86 431 85193421.
E-mail address: sun_junqi@jlu.edu.cn (J. Sun).

0032-3861/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.polymer.2013.06.002

precisely controlled film structure and compositions [16–24]. By deliberately tailoring deposition parameters, the LbL assembly enables controlling the interdiffusion of polyelectrolytes within polyelectrolyte multilayer films [25,26]. Taking advantage of the interdiffusion of polyelectrolytes, we successfully fabricated polyelectrolyte films capable of healing damage such as deep cuts and scratches [27]. Adhesion of two physically contacted solid substrates covered with LbL assembled polyelectrolyte films such as poly(diallyldimethylammonium chloride) (PDDA)/poly(sodium styrenesulfonate) (PSS) or poly(allylamine hydrochloride) (PAH)/poly(acrylic acid) (PAA) was conveniently realized in the presence of water and pressure, thanks to the interdiffusion of polyelectrolytes [28,29]. These previous studies show that LbL assembled polyelectrolyte films are promising as adhesives. However, considering the wealth of functions of LbL assembled polyelectrolyte films, their functions as adhesive films have not been fully explored because no other function has been integrated into the LbL assembled adhesive films. Moreover, the objects to be bonded must be pre-covered with polyelectrolyte adhesive films, making the adhesion process largely inconvenient. It will be convenient if free-standing polyelectrolyte films can be directly used for adhesion purpose. Here, a new type of highly adhesive microgel films are fabricated by LbL assembly of chemically cross-linked poly(allylamine hydrochloride)-dextran microgels (named PAH-D) with hyaluronic acid (HA). The PAH-D/HA adhesive films deposited on solid substrates can adhere strongly when they are slightly pressed with their surfaces getting wet with water. More importantly, free-standing PAH-D/HA films can be directly used as adhesives. The abundance of amine groups in PAH-D microgels allows the incorporation of drugs in PAH-D/HA adhesive films, imparting the adhesive films with drug delivery ability. Ibuprofen-loaded PAH-D/HA free-standing films can firmly bond periostea, promising their application as bioadhesives with drug delivery ability.

2. Experimental section

2.1. Materials

Poly(allylamine hydrochloride) (PAH, Mw *ca.* 56 000), hyaluronic acid sodium (HA, Mw *ca.* 1 630 000) were purchased from Sigma–Aldrich. Lucifer yellow cadaverine (LYC) was purchased from Biotium. Dextran (Mw *ca.* 40 000) was purchased from Tokyo Chemical Industry Co., Ltd. Ibuprofen sodium was purchased from Fluka. All chemicals were used without further purification. PAH-D microgels were synthesized by chemical cross-linking of PAH and dextran according to our previously reported method [30]. The cross-linking was conducted by first partially oxidizing hydroxyl groups of dextran to produce aldehyde groups, which then reacted with amine groups of PAH via the formation of imine (–N–C–) bonds. Finally, the –N–C– bond in the cross-linked PAH and dextran microgel was reduced into –N–C–. The synthesized PAH-D microgels contain PAH and dextran with a monomer molar ratio of 1.5:1. LYC-labeled HA (HA-LYC) was synthesized according to a literature method and was briefly described in our previous work [27]. The molar ratio of LYC to carboxylate groups of HA was chosen at 1:50. The unreacted LYC was removed from the reaction solution by dialyzing against deionized water for one week. Periostea were torn away from fresh bovine ribs.

2.2. Preparation of PAH-D/HA adhesive films

Glasses and silicon wafers were first immersed in piranha solution (1:3 mixtures of 30% H_2O_2 and 98% H_2SO_4) and heated until no bubbles released. Then they were rinsed with copious amounts of water and finally dried by N_2 flow. *Caution: Piranha solution reacts violently with organic material and should be handled carefully.* The newly cleaned glass or silicon substrate was first immersed in PAH-D aqueous solution ($\sim$1 mg mL^{-1}, pH 7.4) for 15 min to obtain a layer of PAH-D, followed by a rinsing and drying step using water and N_2 flow. The substrate was then transferred to an aqueous HA solution (1.0 mg mL^{-1}, pH 7.4) for 15 min, followed by another water rinsing and N_2 drying step. (PAH-D/HA)*n multilayer films can be deposited on the substrate by repetition of the above deposition processes in a cyclic fashion until a desirable thickness is achieved (n refers to the number of film deposition cycles). Free-standing PAH-D/HA adhesive films were produced by employing a sacrificial cellulose acetate (CA) layer [31]. Acetone solution of CA (30 mg mL^{-1}) was spin-coated on a newly cleaned glass substrate at 1000 rpm to obtain a homogeneous CA layer ($\sim$1 μm). The CA layer was further treated with oxygen plasma for 3 min to obtain a negatively charged hydrophilic surface, which can facilitate the deposition of PAH-D layer. The deposition process of the PAH-D/HA film on the oxygen plasma-treated CA layer was the same as that on the bare glass substrate. Large-area free-standing PAH-D/HA film was exfoliated from the substrate by immersing the resultant film in acetone solution to dissolve the sacrificial CA layer.

2.3. Loading and release of ibuprofen

Ibuprofen was loaded into PAH-D/HA films by immersing the films into an aqueous solution of ibuprofen sodium (15 mM, pH 7.4) for 3 h [32]. The release of ibuprofen from PAH-D/HA film was conducted by immersing the film into a vial containing 3 mL of phosphate buffered saline (PBS) at 37 °C, which was replaced by a fresh one after an appropriate time to ensure constant release conditions. The releasing profile of ibuprofen was obtained by monitoring the absorbance of ibuprofen at 220 nm in PBS. As the absorbance of ibuprofen at 220 nm in PBS obeys Lambert–Beer law, the amount of released ibuprofen can be determined using the calibration curve for ibuprofen in PBS.

2.4. Characterization

Scanning electron microscopy (SEM) images were recorded on a XL30 ESEM FEG scanning electron microscope. Ultraviolet-visible (UV–vis) absorption spectra were collected on a Shimadzu UV-2550 spectrophotometer. The cross-section of glued (PAH/HA)*30 films deposited on two silicon wafers was viewed by an Olympus FV1000 confocal laser scanning microscope (CLSM). The thickness of the films deposited on glass substrates was determined by a Veeco Dektak 150 surface profiler. Adhesion strength measurements were taken with an autograph universal testing machine (Shimadzu AG-I 1 kN) at ambient environment. The stretching velocity was set as 1 mm min^{-1}. A PDC-002 plasma cleaner (Harrick Plasma company, US) was used for oxygen plasma treatment of CA films. The stress–strain curves of PAH-D/HA free-standing films were measured with a mechanical strength microtest device (410R250, Test Resources, Shakopee, MN).

3. Results and discussion

3.1. Preparation of PAH-D/HA adhesive films on solid substrates

Glass and silicon wafers are selected as substrates to examine the adhesive ability of LbL assembled PAH-D/HA films. Amine-containing PAH-D microgels and glucuronic acid-containing HA are positively and negatively charged in aqueous solution with pH of 7.4, respectively. Therefore, PAH-D and HA can be LbL assembled on glass or silicon substrates based on electrostatic interaction