Applied Clay Science 99 (2014) 119–124

Contents lists available at ScienceDirect

Applied Clay Science

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

Research paper

Palygorskite polypyrrole nanocomposite: A new platform for electrically tunable drug delivery

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ARTICLE INFO

Article history:
Received 23 January 2014
Received in revised form 15 June 2014
Accepted 17 June 2014
Available online 2 July 2014

Keywords:
Polypyrrole
Palygorskite
Aspirin
Drug-delivery
Electrical stimulus

ABSTRACT

A clay polymer nanocomposite (CPN) based on aspirin-loaded palygorskite (Pal) modified polypyrrole (PPy) was prepared by in situ electropolymerization of pyrrole monomer in the presence of Pal as the modifier and aspirin as the drug source. This drug-loading approach was simple and convenient, since colloid templates such as polystyrene microspheres used in conventional drug-loading system were not needed. The resulting CPN was characterized by TEM, XRD, cyclic voltammetry (CV), chronocoulometry, electrochemical impedance spectroscopy (EIS) and FTIR. The CPN was used as a new platform for aspirin delivery, which could significantly enhance aspirin loading capacity of the system and control aspirin release by external electrical stimulus. The results indicated that the proposed novel drug-delivery system might be promising as an implantable device where drug release could be electrically tuned according to the patient's requirement.

1. Introduction

The past decades have seen the development of therapeutically effective, safe, and patient-compliant drug-delivery systems, and researchers still continue to design novel tools and strategies for improving such systems. Recently, conducting polymers have gained much attention as stimuli-responsive macromolecules for drug delivery because of their inherent electroactive properties (Abidian et al., 2006; Richardson et al., 2009; Svirskis et al., 2010a; Zeng et al., 2003). Among these polymers, polypyrrole (PPy) has emerged as a highly promising material due to its ability to switch between oxidation and reduction states in response to electrical potential, and its good biocompatibility (Cho and Borgens, 2011; Geetha et al., 2006; George et al., 2005). However, due to their quite small specific surface area (SSA), most conducting polymers are limited in the capacity to load drugs, which hinders their application as drug delivery system toward a range of disease states (Sharma et al., 2013).

In order to enhance the drug-loading capacity of the drug-delivery system, a colloid template method was recently proposed (Kang et al., 2011; Pokki et al., 2012). However, this method requires complete removal of the colloid templates from the system, which is difficult and time-consuming (Yang et al., 2004). Alternatively, the drug-loading capacity can be enhanced by increasing the SSA of the matrix. One approach is to use clay materials as the matrix because they exhibit not only excellent stability and high adsorption, but also large SSA (Fan et al., 2008; Kong et al., 2010). For example, the SSA of palygorskite (Pal) is as large as 119 $m^2 g^{-1}$ (Kong et al., 2009). This makes Pal a potential material for modification of the drug-delivery system based on conducting polymers (Aguzzi et al, 2007; Li et al., 2013).

In the present work, PPy was modified with Pal by a simple in-situ electropolymerization technique free of colloid templates, and the resulting Pal PPy nanocomposite combined the advantages of both PPy and Pal. On one hand, PPy could be electrically tuned to efficiently release drug by adjusting the applied potential, on the other hand, Pal was anticipated to increase the overall drug-loading capacity of the developed system. To evaluate the performance of this clay polymer nanocomposite (CPN), aspirin, a commonly used anti-inflammatory drug that can be easily detected, was used as target drug molecule to be delivered (Gupta et al., 2010; Murtaza et al., 2011; Szostak and Mazurek, 2002). The results indicated that modification of PPy with Pal increased both drug-loading capacity and drug-releasing efficiency of the drug-delivery system as compared to PPy alone.

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http://dx.doi.org/10.1016/j.clay.2014.06.020
0169-1317/

2. Materials and methods

2.1. Reagents and apparatus

Pyrrole (Aldrich, 98%) was distilled under reduced pressure and stored at 4 °C prior to use. Pal was purchased from Jiangsu NDZ Technology Company (Changzhou, China) and washed with double distilled water to remove turbidity, and then dried at 80 °C. Aspirin and other chemicals were of analytical grade and obtained from Aladdin Chemicals Reagent Co., Ltd. (Shanghai, China). All solutions were prepared with doubly distilled water.

The Pal, and the prepared CPN were examined for their morphologies by transmission electron microscopy (TEM) using JEM-2000 (JEOL Corporation, Japan), XRD patterns by X-ray diffractometer (D/max 2500 PC, Rigaku Corporation, Japan) using Cu Kα radiation, FTIR analyses by FTIR-8400S spectrophotometer (Shimadzu Corporation, Japan), respectively. All electrochemical measurements were performed by using a CHI 660D electrochemical workstation. The content of aspirin was measured by using a UV-160A UV–Visible spectrophotometer (Shimadzu, Japan).

2.2. Preparation of aspirin-Pal PPy nanocomposites

The preparation of aspirin-Pal PPy nanocomposites was carried out by in situ electropolymerization of pyrrole monomers in the presence of Pal as the modifier and aspirin as the drug source. The electrolytic cell consisted of a piece of indium–tin oxide glass (ITO) as the working electrode, a platinum foil as the auxiliary electrode and a saturated calomel electrode as the reference electrode. The whole procedure was carried out as follows. Firstly, 0.56 g Pal was dispersed in 25 mL phosphate buffer solution (PBS) containing 75 mg aspirin (pH 3.5) and sonicated for 1 h, then 0.34 mL pyrrole was added to this emulsion and dissolved with vigorous magnetic stirring for 30 min. The solution was deaerated by bubbling nitrogen for 10 min before the electropolymerization of pyrrole. Then, PPy was deposited onto the surface of ITO by a potentiostatic method, in which a positive potential of 0.80 V was applied at the ITO working electrode for 500 s. During the polymerization process, Pal and aspirin molecules were incorporated into the PPy film simultaneously. Subsequently, the prepared aspirin-Pal PPy nanocomposites was rinsed thoroughly with doubly distilled water and then dried. For comparison, aspirin-loaded PPy was synthesized by the same procedure except for the addition of Pal to the electrolyte.

2.3. Release of aspirin from the drug-loading system

The release of aspirin was triggered by external electrical stimulus, in which a negative potential of −0.6 V was applied at the aspirin-Pal PPy nanocomposites and a solution of 25 mL PBS was used as the media (pH 7.4). Aliquots were withdrawn from the working solution at specific time points, and replaced with the same amount of fresh media. The content of aspirin in each aliquot was measured by spectrophotometry and calculated by Lambert–Beer's law based on the absorbance at 205 nm. The release of aspirin by electrical stimulus was finished when no significant change was observed on the UV–Visible spectra. Spontaneous release of aspirin from the drug-loading system was measured in the same way but without applying the electrical stimulus, and used as control.

3. Results and discussion

3.1. TEM images of Pal and CPN

TEM micrographs of Pal and CPN were shown in Fig. 1. Pal was fibrillar single crystal with a diameter ranging from 20 to 30 nm (Fig. 1A). The branching single crystal structure of Pal remained unchanged after its combination with PPy and clusters of Pal were embedded in the films of PPy, as can be seen in Fig. 1B. The effective coating of PPy on Pal formed a CPN with a core-shell structure. The resulting CPN combined the advantages of both PPy and Pal, which made the CPN an ideal candidate used in drug delivery by external electrical stimulus.

3.2. XRD characterizations of Pal and CPN

The XRD patterns of CPN, and Pal alone were shown in Fig. 2. Both spectra displayed a polycrystalline structure due to the presence of sharp reflections. The crystalline reflections at 8.3, 19.8, 24.2 and 27.5° (2θ value) on curve a were characteristic of Pal (Cao et al., 2008). The crystalline reflection at 8.3° was still observed clearly for the CPN (curve b), indicating that the incorporation of PPy did not alter the crystal structure of Pal. This unchanged crystal structure of Pal demonstrated that the PPy introduced by rapid electropolymerization acted only as a conducting coating layer of Pal. Liu and Tsai (2003) also reported that PPy played a role as a coating layer in the preparation of PPy/caprolactam-modified montmorillonite.

It was noteworthy that a broad reflection ranging from 15.0 to 37.5° appeared on the XRD pattern of the CPN (curve b), which was attributed to the amorphous structure of PPy (Yang et al., 2002). The amorphous crystallinity of the electrodeposited PPy was further proven by the fact that no other obvious reflections for PPy were observed.

3.3. Electrochemical behaviors of the drug-loading system

PPy was electrically conductive due to its uninterrupted and ordered π-conjugated backbone. As a result, the CPN could be regarded as a good

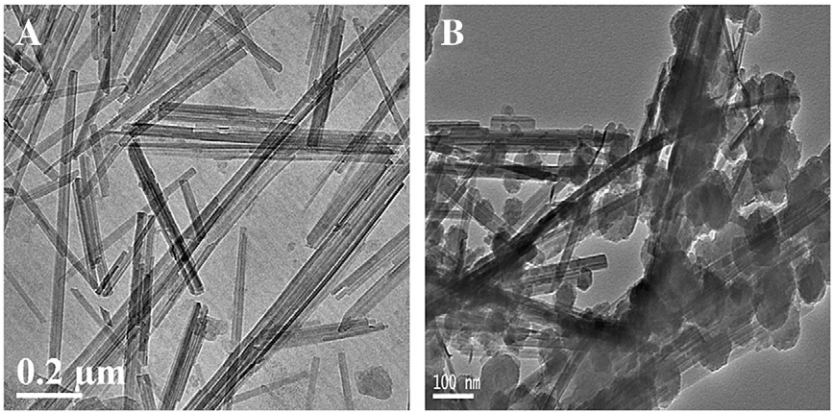

Fig. 1. TEM images of Pal (A) and CPN (B).