Materials Letters 164 (2016) 156–159

Contents lists available at ScienceDirect

Materials Letters

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

Direct synthesis of carbon microspheres under acidic conditions and fenofibrate release

Xiufang Wang, Xiaojing Zhu, Sha Wang, Yufang Pan, Yong Tian *

College of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, China

ARTICLE INFO

Article history:
Received 26 August 2015
Received in revised form
14 October 2015
Accepted 30 October 2015
Available online 31 October 2015

Keywords:
Carbon microspheres
Porous materials
Carbon materials
Fenofibrate
Release

ABSTRACT

Mesoporous carbon microspheres were prepared through a novel direct method under acid-catalyzed conditions, which not only avoided the complicated, time-consuming property of hard-template method, but also avoided the nonporous nature of carbon microspheres by hydrothermal method. Fenofibrate (FFB) was selected as a model drug and was loaded through incipient wetness impregnation. In vitro drug release results further showed that FFB incorporation into the materials significantly increased its release rate compared with that of pure crystalline FFB.

1. Introduction

Carbon microspheres are attracting increased attention because of their potential applications in drug delivery, adsorbent fabrication, and energy storage. Two methods are mainly used to synthesize carbon microspheres [1,2]. One is the hard-template method, which involves numerous experimental steps. Thus, the hard-template method is expensive, complicated, time consuming, and unsuitable for large-scale production. The other method is hydrothermal synthesis, which is widely used to prepare carbon microspheres. However, this method involves high temperature and high pressure. The low pore volume and nonporous nature of carbon microspheres also largely hinder their applications [3].

Combining hydrothermal synthesis with self-assembly process has recently been successfully utilized to synthesize mesoporous carbon microspheres [4]. In literature, most reported mesoporous carbon microspheres have been prepared under alkaline conditions. However, acidic conditions are believed to be preferred over basic conditions because acidity can facilitate and enhance hydrogen and coulombic interactions between phenolic resin precursors and amphiphilic block copolymers [5]. Moreover, methods with easy and generalizable conditions are crucial to the functionalization of mesoporous carbonaceous materials, such as in situ metal-ion introduction [6]. Wei et al. [7] also synthesized mesoporous microspheres by combining hydrothermal treatment with acid-assisted phenol resol and F127 self-assembly approach. However, the direct soft-template synthesis of mesoporous carbon microspheres by self-assembly of copolymer and carbon precursors is challenging because of the rapid polymerization of the carbon source (resorcinol/formaldehyde, RF) under strongly acidic conditions. To our best knowledge, mesoporous carbon microspheres are rarely prepared under acidic conditions through direct RF and F127 self-assembly method, particularly with metal content. In the present work, we demonstrated an easy self-assembly approach to preparing Fe-containing mesoporous carbon microspheres under acidic (HCl) conditions. The entire procedure was low cost, simple, convenient, and suitable for large-scale industrial production. FFB, as a poorly H_2O-soluble, was selected as a model drug. Carbon microspheres loaded with FFB were then developed to increase the FFB release rate, for the potential application in targeted drug release.

2. Materials and methods

The synthesis of carbon microspheres is illustrated in Fig. 1. In a typical procedure, 0.46 g of $FeCl_3 \cdot 6H_2O$ was dissolved in 40 mL of HCl solution (6.66 mL of concentrated HCl dissolved in 5 mL of alcohol and 35 mL of H_2O). Then, 0.28 g of F127 was added with stirring, after which 1.25 g of resorcinol was added. Exactly 0.6 mL of formaldehyde (37%) was gradually added to this solution. After filtration, the sample was heated to 800 °C for 3 h under flowing N_2 and was labeled CS.

* Corresponding author.
E-mail address: tian_yong_tian@163.com (Y. Tian).

http://dx.doi.org/10.1016/j.matlet.2015.10.151
0167-577X/

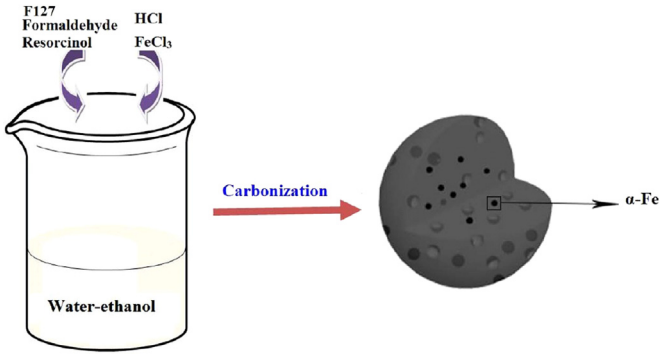

Fig. 1. The illustration for synthesis procedure of carbon microspheres.

In the incipient wetness impregnation, 1 mL acetone solution of FFB (20 mg/mL) was added dropwise to 100 mg CS. The mixture was dried and denoted as FFB-CS. Drug release was conducted by a dissolution apparatus(120 rpm, 37 °C). A 0.15 g FFB-CS was added to 1000 mL of 0.3% sodium dodecyl sulfate (SDS) solution. At predetermined time intervals, 5 mL of the solution was withdrawn, and an equal amount of fresh medium was instantly added. The solution was analyzed by UV–vis spectrophotometry at λ=289 nm. Each experiment was conducted in triplicate.

SEM was performed using LEO 1530VP (Germany).TEM was conducted on a JEOL 2011 microscope. N_2-sorption isotherms were obtained using a volumetric adsorption analyzer (Micromeritics Tristar 3020). XRD patterns were recorded on a multipurpose diffractometer (PAN Analytical Inc. X'Pert Pro., MPD) with Cu radiation. DSC was performed on an STA449C thermal analyzer under N_2 flow at a heating rate of 10 °C/min.

3. Results and discussion

Fig. 2 shows the SEM (a, b) and TEM (c) images of the carbon microspheres. Fig. 2a shows that pure FFB drug was structured as stone-like, non-uniform nanoparticles ranging from 2 μm to 10 μm. The carbon products were dispersed microspheres with around 3 μm diameter and a smooth surface (Fig. 2b). Fig. 2c shows that dark Fe nanoparticles with diameters of around 18 nm were embedded in the carbon substrates. One possible formation mechanism was as follows. EO blocks of pluronic block copolymers F127 and RF were protonated under highly acidic conditions. Coulombic interaction was induced in the self-assembly of F127-resol through the I+X−S+ mechanism, in which the negatively charged Cl^- was the mediator [5]. During cross-linking reaction, resol and $FeCl_3$ molecules were trapped in the spherical micelles of F127 because of strong interactions. F127 decomposed to form mesopores, RF was converted to the carbon framework, and $FeCl_3$ was reduced to Fe nanoparticles during carbonization.

The N_2-sorption isotherms and pore-size distributions (PSD) of CS and FFB-CS are shown in Fig. 3. The N_2-sorption isotherms of the samples (Fig. 3A) were type IV, indicating mesoporous materials. The PSD curves of CS (Fig. 3B) showed pores centered at 6.5 nm, which were mainly derived from the removal of F127 copolymers. Meanwhile, the N_2-sorption isotherms of FFB-CS (Fig. 3A) were also type IV, with pore-size distribution that was similar to that of CS. The isotherm displayed decreased N_2-adsorption capacity after FFB loading, as also reflected by the decrease in pore volume and specific surface area. The pore volume and specific surface area of FFB-loaded carbon decreased from 0.39 cm^3/g to 0.28 cm^3/g and from 668 m^2/g to 515 m^2/g, respectively. These findings confirmed that FFB was successfully incorporated into the mesoporous channels.

Fig. 4A shows that the characteristic diffraction peaks of FFB were observed at 16.6°, 20.7°, 22.1°, 24.6°, 27.3°, 30.3°, and 36.7° (JCPDS Card no. 00-045-1770), indicating a highly crystalline substance.For CS and FFB-CS, angles of 44.7°,65.0°, and 82.3°can be respectively indexed to the (110), (200), and (211) diffraction peaks of body-centered cubic α-Fe (JCPDS Card No. 06-0696). The 26.0° angle can be indexed to the (002) diffraction peak of graphite (JCPDS Card no. 008-0415).Carbon-microsphere graphitization was attributed to Fe catalysis. However, no characteristic peaks of FFB were detected in the pattern for FFB-CS, indicating that FFB was almost completely converted from a crystalline to an amorphous state after loading into carbon microspheres. This finding may be due to the space-confinement effect of pore channels. Crystallization inhibition was typical of confinement in spaces that were smaller than 20 times the molecular size. The molecular dimension of FFB was 1.04 nm × 1.04 nm × 0.62 nm. The pore size of carbon microspheres was 6.5 nm, which was insufficiently large for compounds to form a crystalline state. Fig. 4B shows the DSC results of FFB and FFB-CS. A single sharp endothermic melting peak at 82 °C was observed for original FFB, and this finding agreed with the melting point of crystalline FFB [8]. However, no trace of an endothermic peak at 82 °C was observed for FFB-CS, showing that the drug was in a noncrystalline state.

The cumulative dissolution release of pure FFB did not exceed 40% in 0.3% SDS medium solution after 60 min (Fig. 5). By contrast, the cumulative release of FFB-CS exceeded 80% after 60 min with significant increase. Pure FFB drug was composed of microsized crystalline particles, and nanopores of mesoporous carbon microspheres restricted FFB particles to the nanometer range, whereas particle sizes of the drug incorporated in the pore channels significantly decreased compared with microsized crystalline FFB particles. The decrease in particle size significantly promoted the dissolution rate of drugs. Reduction of FFB particle size can also be achieved by milling. The advantage was that the procedure for drug loading was omitted. The disadvantage was that the approach required special apparatus such as bead milling or high pressure homogenization [9]. The resultant small particles with high surface energy were easy to aggregate, due to the reason that

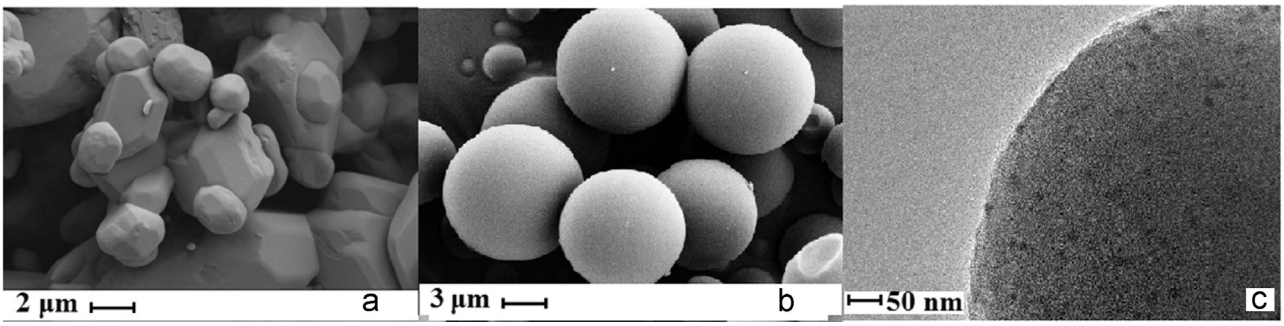

Fig. 2. SEM (a, FFB; b, CS) and TEM (c, CS) images of the carbon microspheres.