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A geometric pore adsorption model for predicting the drug loading capacity of insoluble drugs in mesoporous carbon

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ABSTRACT

In this work, a simple and accurate geometric pore-adsorption model was established and experimentally validated for predicting the drug loading capacity in mesoporous carbon. The model was designed according to the shape of pore channels of mesoporous carbon and the arrangement of drug molecules loaded in the pores. Three different small molecule drugs (celecoxib, fenofibrate and carvedilol) were respectively loaded in mesoporous carbon with different pore sizes. In order to test the accuracy of the established model, nitrogen adsorption–desorption analysis was employed to confirm the pore structure of mesoporous carbon and to calculate the occupation volume of the adsorbed drugs. The adsorption isotherms of celecoxib were systematically investigated to describe the adsorption process. It was found that the experimental results of adsorption capacity were all in the range of the predicted values for all the tested drugs and mesoporous carbon. The occupation volumes calculated from the model also agreed well with the experimental data. These results demonstrated that the established model could accurately provide the range of drug loading capacity, which may provide a useful option for the prediction of the drug loading capacity of small molecule drugs in mesoporous materials.

1. Introduction

In recent years, inorganic porous materials such as porous silica and porous carbon have opened up a new path for the development of drug delivery system (Zhang et al., 2013; Chen et al., 2004; Niu et al., 2013; Hu et al., 2014; Zhang et al., 2014). Among those materials, mesoporous carbon has gained tremendous attention owing to its distinct characteristics, such as easy shape control, large surface area and huge pore volume. A lot of small molecule insoluble drugs, such as anti-cancer drugs (Rodney et al., 2007), antimicrobials (Monica et al., 2011) and anti-inflammatory drugs (Luo et al., 2011; Chia-Hung et al., 2008; Wang, 2011; Heister et al., 2012) have been successfully loaded into mesoporous materials and gained improved dissolution rate and efficacy. The factors that govern the adsorption of drugs on mesoporous materials play an important role in understanding the drug loading process. Heister et al. (2012) reported that the high drug loading capacity of carbon nanotubes was due to their high surface area. Zhao et al. (2012a) reported that the drug loading capacity of mesoporous carbon was directly correlated to its pore volume. Though significant efforts have been taken to study the relationship between the drug loading capacity and the properties of mesoporous materials, the maximum drug loading capacity still can not be accurately predicted. So establishing an accurate model to predict the drug loading capacity as well as to show the correlation of the capacity and material structure is of great importance to the selection of a suitable mesoporous material for a given drug and to meet the clinical dosage requirements of the drug.

There have been several studies of geometric model describing the loading process of protein drugs in mesoporous materials and predicting the amount of adsorption (Lung-Ching et al., 2011; Miyahara et al., 2007). However, the established models for protein drugs may not be quite suitable for small molecule drugs because the structure, size and properties of protein drugs are completely different from that of small molecule drugs (George and Abraham, 2006; Whittleseya and Sheaa, 2004).

The purpose of this study is to establish a geometric model to predict the drug loading capacity of small molecule drugs in mesoporous materials. The model was constructed based on the

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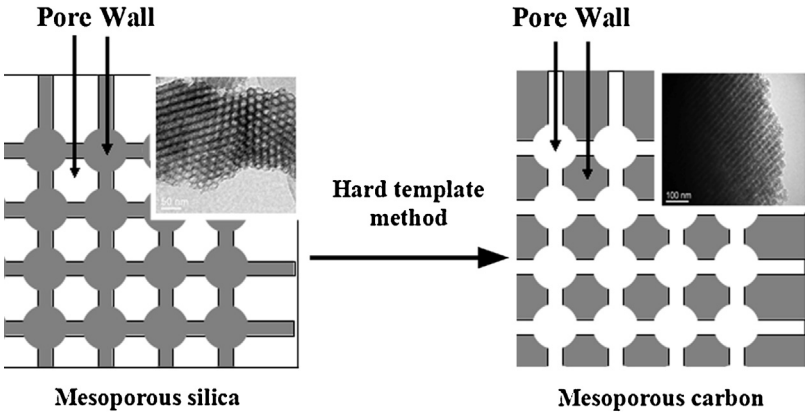

Fig. 1. The synthesis process of mesoporous carbon.

size of the adsorbed drug and the pore structure of mesoporous carbon. Mesoporous carbon with different pore sizes was prepared using mesoporous silica as a template. Celecoxib (CEL) were loaded into mesoporous carbon then the adsorption capacity of the drug was predicted. Nitrogen adsorption–desorption analysis was carried out to validate the accuracy of the model. To further confirm the suitability of the model, another two small molecule drugs, fenofibrate and carvedilol, were also tested.

2. Experimental

2.1. Materials

Celecoxib (purity>99.0%) and carvedilol (purity>99.0%) was kindly supplied by Shenyang Funing Pharmaceutical Co., Ltd., fenofibrate (purity>99.0%) was kindly supplied by Yinhe Pharmaceutical Factory (Wuhan, China). All other chemicals were of analytical grade.

2.2. Synthesis of mesoporous carbon with different pore sizes

Mesoporous carbon with different pore sizes was synthesized on a hard template method. The template of face-centered cubic mesoporous silica with different pore sizes was prepared using a temperature-regulation method as reported (Zhu et al., 2014). Then, 1 g of mesoporous silica was impregnated with a solution containing 1.0 g sucrose, 0.1 g H_2SO_4 and 2.4 g H_2O. The obtained mixture was reacted in an oven at 80 °C for 6 h and then at 160 °C for another 6 h. After that, a solution containing 0.6 g sucrose, 0.06 g H_2SO_4 and 1.6 g H_2O was used to impregnate the mixture. The obtained solid powder was carbonized at 700 °C for 3 h under N_2. The silica template was removed by 10% hydrofluoric acid at 25 °C. Then the mesoporous carbon with different pore sizes was obtained.

2.3. Nitrogen adsorption–desorption analysis

Nitrogen adsorption–desorption analysis was conducted using a nitrogen adsorption analyzer (V-Sorb 2800P, China). The mesoporous carbon samples were degassed at 120 °C for 12 h, while the drug loaded samples were degassed at 50 °C for 12 h to remove the physically adsorbed water. Information about the pore structure of mesoporous carbon was obtained and the amount of the adsorbed drugs on mesoporous carbon was calculated.

2.4. Drug adsorption on mesoporous carbon

A series of drug solutions with concentrations ranging from 0.25 to 20 mg/mL were prepared. 20 mg of mesoporous carbon with different pore sizes and 4 mL drug solution were respectively mixed in plastic tubes and then placed in a shaking bed incubator

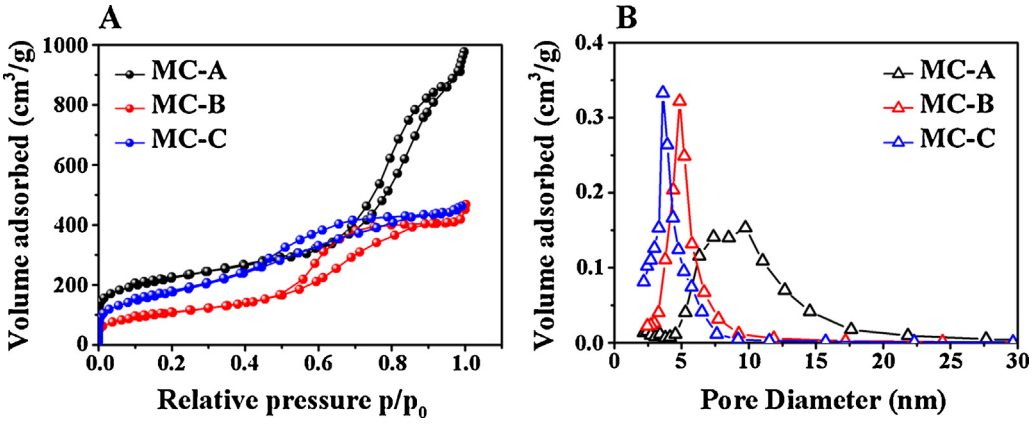

Fig. 2. Adsorption–desorption isotherms (A) and pore size distributions (B) of mesoporous carbon with different pore sizes.