Materials Science and Engineering C 59 (2016) 43–52

Contents lists available at ScienceDirect

Materials Science and Engineering C

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

Impact of pore characteristics of silica materials on loading capacity and release behavior of ibuprofen

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ARTICLE INFO

Article history:
Received 28 April 2015
Received in revised form 30 August 2015
Accepted 26 September 2015
Available online 30 September 2015

Keywords:
Dissolution efficiency
Solid dispersion
Physical stability
Ibuprofen
Bimodal porous silica

ABSTRACT

Impact of pore characteristics of porous silica supports on loading capacity and release behavior of ibuprofen was investigated. The porous silica materials and ibuprofen-loaded porous silica materials were thoroughly characterized by N_2-sorption, thermal gravimetric and derivative weight analyses (TG-DTW), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR), scanning electron microscope (SEM), transmission electron microscope (TEM) to determine the physical properties of materials, amount of ibuprofen adsorbed and position of ibuprofen. The detailed characterization reveals that the ibuprofen molecules adsorbed inside the mesopores. Increasing the mesopore size from 5 nm to 10 nm increased the ibuprofen loading from 0.74 to 0.85 mmol/g, respectively. Incorporation of macropore into the structure of porous silica materials enhanced the ibuprofen loading capacity of 11.8–20.3%. The ibuprofen-loaded bimodal meso-macroporous silica materials exhibited the highest dissolution of 92 wt.% within an hour. The ibuprofen particles deposited on the external surface of the porous silica materials showed a lower dissolution rate than the ibuprofen adsorbed inside the mesopores due to the formation of ibuprofen crystalline.

1. Introduction

The majority of novel innovative drug candidates suffer from poor solubility which reduces their bioavailability, especially in oral drug delivery that is still the most common and preferable administration route [1,2]. Numerous techniques are now available that can enhance solubility of such compounds [3,4]. These include changing their physicochemical properties such as increasing the exposed surface area by reducing the particle size or using a form that possesses a less ordered crystal structure [5,6]. The solubility of amorphous form of drug was typically 2–4 times higher than that of the crystalline form [7]. However, the use of pharmaceuticals in the amorphous form is limited owing to their low stability [7]. Therefore, the improvement of solubility of poorly water soluble drug without compromising the stability remains a challenge for pharmaceutical industry.

Immobilization of drug compounds into porous carrier materials can overcome the stability problems due to the interaction between drug molecules and the surface of the porous materials [8–10]. Microporous and mesoporous materials such as zeolites and mesoporous silica are widely used as drug delivery carriers due to their potential applications including biocompatibility, low toxicity, large surface area, and the ability to modify the physicochemical properties [11,12]. It has been reported that the surface area and the pore size of the porous materials have a great effect on the drug loading capacity and the dissolution rate. For instance, the amount of drug adsorbed is proportional to the surface area of the materials, i.e., the large surface area of the materials can uptake the large drug molecules in case of complete monolayer adsorption. The material with the large surface area usually contains micropores, resulting in poor diffusion of dissolution media and drug molecules. Increasing pore size of the material can diminish diffusion limitation. However, the material with large pore size might be not able to maintain the drug in the amorphous form, i.e., the possibility for the formation of an organized crystal structure inside the pore.

It has been shown recently that the materials with bimodal (meso-macro) pore size could enhance mass transfer due to the presence of macropores while maintaining the large surface area simultaneously [13]. Despite the significant number of papers reporting the advantage of bimodal meso-macroporous materials for catalysis [13,14] and adsorption [15,16], a few studies have considered the use of such materials as porous material carriers for drug delivery systems, and the effect of the presence of macropores on the loading capacity and releasing behavior of drug is not particularly well understood. In this work, comparative investigations of the adsorption capacity and release of a typical poorly soluble model compound, ibuprofen, over unimodal mesoporous and bimodal meso-macroporous silica materials were conducted. The porous silica materials before and after ibuprofen loading were

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http://dx.doi.org/10.1016/j.msec.2015.09.095
0928-4931/

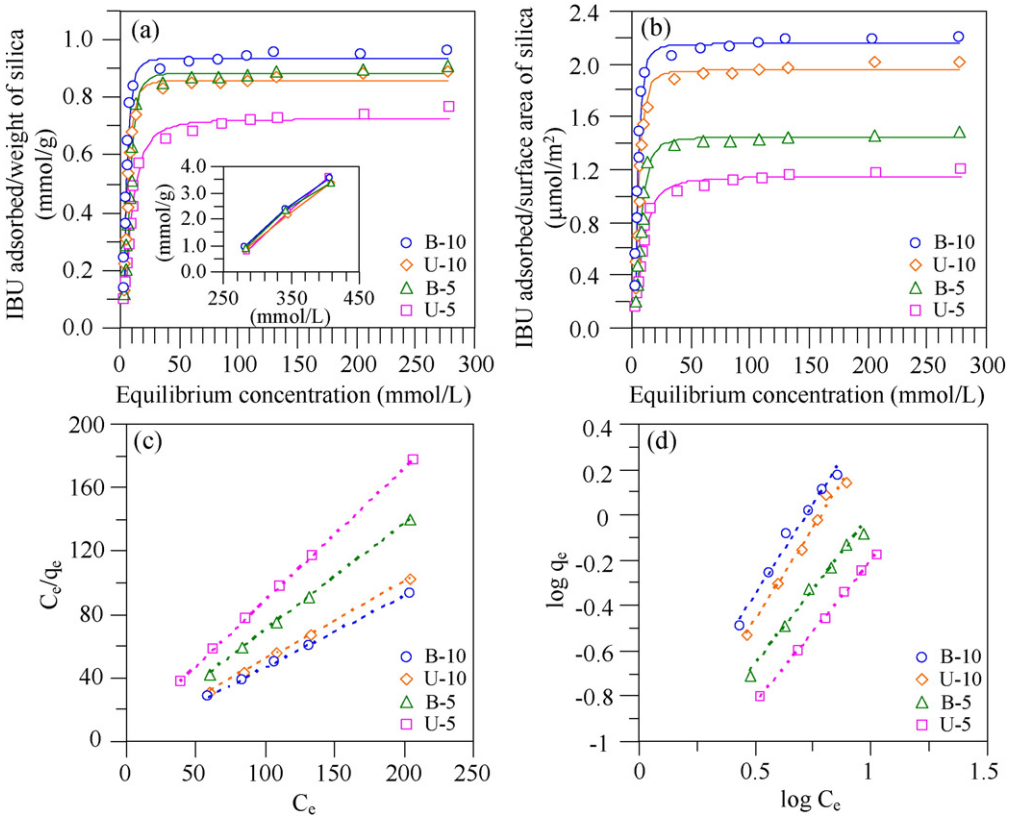

Fig. 1. Ibuprofen adsorption isotherms of the studied porous silica materials expressed as the amount of adsorbed ibuprofen/weight of silica (a) and as the amount of adsorbed ibuprofen/surface area of silica (b). The inset in Fig. 1a is the amount of ibuprofen precipitated onto the porous silica materials because the concentration of ibuprofen exceeds the saturated concentration. The Langmuir (c) and Freundlich (d) isotherm plots of ibuprofen adsorption onto the studied porous silica materials.

systematically characterized by means of N_2-sorption, X-ray diffraction, thermal gravimetric analysis (TGA), scanning electron microscope (SEM). The results showed that the pore structure of silica materials really make a significant difference on the adsorption capacity and release profile.

2. Experimental

2.1. Materials

Chitosan with 80% deacetylation was purchased from Eland Corporation. Acetic acid, hydrochloric acid, and sodium hydroxide were purchased from Sigma–Aldrich Company. Sodium silicate ($Na_2Si_3O_7$: 30 wt.% SiO_2, 4 wt.% NaOH) was obtained from Thai Silicate Company. All chemicals and reagents are of analytical grade and used without any further purification.

2.2. Preparation of unimodal and bimodal porous silica materials

Bimodal (meso–macro) porous silica materials were synthesized via a sol–gel process using sodium silicate as a silica source and chitosan as a template. In a typical synthesis, 0.4 g chitosan was dissolved in 100 mL of 1% *v*/*v* acetic acid in deionized water at room temperature for 12 h. Then 5.5 g sodium silicate, primarily diluted with 10 mL deionized water, was slowly added to the chitosan solution under vigorous stirring. Subsequently, the pH value of the mixture was quickly adjusted to 6 by the addition of 2 M HCl. The mixture was stirred at 40 °C for 3 h and after that it was poured into a Teflon container and aged in autoclave at either 60 or 100 °C for 24 h in order to vary mesopore size of the materials. The obtained product was filtered, washed several times with deionized water, dried at 120 °C for 12 h and calcined at 600 °C for 4 h at a heating rate of 2 °C/min. Unimodal porous silica materials having equivalent mesopore size to the bimodal porous silica materials were synthesized using the similar condition as mentioned above except for the addition of chitosan. The unimodal and bimodal porous silica materials are denoted as U-*X* and B-*X* in which *X* is the mesopore size.

2.3. Drug loading

The ibuprofen-loaded porous silica materials were prepared by impregnation method. 1 g calcined porous silica power was suspended in 30 mL hexane containing different ibuprofen concentrations (1, 1.5,

Table 1
BET surface area, pore diameter, total pore volume, mesopore volume and macropore volume of different porous silica materials and ibuprofen-loaded porous silica materials.

Sample	BET surface area (m^2/g)	Mean pore diameter (nm)	Total pore volume (cm^3/g)	Mesopore volume (cm^3/g)[a]	Macropore volume (cm^3/g)[b]
U-5	634	5.0	0.85	0.82	0.03
30-IBU/U-5	412	3.9	0.42	0.41	0.01
U-10	441	12.2	1.18	1.13	0.05
30-IBU/U-10	324	10.0	0.65	0.63	0.02
90-IBU/U-10	24	–	0.09	0.09	–
B-5	615	5.0,90	2.36	1.38	0.98
30-IBU/B-5	366	3.9,90	1.55	0.63	0.92
B-10	436	12.2,140	2.05	1.02	1.03
30-IBU/B-10	294	10.0,140	1.45	0.54	0.91
90-IBU/B-10	36	90	0.24	0.09	0.15

[a] Mesopore volume was calculated at pores smaller than 50 nm determined by N_2-sorption.
[b] Macropore volume was calculated at pores larger than 50 nm determined by N_2-sorption.