Nanoporous Silica and Its Application in Drug Delivery

Chanatip Samart[1*], Weerayut Srichaisiriwech[1]
and Chatchawan Sookman[2]

[1]Department of Chemistry, Faculty of Science and Technology, Thammasat University, Pathumtani 12121, Thailand

[2]Chemical Engineering Division, Faculty of Engineering, Rajamangala University of Technology Krungthep, Bangkok 10120, Thailand

**Corresponding author. E-mail: chanatip@tu.ac.th*

ABSTRACT

Nanoporous silica was prepared and tested for its application in drug delivery. In the synthesis, tetraethyl orthosilicate (TEOS) was employed as a silica source and pluronic (P123) was chosen as a structure directing agent. The mixture was heated at various temperatures (30°C -60°C) and reaction times (2-4 hours). The obtained product was treated by hydrothermal and dried in hot air oven. Finally, it was calcined at 600°C to yield nanoporous silica of different physical properties. Indigo carmine was subsequently loaded by soaking the silica in the solution of indigo carmine for 48 hours. The releasing rate of the model drug was evidently affected by the physical properties of the nanoporous silica prepared. At the condition of 60°C for 4 hours, the releasing was high because the pore size of the silica was too large comparing with the molecular size of indigo carmine. Furthermore, high temperature also increased the polymerization resulting in a reduction of silanol group (Si-OH) need for binding with the model drug. At temperature of 30°C, the pore size was too small for indigo carmine. However, after hydrothermal step the pore diameter was enhanced which is suitable for indigo carmine.

Key words: Nanoporous silica, Drug releasing, Drug delivery system

INTRODUCTION

Mesoporous silica is a material which have pore diameter in the range of 2-50 nm. It has attractive features, such as large pore volume, uniform pore size distribution, and large surface area. Furthermore, it is also non-toxic and biocompatibility material. All these properties promote many research themes. Mesoporous silica is used versatile such as catalyst support (Subrahmanyam, 2004; Ooi et al., 2005), CO_2 capture (Khatri et al., 2005), remove of heavy metal in waste water (Sayari et al., 2005), and template of carbon nanotube synthesis (Zhu et al., 2002).

Application in drug delivery of mesoporous silica is very interesting because the uniform of pore size can control the releasing rate of drug. Moreover, silica has high stable structure. Porous hollow silica can be used as drug carrier. The drug was collected in the cavity and released through the pore (Li et al., 2004; Chen et al., 2004) The effect of coating conditions and media conditions on controlling vitamin B1 released of tablet silica was studied (Wu et al., 2007). Qu et al., (2006) used mesoporous silica type MCM-41 to study the effect of pore regulating and morphology on controlled release of captropil. The largest and smallest pore size gave the fast releasing rate. Therefore, pore structure regulation can controll releasing rate. This work synthesizes nanoporous silica (2-10 nm) and studies the effect of synthesis conditions on its physical properties which affect indigo carmine releasing.

MATERIALS AND METHODS

Synthesis of nanoporous silica

The mixture of 2 g pluronic P123 (Aldrich, USA) and 72 ml of 2 M HCl was stirred at the reaction temperatures (30-60°C) for 4 hrs. Tetraethoxysilane (Fluka, Italy) and Pluronic P123 (Aldrich, USA) at the ratio of 3:1 poured in the previous mixture and stired for the reaction times (2-4 hrs). Hydrothermal treatment was applied after the end of reaction time for 0-3 hrs. The mixture was filtered to obtain the silica solid particle and dried at 100°C for 6 hrs. The dried solid particle was calcined at temperature of 600°C for 4 hrs. The nanoporous silica was characterized for pore diameter, surface area, pore volume, and pore size distribution by nitrogen adsorption desorption technique using Autosorb-1c. The pore diameter pore volume and pore size distribution were calculated by Barret-Joyner-Halenda (BJH) model. The surface area was given by Brunauer-Emmet-Teller (BET) model.

Loading and release study

The nanoporous silica was soaking in 10% wt of indigo carmine (Himedia, India), a drug model for 48 hrs. It was filtered and dried at temperature of 60°C for 6 hrs. After drug loading, the sample was weighed about 0.5 g and put in to phosphate buffer as simulated body fluid. The releasing of indigo carmine, at time intervals, was measure by UV-vis spectrophotometer (CECIL, CE1010) at λ= 610.2 nm.

RESULTS AND DISCUSSION

Physical properties of nanoporous silica

Figureure 1 showed the surface area of nanoporous silica at various reaction times with and without hydrothermal treatment. The surface area increased when the reaction time was increased. Hydrothermal treatment can improve surface area from 400-550 m2/g at without treatment to 700-800 m2/g at 3 hrs treatment. The high reaction temperature (60°C) decreased surface area, however, the high reaction temperature provided the large surface area after hydrothermal treatment.

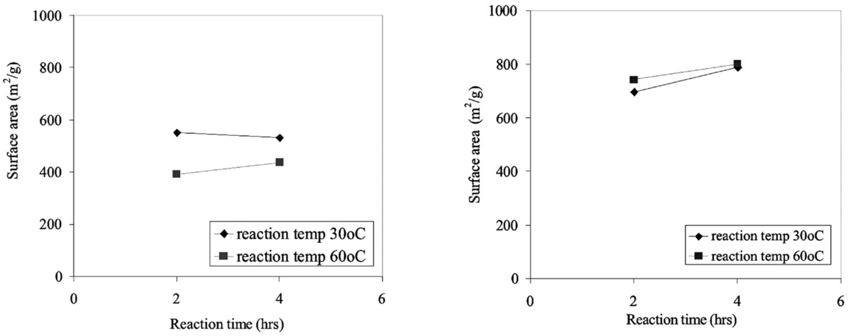


Figure 1. Surface area of nanoporous silica at various reaction times and reaction temperature: (a) without hydrothermal (b) with hydrothermal 3 hrs.

Pore volume also had to concern because large volume can more drug loading. The reaction temperature of 30°C showed decreasing of pore volume when the reaction time was increased but the higher reaction temperature (60°C) gave the larger pore volume at longer reaction time as show in Figure 2a. Hydrothermal treatment enlarged pore volume 100% and showed increasing of pore volume when the reaction time was increased at all reaction temperatures (Figure 2b).

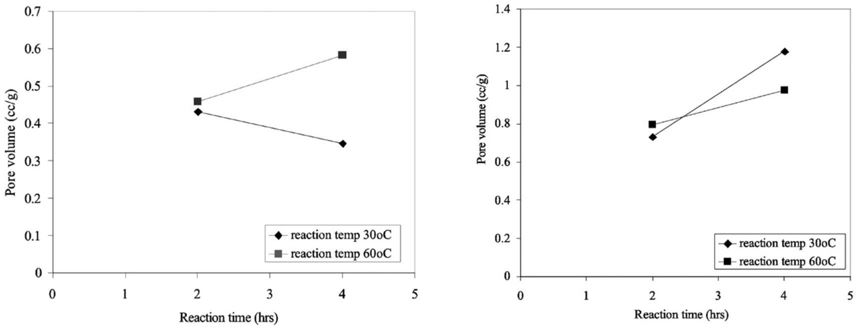


Figure 2. Pore volume of nanoporous silica at various reaction times and reaction temperatures: (a) without hydrothermal (b) with hydrothermal 3 hrs

Figureure 3 presented the pore size distribution of nanoporous silica at reaction temperature of 30°C and reaction times of 2 and 4 hrs after hydrothermal treatment for 3 hrs. The uniform pore size was obtained at all conditions. The longer reaction time (4 hrs) provided shifting the distribution curve to smaller pore diameter because it showed the more complete polymerization of silica molecule to obtain compact structure.

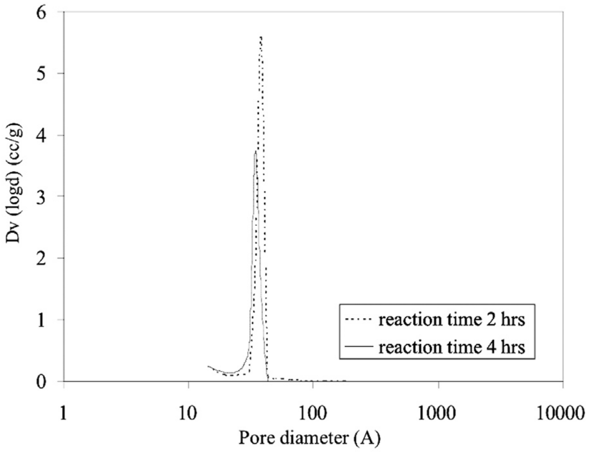
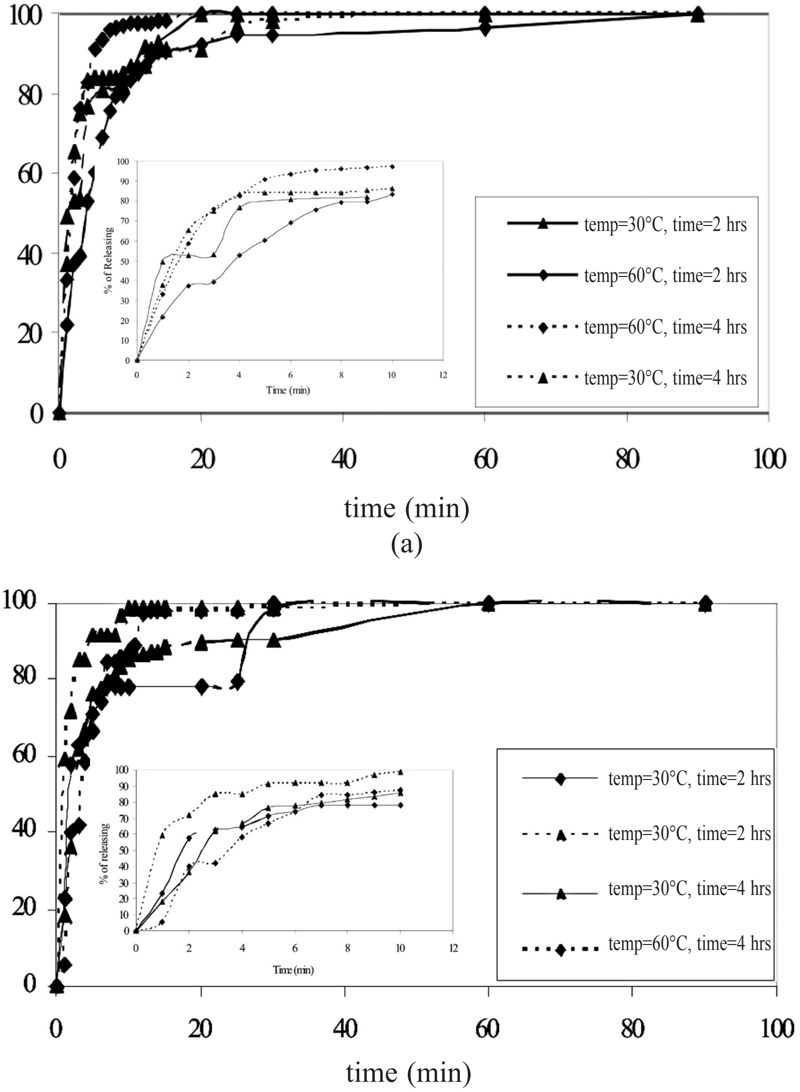


Figure 3. Pore size distribution of nanoporous silica at reaction temperature of 30°C and reaction time of 2 and 4 hrs.

Study of indigo carmine releasing

The releasing behavior was affected by physical properties of nanoporous silica. Figure 4a showed the releasing profiles of indigo carmine from nanoporous silica synthesized with various reaction times and reaction temperatures without hydrothermal treatment. The lower reaction temperature (30°C) gave pore diameter less than 4 nm, therefore, molecule of indigo carmine can not go through the pore cavity to represent fast releasing as shown in triangle with lines. However, the high reaction temperature (60°C) provided large pore diameter (Figure 1a) and the longer reaction reduced the amount of silanol group (Si-OH) which it can not bind indigo carmine. The releasing profile which showed in square with dash line is very fast. The square with solid line is the releasing profile from nanoporous silica in the condition reaction temperature of 60°C and reaction time of 2 hrs to remain more silanol group and suitable pore diameter, there by indigo carmine released slowly. The effect of hydrothermal reduced silanol group to polymerize remaining silanol group, the increasing rates of releasing were obtained as showed in Figure 4b. However, hydrothermal still need in the synthesis nanoporous silica since it gave large pore volume (Figure 2b) which it provided high drug loading.



(a)

(a)

Figure 4. Releasing profiles of indigo carmine from nanoporous silica at various reaction times and reaction temperatures (a) non-hydrothermal (b) hydrothermal at 3 hrs.

CONCLUSION

The releasing behavior of indigo carmine was affected by pore diameter and amount of silanol group. The low synthesis temperature (30°C) provided small pore diameter. The drug can not go through the pore cavity thus, the drug on external surface only released. Pore size can not control the rate of releasing which showed fast rate. The longer reaction time showed the reduction of silanol group due to over polymerization. The interaction between drug and silanol group was reduced which fast releasing still obtained. Therefore, the suitable conditions should to be high temperature but short reaction time. This condition gave the slowest releasing. The effect of hydrothermal treatment expanded pore size and increased pore volume. The drug can transfer to inside easily and large pore volume collected large amount of drug loading. However, the hydrothermal treatment affected silanol group reduction. From this study, nanoporous silica should to develop surface feature such as functionalize on the surface to obtain more interaction between drug and surface which will reduce releasing rate.

ACKNOWLEDGEMENTS

This research have been supporting by Thammasat University Research Fund and Department of Chemistry, Thammasat University.

REFERENCES

Chen, J. F., H. M. Ding, J. X. Wang, and L. Shao. 2004. Preparation and characterization of porous hollow silica nanoparticles for drug delivery application. Biomater. 25: 723-727.

Khatri, R. A., S. S. C. Chuang, Y. Soong, and M. Gray. 2005. Carbon dioxide capture by diamine-grafted SBA-15: a combined fourier transform infrared and mass spectrometry study. Indust. & Eng. Chem. Res. 44: 3702-3708.

Li, Z. Z., L. X. Wen, L. Shao, and J. F. Chen. 2004. Fabrication of porous hollow silica nanoparticles and their applications in drug release control. J. Control. Releas. 98: 245-254.

Ooi, Y. S., R. Zakaria, A. R. Mohamed, and S. Bhatia. 2005. Catalytic conversion of fatty acids mixture to liquid fuel and chemicals over composite microporous/mesoporous catalysts. Energy & Fuels 19: 736-743.

Qu, F., G. Zhu, S. Huang, S. Li, J. Sun, D. Zhang, and S. Qiu. 2006. Controlled release of captopril by regulating the pore size and morphology of ordered mesoporous silica. Microporous & Mesoporous Mater. 92: 1-9.

Sayari, A., S. Hamoudi, and Y. Yang. 2005. Applications of Pore-Expanded Mesoporous Silica. 1. Removal of Heavy Metal Cations and Organic Pollutants from Wastewater. Chem. Mater. 17: 212-216.

Subrahmanyam, Ch., B. Viswanathan, T. K. Varadarajan. 2004. Alkylation of naphthalene with alcohols over acidic mesoporous solids. J. Molec. Catalys. A: Chemical 226: 155-163.

Wu, Z., Y. Jiang, T. Kim, and K. Lee. 2007. Effects of surface coating on the controlled release of vitamin B1 from mesoporous silica tablets. J. Control. Release 119: 215-221.

Zhao, D., J. Feng, Q. Huo, N. Melosh, G. H. Fredrickson, B. F. Chamelka, and G. D. Stucky. 1998. Triblock copolymer syntheses of mesoporous silica with periodic 50 to 300 angstrom pores. Science 279: 548-552.

Zhu, H. W., C. L. Xu, D. H. Wu, B. Q. Wei, R. Vajtai, and P. M. Ajayan. 2002. Direct synthesis of long single-walled carbon nanotube stands. Science 296: 884-885.