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Mesoporous silica nanoparticles as vehicles for drug delivery

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Mesoporous silica nanoparticles as vehicles for drug delivery

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Abstract. Silica-based materials such as mesoporous silica nanoparticle MCM-41 and hollow mesoporous silica have been synthesized at room temperature. Several characterization techniques such as N_2 adsorption-desorption analysis, SEM and FTIR have been employed to assess the formation of the nanoparticles. Rifampicin, commonly used in tuberculosis treatment, was selected as the target drug to assess the ability of the two nanoparticles to host this antibiotic. Following the loading of rifampicin on the particle surface, the dissolution behaviour of rifampicin in a media was investigated. Surface characterizations show HMS exhibits higher surface area as well as pore size and volume compared to MCM-41. However, rifampicin was not attached on the latter particles until it was modified with APTES. HMS particles store more rifampicin molecules on the particle surface than the modified MCM-41. The in-vitro drug release was investigated with buffer phosphate (pH=7.4) and the results shown that the rifampicin-loaded HMS particles were capable of releasing 18% rifampicin content after 77 h. Further investigation was necessary to support the promising application of mesoporous silica nanoparticles for pulmonary drug delivery.

1. Introduction

Silica-based nanoparticles has gained interest due their high performances on surface area, pore volume, pore size as well as loading capacity and biocompatibility [1,2]. Several mesoporous silica nanoparticles such as MCM-41, MCM-48, SBA, FSM and others as well their promising applications have well been documented [3-8]. A unique core-shell structured of mesoporous silica nanoparticles, i.e. hollow interior structure offers higher performance to load drugs on the particle surface [9]. This can help patient during chemo or tumor therapy [10] by increasing the treatment efficiency.

In this study, two different silica-based particles, i.e. MCM-41 with hexagonal structure and hollow mesoporous silica particles have been investigated to assess the ability of the particles to host rifampicin ($C_{43}H_{58}N_4O_{12}$) as the target drug. Rifampicin is an antibiotic drug to treat tuberculosis disease. Previous report on rifampicin loaded on mesoporous silica nanoparticles found that methanol is the best solvent that allow the drug loading up to 52% [11]. However, the use of methanol may need to be inhibited due to the toxic reason. Therefore, we use different solvent in this study. In addition, we also compared different silica nanoparticle structure to assess the particles ability to attract rifampicin as well as their release profile from the particle surface.

2. Experimental

2.1. Materials

Cetyltrimethyl-ammonium bromide (CATB), tetra ethyl ortho silicate (TEOS) and 3-aminoprophyl triethoxysilane (APTES) were purchased from Sigma-Aldrich. Other reagents were analytical grade and were used without further purification.

2.2. Procedures

Two different silica nanoparticles were prepared in this study. Firstly, mesoporous MCM-41 was prepared by dissolving in CTAB in water under constant stirring, followed by the addition of sodium hydroxide solution (2 M) and the mixture was stirred at 80ºC for 1 h. Then TEOS was added slowly and the mixture was further stirred for another 3 h. The solid part was separated, washed and dried in an oven at 328K for 24 h. Finally the particles were calcined at 823K for 5 h to remove the template. In this study, the name of MCM-41 was simplified to MCM. Secondly, hollow mesoporous silica (HMS) was prepared by mixing NaOH, PVP-K30 and CTAB prior to the addition of TEOS. The mixture was then put in the autoclave and heated up to 120ºC for 48 h. The solid part was separated and dried prior to calcine the particles at 630ºC for 10 h.

Rifampicin was loaded by soaking the mesoporous silica nanoparticles into 500 mL ethanol solution containing 1 g of rifampicin under ultrasonic treatment for 5 min. The mixture was further stirred for 24 h. The solid part was separated, dried and stored for further use. The particles and loaded-particles were characterized using Fourier Transform Infrared (FTIR), Scanning Electron Microscope (SEM) and nitrogen sorption.

For release assessment, the rifampicin-loaded particles were placed in a dialysis bag prior to immerse the bag in 200 mL of PBS solution containing tween 80 (pH 7.4). The solution was stirred at room temperature and 400 rpm for dissolution testing. 0.5 mL of dissolution samples were withdrawn regularly followed with media replacement. The samples were analysed by using a UV-vis spectrophotometer (Shimadzu, UVmini-1240).

3. Results and Discussion

3.1. MSN Characterization

Figure 1 displays SEM micrograph of the two silica nanoparticles investigated in this study.

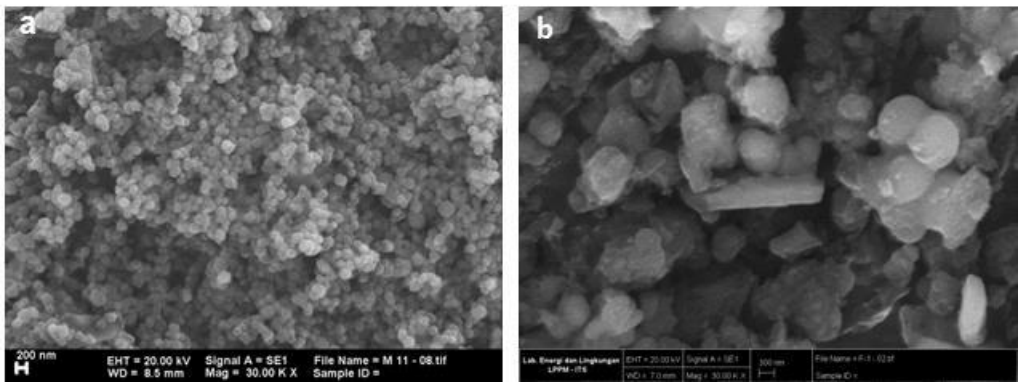

Figure 1. Scanning electron micrographs of (a) MCM and (b) HMS

It can be seen that the MCM silica has spherical morphology and these spheres are uniform with sizes around 150 to 200 nm and they are agreeing with previous reports [11-12]. For HMS particles, the irregular shapes were observed with particle size around 500 nm.

Table 1 shows the BET surface area, pore diameter and pore volume of the MCM and HMS.

Table 1. Properties of the two synthesized particles

Sample	Surface area (m^2/g)	Pore size (nm)	Pore volume (cm^3/g)
MCM	470	6.46	0.901
HMS	309	2.68	0.153

The surface area of MCM was found 470 m^2/g which is lower than reported in literature [11, 13]. For HMS, the surface area was 309 m^2/g while others reported slightly higher (410 m^2/g) [12]. The pore size distribution of MCM and HMS particles observed at around 6.46 and 2.68 nm, thus suggesting the formation of mesoporous structure at the particle surface. Pore volume of MCM and HMS were around 0.9 and 0.15 cm^3/g, respectively. Pore volume of the synthesized particles was slightly higher (0.7-0.8 cm^3/g [13-14]) for MCM, but much lower for HMS (0.34 m^3/g) [15].

3.2. Rifampicin loading and release

Rifampicin loaded onto the particle surface was quantified by using a spectrophotometry method. The amount of rifampicin loaded on the particles surface is shown in figure 2.

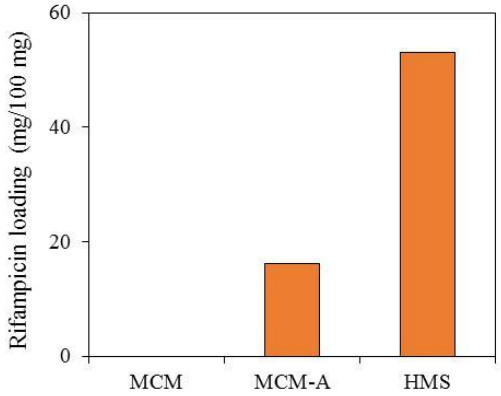

Figure 2. Rifampicin loaded on the particle surface

As seen in figure 2 that MCM and HMS exhibited different characteristics as the host for rifampicin. The amount of rifampicin loaded on the MCM surface was neglected; however, the target molecule was successfully loaded on the surface of HMS with a capacity loading of 53 mg/100 mg. However, Mohseni *et al*. (2015) reported MCM particles can be acted as a host for rifampicin [11]. The low concentration of rifampicin in the release solution maybe below the detection limit of our instrument and thus, no rifampicin reported during our study. To improve the ability of MCM to hold rifampicin, the particle surface was modified with APTES [15-17]. The amount of rifampicin loaded on the MCM surface was around 16 mg of rifampicin/100 mg (figure 2), suggesting a considerable effect of surface functionalization on the uptake of rifampicin. The difference can be explained by the interactions of rifampicin functional groups with MCM surface. Amine modification enhances the particle surface charge which in turn results stronger interaction between the target molecule and the silica surface

[18]. Different case with MCM, HMS particles are able to host rifampicin without any surface modification. Different particle morphology influences the uptake of the target molecule [19].

To confirm the presence of rifampicin in the particle surface, the particles were subjected to FTIR analysis. Figure 3 shows the FTIR spectra of MCM loaded with rifampicin. The presence of carboxyl vibration bands at 1720 cm^{-1} together with C-H stretching vibrations at 2850-2950 cm^{-1} suggested the alkyl group of rifampicin has been incorporated into the host matrix. Similar results were observed for HMS (not shown).

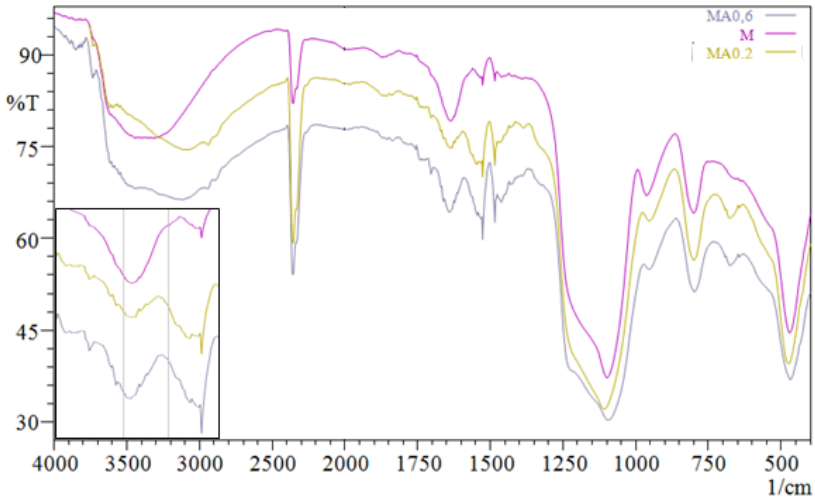

Figure 3. FTIR analysis of MCM and modified MCM-rifampicin

3.3. Rifampicin release study

The release studies of rifampicin from both modified MCM and HMS particles at room temperature were performed in inorganic solution of PBS. Figure 4 shows the cumulative release kinetics of rifampicin from the two particles.

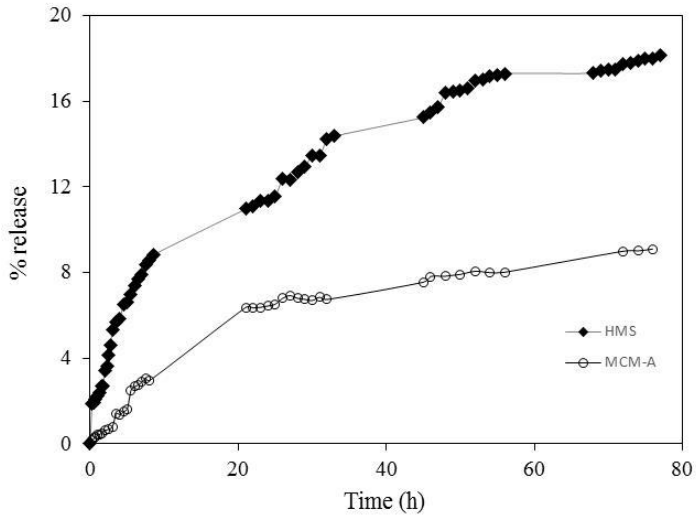

Figure 4. Cumulative release profiles of rifampicin from modified MCM and HMS surface

As seen in figure 4, the amount of rifampicin released from the particle surface was increased with time. However, rifampicin was released from the two particle surface with different rate. Generally, the release rate of rifampicin from HMS was relative rapid than the modified MCM, showing a two-stage release pattern with a rapid initial burst release, followed with slower rate over three days. The initial burst observed in the first 8 h, equivalent to 8.8% of the loaded rifampicin has been released from HMS soaked in PBS (pH 7.4). Thereafter, slower release rate was observed until 77 h of release period. Total rifampicin released at this condition was 18% (equivalent to 0.49 mg rifampicin). For the modified MCM, rifampicin has a slower release rate. For example, at 1 h only 0.4% of rifampicin can be released out from the particle surface. Prolonged the period up to 8 h lets 3% rifampicin was observed in the solution. Finally, after 76 h the amount of rifampicin released from the particle surface was only 3%. The results suggest that some fraction of rifampicin loaded on the particle surface cannot be extracted during release experiment. Compared to other report [11] approximately 4.5 mg of rifampicin can be released from the mesoporous silica nanoparticles over 24 h. Design on mesoporous silica nanoparticles reported that particle surface decoration with organic or inorganic compounds will regulate the release of target drugs under specific conditions such as pH [20], chemicals [21], redox reaction [22], etc. Therefore, this preliminary investigation needs to be further developed to improve both the loading capacity and controlled release rate.

4. Conclusions

Rifampicin loading into MCM and HMS particles, followed by subsequent release test was analyzed to assess the effect of different mesoporous silica nanoparticles on the ability of the particles to attract rifampicin molecules. MCM-41 materials were not able to be acted as host for rifampicin molecules and thus, amine-functionalization of MCM-41 has enhanced the loading capacity of rifampicin by 16%. In the case of pure HMS, the particle surface attracts rifampicin molecules 3.3 times than the functionalized MCM. Accordingly, the release rate of rifampicin from HMS surface was observed much higher. Further analysis was necessary to be investigated to get insight of study of particle morphology for drug delivery. However, the results observed here suggest the particles can be further investigated to be able to act as a drug delivery control, especially for pulmonary treatment.

References

[1] Angelos S, Liong M, Choi E and Zink JI 2008 *Chem Eng J* **137** 4-13
[2] Sun B, Zhou G and Zhang H 2016 *Prog Solid State Ch* **44** 1-19
[3] Wang Z, Zong S, Yang J, Li J and Cui Y 2011 *Biosens Bioelectron* **26** 2883-9
[4] Gonzalez G, Sagarzazu A, Cordova A, Gomes ME, Salas J, Contreras L, Noris-Suarez K and Lascano L 2018 *Micropor Mesopor Mat* **256** 251-65
[5] Shariatinia Z and Zahraee Z 2017 J Colloid Interface Sci **501** 60-76
[6] Yang X, He C, Li J, Chen H, Ma Q, Sui X, Tian S, Ying M, Zhang Q, Luo Y, Zhuang Z and Liu J 2014 *Toxicol Lett* **229** 240-9
[7] Freitas LBO, Corgosinho LM, Faria JAQA, Santos VM, Resende JM, Leal AS, Gomes DA and Sousa EMB 2017 *Micropor Mesopor Mat* **242** 271-83
[8] Park HJ, Sohn JH, Kim YJ, Park YH, Han H, Park KH, Lee K, Choi H, Um K, Choi IH, Park JW and Lee JH 2015 *Exp Mol Med* **47** e173
[9] He D, Wang S, Lei L, Hou Z, Shang P, He X and Nie H 2015 *Chem Eng Sci* **125** 108-20
[10] Liu J., Luo Z, Zhang J, Luo T, Zhou J, Zhao X and Cai K 2016 *Biomat* **83** 51-65
[11] Mohseni M, Gilani K and Mortazavi SA 2015 *Iran J Pharm Res* **14** 27-34
[12] Melendez-Ortiz HI, Garcia-Cerda LA, Olivares-Maldonado Y, Castruita G, Mercado-Silva JA

and Perera-Mercado YA 2012 *Ceram Int* **38** 6353-8
[13] Manzano M, Aina V, Arean CO, Balas F, Cauda V, Colilla M, Delgado, MR and Vallet-Regi, M 2009 *Chem Eng J* **137** 30-7 *Mat Sci Eng C* **78** 674-81
[14] Cuello, NI, Elias VR, Mendieta SN, Longhi M, Crivello ME, Oliva MI and Eimer GA 2017
[15] Hao N, Jayawardana KW, Chen X, Zoysa TD and Yan M 2015 *ACS Appl Mater Interfaces* **7** 1040-5
[16] Szegedi A, Popova M, Goshev I, Klébert S and Mihály J 2012 *J Solid State Chem* **194** 257-63
[17] Manzano M, Aina V, Arean CO, Balas F, Cauda V, Colila M, Delgado MR and Vallet-Regi M 2008 *Chem Eng J* **137**30-7
[18] Zelenak V, Halamova D, Almasi M, Zid L, Zelenakova A and Kapusta O 2018 *App Surf Sci* **443** 525-34
[19] Maleki A, Kettiger H, Schoubben A, Rosenholm JM, Ambrogi V and Hamidi M 2017 *J Control Release* **262** 329-47
[20] Li T, Chen X, Liu Y, Fan L, Lin L, Xu Y, Chen S and Shao J 2017 Eur. J. Pharm. Sci. **96** 456-63
[21] Yu E, Lo A, Jiang L, Petkus B, Ercan NI and Stroeve, P 2017 *Colloids Surf. B Biointerfaces* **149** 297-300
[22] Hernandez R, Tseng HR, Wong JW, Stoddart JF and Zink JI *2004 J Am Chem Soc* **126** 3370-1

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