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Drug loading-release behaviour of mesoporous materials SBA-15 and CMK-3 using ibuprofen molecule as drug model

Maria Ulfa¹ and Didik Prasetyoko²

¹Study Program of Education Chemistry, Faculty of Teacher Training and Education Sebelas Maret University, Jl. Ir. Sutami 36A, Surakarta 57126, Central Java Indonesia
²Department of Chemistry, Faculty of Mathematics and Natural Sciences, Institute Technology Sepuluh Nopember, JI Keputih, Surabaya, 61115, East Java Indonesia

E-mail : ulfa.maria2015@gmail.com

Abstract. The well-ordered mesoporous silicate (SBA-15) was synthesized via soft-templating route using block copolymer P-123 as directing agent and tetraethoxysilane as the silica source. The ordered mesoporous carbon (CMK-3) was synthesized via a hard casting route using SBA-15 as nano-template and sucrose as carbon source. The character of mesoporous structure of the samples was investigated by scanning electron microscopy, FTIR and element analysis. The loading release performance using SBA-15 and CMK-3 was investigated by ibuprofen molecule as the drug model. The results illustrated a unique trend of impregnation phenomenon from both of SBA-15 and CMK-3 which was closely related to the mesoporous structure of the materials. When the mesoporous carbon SBA-15 and CMK-3 were loaded by ibuprofen molecule, the agglomeration of ibuprofen did not appear on the outer surface of carbon with the increase of ibuprofen concentration. Our results indicated that mesoporous structure could influence the phase transformation behavior of ibuprofen, which can effectively decrease the drug release time of drug in delivery system.

1. Introduction

Mesoporous material have attracted premium attention in pharmacy field due the the unique character such as large pore diamater, high stability and ordered uniformity of space [1-3]. Mesoporous carbon and mesoporous silica are the twins material which is have started as carrier medical material in last ten years, the most wanted material from mesoporous family in this decade are SBA-15 and CMK-3 which is based on silica and carbon, respectively. The other application of molecular sieve of mesoporous silica SBA-15 and mesoporous carbon CMK-3 used as energy storage material, catalysis, adsorption and enviromental issue [4-5]. The unique character of molecular sieve of both mesoporous material including high thermal stability, inertness, high specific surface area, the unique honeycombstructure, regularity and sharp pore size distribution was make molecular sieve of mesoporous silica be a fovourite material in last decade [6-7]. Syntesis of molecular sieve of mesoporous silica SBA-15 has been reported not only by calcination of silica source but also of self assembly of polymer such as poly(propylene oxide)-block-poly(ethylene oxide)-block-poly(propylene oxide) triblock copolymer Pluronic F127. The block-copolymers of poly ethilene glycol PEG and triblock copolymer Pluronic P123 (EO₂₀PO₇₀EO₂₀). However, the high cost of mesoporous silica SBA-15 and mesoporous carbon CMK-3 in pharmacology term should be replace by the optimum loading release behaviour.
Ibuprofen is the most popular of anti-inflammatory and antipyretic drug in medical field. The drug delivery system was need modified by carrier material to increase efficiency of drug consumption. This step have urgent realized due to the toxic effects of ibuprofen as pharmaceutical drug on vital organ beings. One of the method which had been investigated to minimized degree of ibuprofen molecule in health vital organ is optimization the loading release behaviour [8-10]. Previous reportation has been used microporous material but not work properly due to the low efficiencies for control release of ibuprofen molecule [11-13]. To solve this problem, loading release of ibuprofen molecule in body system need material which is have not only accessible pore but also controlling pore system. Mesoporous silica SBA-15 and mesoporous carbon CMK-3 can be act as the twins carrier and controlling drug release of ibuprofen molecule in drug delivery system. In our best knowledge, these twins mesoporous material have not been compared yet in before in the loading release ibuprofen molecule term.

The attention of our study will focus on investigating the comparation of microstructure of SBA-15 and CMK-3 in loading release ibuprofen molecule. The mesoporous silica SBA-15 sample synthesized using P123 and TEOS and mesoporous carbon CMK-3 sample synthesized using mesoporous silica SBA-15 as template. Characterization was investigated by SEM, EDX and FTIR. The loading release kinetics studied in the end of the work to get behaviour of both material.

2. Experimental Methods

2.1 Material
The non ionic triblock copolymer poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) known as Pluronic F123 surfactant with molecular weight 5800 was purchased from Merck which is used as a syntetic directing agent in syntesis silica. The sucrose with molecular weight 342 has been used as carbon precursor was purchased from Aldrich. All chemicals including HCl, H2SO4, NaOH were purchased from Sigma-Aldrich. Deionized water and tetraethyl orthosilicate as source of silica were purchased from Merck.

2.2 Synthesis of mesoporous silica SBA-15
The mesoporous silica SBA-15 sample synthesized based on Nejad et al. procedure with small part modification8. The pluronic p123 was mixed in hydrocloric acid solution to obtain P123 solution. The tetraethyl orthosilicate drop slowly into P123 solution under stirring 150 rpm for 24 h. The ratio of pluronic p123: tetraethyl orthosilicate: hydrocloric acid solution is 1:5:30 (w/w/v). The mixture was transfered into steel container and aged at 100°C for 24 h as hydrotermal step. The white composite separating with vacum apparatus, washing with distilled water and drying in oven at 100°C for 24 h. Then, for removing p123 part, the grey-white powder was calcined at 550 °C in air for 24 h. the resulting sample then kept on desicator until next application process.

2.3 Synthesis of mesoporous carbon CMK-3
The mesoporous carbons CMK-3 synthesized based on Nejad et al. using mesoporous silica SBA-15 which was obtained in first synthesis as hard template and sucrose as precursor carbon. The white powder SBA-15 mixed to sucrose solution which is contain sulfuric acid and deionized water. The ratio of SBA-15: sucrose: sulfuric acid: deionized water is 1.7 10^{-2}:3.6 10^{-3}:1.4 10^{-3}:2.8 10^{-1} (mol/mol). The resulted mixture was carbonized partially at 100°C for 6 h then temperature increased up to 160°C for 6h to obtained clear dark powder. From partial to full polymerization, sucrose solution (64% from first sucrose solution concentration) has been incorporated to resulted dark powder composite followed by partial carbonization at 100°C for 6 h which then temperature increased as the first step. The night dark powder has been pyrolized in carbolite furnace at 900°C wit ramp temperature 5C/min for 8 h under nitrogen flow and prepared by holding time in 300°C and 600°C for 3 h. the black powder then removed from silica particle by 2M natrium hydroxide solution under vacuum apparatus. Sample has been washed by deionized water and ethanol then filtered by Whatman paper filter. In the end of synthesis step, the pure dark powder of CMK-3 was dried at 100°C for 24 and kept in desicator for next application.
2.4 Characterization
The microscopic features of the samples were observed with a field-emission scanning electron microscope (FESEM) (JSM-6700F, JEOL Japan) operated at 10 kV and a field-emission transmission electron microscopy (FETEM) (JEM 2010F, JEOL, Japan) operated at 200 kV. The observations were backed by phase and chemical analysis carried out with the electron diffraction and energy dispersive X-ray spectroscopy (EDS) measurements. The measurements of EDS has been complete by ZAF software (10 kV, the current is 10 and fixed 10mm working distance) for elemental analysis.

2.5 Adsorption of ibuprofen
The ibuprofen solution was obtained by mixing hexana and ibuprofen powder 100 ppm. The adsorption studies was started by adding 20 mg Unique Natural Silica (UNS) sample powder into 30 ml ibuprofen solution and stirring at room temperature for 60 minute. The separation of white adsorbent was done by using Whatman Paper then the resulting solution was measured by UV-Vis Instrument to get the amount of ibuprofen adsorbed not only at any time but also at equilibrium stage. Weight of ibuprofen that adsorbed onto Unique Natural Silica (UNS) sample at equilibrium stage labelled as \( q_e \) which is measure equation (1).

\[
q_e = \frac{(C_o - C_e)w}{m}
\]  

(1)

Where \( C_o \) dan \( C_e \) is initial and equilibrium concentration, respectively. The symbol of \( w \) and \( m \) representation of liquid volume (L) and adalah weight of ibuprofen (g). Weight of ibuprofen that adsorbed onto Unique Natural Silica (UNS) sample at time labelled as \( q_t \) which is measure equation (1).

\[
q_t = \frac{(C_o - C_t)w}{m}
\]  

(2)

Where \( C_t \) is concentration at certain time.

3. Result and Discussion
Figure 1. is spectra of mesoporous SBA-15 and CMK-3 samples showing bands at wave numbers 354, 749 and 993 cm\(^{-1}\) representing C-H vibrations. The CMK-3 (Figure 1.a) sample show high intensity at 1627 cm\(^{-1}\) shows the presence of C = C vibration in the C = C olefin terminal bond. The 2337 cm\(^{-1}\) band represents the vibration of C = O on the carbonyl group. The bands 1342 and 1134 cm\(^{-1}\) arose because of the group vibrations -CH\(_2\) or CH\(_3\). The ribbon character due to the C-O vibrational strain observed in the range of 500-1300 cm\(^{-1}\) representing the carboxylic, phenol and alcohol groups. The bands in 1134, 1342, 2924 and 3749 cm\(^{-1}\) may represent vibrational strains of C-O-H phenolic and carboxylic alcohol groups. The bands at 1134, 3425 cm\(^{-1}\) represent the O-H bonds on the structure of the carboxylate group [14-16].

Figure 1.b show the silanol peak at 1627 cm\(^{-1}\) [16-18]. The silanol peak also appear at 3400 cm\(^{-1}\) show the uniformity of the functional group especially long chain of silica binding with oxygen on the ibuprofen have great impact in loading process as SEM result (Figure 2). For a compare, the density of the rich oxygen functional group on the CMK-3 surface plays a significant role in drug loading system due the high affinity of ibuprofen to attract with carbonyl group when it use as carrier substance. Various functional groups especially oxygen rich available as a bridge between ibuprofen and silanol in SBA-15 and CMK-3 could be enhanced the loading performance.

Figure 2 presenting the effect of stirrer time on the amount of ibuprofen adsorbed onto mesoporous silica SBA-15 and mesoporous carbon CMK-3. The investigation was ranged at 0 to 80 min with initial concentration 100 ppm. The kinetic trend showed that both of SBA-15 and CMK-3 has not only fast adsorption in the first 20 min but also has equilibrium rate after 30 min adsorption. In the other words, the properly concentration of ibuprofen was adsorbed is 62.3 mg and 86.1 mg ibuprofen onto one gram of SBA-15 and CMK-3 respectively. In our suggestion, increasing ibuprofen concentration after this level could decrease the capacity of material. It is logic because in the first adsorption step, material has rich of slit and space on the inner and outer surface which is accessible for ibuprofen molecule. Then, ibuprofen adsorbed onto the material pore in both of micro and mesospace to form single layer. The inner and outer surface which was covered by ibuprofen in single layer, will tranform into multilayer which is decrease the adsorption rate. At the constant adsorption rate, inner or outer surface of material could not adsorbed anything as we called equilibrium state. As can be seen from fig. 2a, ibuprofen concentration adsorbed onto CMK-3 is higher than SBA-15 due to
the larger surface area. Not only from surface effect but also functional group effect of CMK-3 (as can be seen in FTIR trend at Figure 1) have great impact to increase interaction of ibuprofen and oxygen part in carbon functional group.

**Figure 1.** Spectra of SBA-15 and CMK-3 after ibuprofen adsorption

**Figure 2.** The ibuprofen adsorption curve when using a. CMK-3 and b. SBA-15
Figure 3. SEM image of mesoporous sample of a. pure SBA-15 before ibuprofen adsorption, b. SBA-15 after ibuprofen adsorption, c. pure CMK-3 before ibuprofen adsorption, d. CMK-3 after ibuprofen adsorption.

Figure 3 is microimage of CMK-3 and SBA-15 sample observed by SEM. The image show that when SBA-15 sample viewed from the perpendicular point, material has micropipe structure. The mesoporous carbon CMK-3 shows a well ordered nanopipe structure in which arranged of the carbon monopencil. The nanopipe of CMK-3 are separated by the ibuprofen agglomeration in outer surface which is showing the the half part of the covered adsorption system. As can be seen in Figure. 3, the types of nanopipe system in CMK-3 can be clearly identified having the same structure with SBA-15 as replication effect. As we know in experimental section, mesoporous carbon CMK-3 generated by SBA-15 as hard templating system via replication process. It can be observed by pore diameter comparation between CMK-3 and SBA-15 which is the pore diameter of SBA-15 is 8.5 nm and
CMK-3 is 4.2 nm. The other phenomenon can be identified clearly by the number of ibuprofen agglomeration which is figured out as soft cotton-like in SEM image. The ibuprofen soft cotton-like in SBA-15 was observed greater than in CMK-3 due to the high surface of CMK-3 that available for ibuprofen molecule. In the other word, the minimized space in SBA-15 making agglomeration of ibuprofen after equilibrium section that appear as overlapped soft cotton in nanopipe of SBA-15. For a sum, SBA-15 and CMK-3 could be the potential material in drug delivery system in the future with the optimum condition during loading release process.

4. Conclusion
The whole results show that the a carbonyl in CMK-3 and silanol group in SBA-15 could be good agent to increase adsorption capacity in ibuprofen delivery system. The mesoporous silica SBA-15 and mesoporous carbon CMK-3 material has a nanopipe structure as replication effect. In the equilibrium stage, The mesoporous silica SBA-15 and mesoporous carbon CMK-3 has adsorption capacity of ibuprofen up to 62.3 and 86.1 mg/g with spontaneous adsorption. The high adsorption capacity resulted by not only the surface and morphology effect but also chemical structure of CMK-3 and SBA-15.

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