Synthesis and Characterization of Ordered Mesoporous Carbon CMK-3 with a High Loading Capacity of Ibuprofen and its Release Performance at Simulated Body Fluid

Maria Ulfa¹ and Didik Prasetyoko²

¹ Study Program of Chemistry Education, Faculty of Teacher Training and Education, the March University, Jl. Ir. Sutami 36A, 57126 Surakarta, Central Java Indonesia
² Department of Chemistry, Faculty of Mathematics and Natural Sciences, Institute of Technology Ten November, Jl. Keputih, Surabaya, East Java Indonesia
E-mail: ulfa.maria2015@gmail.com

Abstract. In this paper, ordered mesoporous carbon CMK-3 have been synthesized via hard templating method using mesoporous silica as template followed by thermal carbonization. The resulting ordered mesoporous carbon sample have been loaded by ibuprofen as anti inflammatory drug model up to 75% (w/w). Characterization of textural and structural resulting ordered mesoporous carbon was examined by transmission electron microscopy, small angle X-ray scattering, Fourier transform infrared spectroscopy and nitrogen adsorption-desorption. The high loading ibuprofen effect in release performance have been reviewed and it appears that ibuprofen loading on ordered mesoporous carbon surface can be released up to 50% in simulated body fluid at pH 7.4 for 200 min. Result shows that high ibuprofen loading not only change the textural and structural material but also have great impact for release performance. Key Word: ordered mesoporous carbon, CMK-3, ibuprofen, high loading, release.

1. Introduction
Ordered mesoporous carbon (CMK-3) is a large porous adsorbent from the group nanomaterial which is considered as effective adsorbent, catalysis, energy storage and medical field [1]. The unique of CMK-3 is due to not only the availability of pores with a size range of 2-10 nm as access to large molecules but also regular pore structure, high surface area, inert and high thermal stability [2]. The pore size and surface area of ordered mesoporous carbon (CMK-3) can be good carrier for drug delivery material [3-4]. However, the using of CMK-3 for drug delivery system is high cost due to the complicated the synthesis process. To solve this problem, regeneration step is the best way to decrease the consume of CMK-3 but is not easy for oral drug consume. The alternative solution is how to control the CMK-3 pore in the releasing drug molecule which is need the information about the the change of structural and textural of material after drug loading process.

The popular anti inflammatory and antipyretic drug which is most used by all people around the world is Ibuprofen [5]. The pharmaceutical research was tried to increasing ibuprofen molecule loading for highly drug efficiencies by drug delivery system. Patient not need to consume drug gradually due to the high loading ibuprofen in carrier material only if releasing process in long time period [6]. The various technique had been investigated to maximized the ibuprofen loading as adsorption and coagulation. Mesoporous carbon can be act as carrier of ibuprofen molecule in drug delivery system. However, nothing research was studied about the structural change of carrier material after loading.
process, microporous activated carbon adsorbent had low efficiencies for decreasing ibuprofen molecule. The control of loading process is required for the drug delivery applications [7-9]. Mesoporous carbons with uniform pores are expected to be carrier material for ibuprofen with high loading capacities [10]. The high loading depend on pore size, surface area and surface chemistry of material [11-12]. However, in the best of our knowledge, comparison between material before and after loading process and its impact in realizing process have been not studied before. Herein, we report a simple synthesis of CMK-3 via self-assembly route using hard templating method followed by loading profen using ibuprofen. The comparison character of material before and after loading process have been measured by characterization with X-ray diffraction (XRD), FTIR, N2 adsorption-desorption isotherms and transmission electron microscopy (TEM). Release capacity of CMK-3 have been observed by simulated body fluid to dissolve ibuprofen from CMK-3.

2. Experiment

2.1 Material

The materials used in this study tetraethylortosilicate (Merck, 98%), sulfuric acid, hydrochloric acid, n-hexane, NaOH (Merck, 99%), Pluronic P123, HF, hydrochloric acid, ethanol, methanol, acetone and aquabides, Ibuprofen (Merck, 98%).

2.2 Synthesis CMK-3

The mesopore carbon synthesis begins by SBA-15 synthesis according to the procedure elsewhere [14]. For CMK-3 synthesis was firstly started by mixing sucrose powder about 1.04 g in a 0.2 g mixture of concentrated sulfuric acid in 100 g air while stirring to produce a homogeneous sucrose solution. Then 1 g of SBA-15 was added to the sucrose solution and added homogeneously for 2 hours. Mixing until homogeneous. So that carbon is infiltrated into the mold and coating the mold walls. The bone mixture is then heated in an oven at 100 °C for 7 hours then the temperature is raised to 160 °C for 7 hours to dehydrate. After the sucrose / SBA-15 composite contains a period of partial carbonized organic, then added sucrose solution containing 0.92 g of sucrose into a mixture of 0.08 g sulfuric acid and 100 g of water. sucrose / SBA-15 composites were then heated again at 100 °C for 6 hours followed by a temperature of 160 °C for 6 hours into black powder, carbonization begins with carbonization of samples temperature of 30-300 °C. The holding time is carried out for 1 hour at 300 °C. Furthermore, carbonization is continued in the range of 300-600 °C and is held for 1 hour at 600 °C. Furthermore, the black powder is carbonized by heating 900 °C for 3 hours. The entire carbonization is carried out at a heating rate of 5 °C / min under the N2 gas flow. The carbonized sample is then washed with 1M NaOH (in ethanol and water 50:50) temperature 70 °C to release the silica mold. In the next synthesis washing is done with HF with a concentration of 10-40% for 2-24 hours. Washing is done 3 times to make sure the silica is released all, followed by washing using ethanol. The resulting sample is then dried at 110 °C and stored in the desiccator. The resulting sample was labelled as CMK-3 before loading.

2.3 Ibuprofen loading-release

Ibuprofen-loaded CMK-3 was prepared as follows: 0.075 g of Ibuprofen was dissolved in 20 mL of ethanol, and 0.100 g of CMK-3 powder was then added under constant stirring for 24 h at room temperature. The solid part of the dispersion was separated using centrifugation and dried overnight at room temperature. The resulting sample was labelled as CMK-3 after loading. The drug release experiments were performed by immersing the drug loading samples into simulated body fluid (pH 7.4 at 37 °C). Several sample were tested in each 10 min and examined by UV–Vis spectroscopy.

3. Result and discussion

TEM results of CMK-3 before loading and CMK-3 after loading mesoporous carbon samples are shown in Figure 1. TEM images show the presence of uniform pores on CMK-3 before loading and CMK-3 after loading sizes of 4.5 and 3.8 nm seen from the vertical and horizontal directions.
Uniformity of the pore size was confirmed by the particle size histogram processed from TEM images. The particle size distribution of CMK-3 before loading samples shows the dominance of uniform particles measuring 1-5 nm. Meanwhile, the particle size distribution at CMK-3 after loading shows the dominance of uniform particles in the range of 5-10 nm. This is not much different from the pore size distribution resulting from the calculation of nitrogen adsorption-desorption data in the CMK-3 before loading and CMK-3 after loading samples which were 4.06 nm and 8.5 nm respectively. This fact reinforces the conclusion that the results of the CMK-3 before loading and CMK-3 after loading sample pore measurements are not much different despite using 2 different instruments.

Figure 1. Illustration of mesoporous carbon CMK a. before and b. after ibuprofen loading

Figure 1 shows CMK-3 before loading mesoporous carbon samples which imply regular hexagonal structures with p6mm group space based on the pattern of black dots shown by FFT. The TEM image pattern shows that CMK-3 have a honeycomb structure as represents a hexagonal pore arrangement. CMK-3 morphology of parallel points representing the arrangement of carbon bars when observed from the horizontal direction. Figure 1 also shows a small number of irregular stacks (stacking faults) of CMK-3 after ibuprofen loading due to some skeletons experiencing little damage came from ibuprofen desposition in inner pore at high loading up to 75% w/w. The TEM observations on CMK-3 before loading provide the conclusion that mesoporous carbon has the same morphology as CMK-3 after loading silica which could be said that not only nothing significant big destruction after ibuprofen loaded onto CMK-3 but also this implies the stability of CMK-3.

Figure 2. Illustration of mesoporous carbon CMK during synthesis and ibuprofen loading.

Figure 2 is an illustration that represents the SBA-15 replication process to become mesoporous carbon CMK-3. In the illustration, SBA has a pore structure arrangement that forms a hexagonal structure which is have small micropores or mesopores on the wall as bridges connecting the main
channels of the mesoporous tube. If the carbon precursor fills the entire inner chamber of the SBA-15, a carbon frame will form with a solid stem. This process is enhanced by the release of the silica skeleton. When the silica wall has been released, the silica wall changes into an empty carbon pore channel. This means that the actual carbon pore is the former position of the released silica wall which is in next application has been used by ibuprofen as accessible pore during loading process. The ibuprofen have been loaded onto CMK-3 by fills larger the meso-empty carbon than micro-empty channel. It is logic because the ibuprofen size in more small than the mesoporous space in CMK-3.

The high loading of ibuprofen in our prediction would be have great impact on surface chemistry of CMK-3 as FTIR observation below.

Figure 3. Spectra of FTIR on CMK-3 sample.

FTIR spectra in all CMK-3 samples showed wide absorption peaks at 3600-3100 cm⁻¹ wave number not only indicates the presence of a number of hydrogen bonds but also describes the amount of water absorbed on the surface of the sample. The absorption band in the range of 1300-1000 cm⁻¹ shows the vibration of the CO bond strain presented in the following functional groups: anhydride (980-1300 cm⁻¹), ester (1150-1080 cm⁻¹), lactone (1160-1370 cm⁻¹), alcohol (1280-1050 cm⁻¹), phenol (1220-1000 cm⁻¹), and ether (1300-1000 cm⁻¹) [12]. The absorption area at the wavelength range 2000-1500 cm⁻¹ with small intensity shows the characteristic character of double bond vibration. In the range of these wavelengths, there are several vibrations observed, including vibrations C = C (1680-1620 cm⁻¹), aromatic rings (1600-1585 cm⁻¹), C = O from carboxylates (1760-1665 cm⁻¹), carbonyls (1600-1590 cm⁻¹), quinones (1680-1550 cm⁻¹), lactone groups (1790-1675 cm⁻¹), and anhydrides (1880-1740 cm⁻¹) [13]. The vibration of the CH3 and CH2 groups appears in the range of 3000-2800 cm⁻¹. Nothing significant differences was observed but the intensity of CMK-3 after loading is slightly lower than before loading due to the ibuprofen was filled the CMK-3 pore.
In this study, observations with the scattering results of SAXS were carried out on sample CMK-3 before and after ibuprofen loading. Figure 4 both samples show peaks (100), (110) and (200) which describe regular two-dimensional hexagonal mesopore arrangements. The intensity of the q values at the top (100), (110) and (200) positions observed are 0.72; 0.79; and 1.09 where the q peak at CMK-3 after ibuprofen loading is lower than CMK-3 after ibuprofen loading as the effect of the former of ibuprofen sites. The SAXS scattering results in all samples showed peaks with sufficiently strong intensity at (100) and (200) which indicated the regularity of the mesoporous structures formed. The size of the pore CMK-3 before and after ibuprofen loading is 3.39 and 3.16 nm. The pore of CMK-3 before ibuprofen loading is greater than after which indicates that small part of CMK-3 frame work may destructed by ibuprofen after loading. This phenomenon is consistent with the explanation of next nitrogen adsorption-desorption isotherm data and TEM observations. Overall, CMK-3 before not significantly different from CMK-3 before ibuprofen loading, so it can be concluded that the ibuprofen loading at 75% w/w remaining the the CMK-3 structure.

Figure 4. SAXS of CMK-3 before and after ibuprofen loading.
Figure 5. Isotherm-adsorption-desorption nitrogen CMK-3 before and after ibuprofen loading.

Figure 5 shows the nitrogen adsorption isotherm in the CMK-3 sample. The successful synthesis of mesoporous carbon can also be seen by observing the inflection point of the nitrogen adsorption isotherm in the CMK-3 sample. The position of P / Po at the inflection point is a function of pore diameter due to the presence of surface adsorption procedures along with the formation of mono and multilayer [14-15]. Inflection of the isotherm of mesoporous CMK-3 carbon samples at P / Po 0.0-1.0 is divided into 3 areas. First, the inflection point at P / Po <0.5 where nitrogen fills a small portion of the pore volume in small pores representing the formation of a monolayer on micropore carbon. Furthermore, most of the porous space with a larger size is filled with nitrogen along with the increase in pressure (P / Po 0.4-0.8) which reflects the contribution of mesoporous to carbon during adsorption. In this area there is a sharp inflection on carbon CMK-3 isotherm as more nitrogen enters is estimated due to nitrogen capillary condensation in the mesopore. According to some researchers, this phenomenon is a character of the pore uniformity of a material [16-17]. Sharp inflection in the pressure range is a sign that there is an interconnection of the pores which gives another meaning that in the pore tissue there is a primary pore and there are secondary pores (generally smaller). In some studies, smaller pore on CMK-3 framework have been acted as pore neck or pore bridges that connecting each mesorod carbon which is impact to stability building block [18-19]. The area after the capillary condensation stage appears as a displaying plain at higher relative pressures that are expected to occur due to the formation of multilayer nitrogen adsorption on the external surface and empty slits of CMK-3 samples. Shallow slope in this area indicates that the external surface area in the CMK-3 sample is very small. The desorption branch almost did not coincide with the adsorption branch which revealed that nitrogen adsorption occurred irreversibly in mesopore. This is thought to be due to a pause when capillary condensation occurs. Finally, at high pressure (P / Po > 0.8) an inflection point occurs in the vertical direction which is estimated to be the area of entry of nitrogen in macropore carbon. The isotherm CMK-3 after loading was lower than before loading due to the pore filled by ibuprofen. This loading process have big impact to the CMK-3 pore because inner pore was covered by ibuprofen molecule so nitrogen can not fill the pore.
Figure 6. Release trend of ibuprofen using CMK-3 after high loading process.

Figure 6 shows the ibuprofen release profile with CMK-3 for 500. The ibuprofen release profile with CMK-3 is found to reach 50% at first 200 min and it is fully release at 500 min. This phenomenon indicating that ibuprofen molecule adsorpt onto both of meso and microporous part of CMK-3. The slow release profile in our prediction have been affected by ibuprofen deposition in inner pore of CMK-3. The high deposition may affected by high loading ibuprofen and numerous of mesopore space which is available for ibuprofen as big molecule. The second prediction is ibuprofen have been trapped not only by functional group of CMK-3 surface but also agglomeration of ibuprofen molecule in depth surface. a reduction of% dissolution of original ibuprofen due to the formation of agglomerates. This is in agreement with the nitrogen adsorption data, morphology of material by TEM, structure profile by XRD and implies the presence of free hydroxyl group as active sites on the surface of CMK-3 as evidenced by FTIR spectra. Over all, the textural and structural of CMK-3 before ibuprofen loading was very similar to CMK-3 before ibuprofen loading which is imply the stability of CMK-3 for regeneration carrier material in drug delivery system

4. Conclusion
Ordered mesoporous carbon CMK-3 was succesfully constructed by via hard templating method using mesoporous silica as template followed by thermal carbonization. The result show that at 75% w/w loading capacity of ordered mesoporous carbon by ibuprofen have not dramatically destructed the structure. The characterization of ordered mesoporous carbon show that any small shrinkage part of morphology due to the ibuprofen removing process. Over all, surface chemistry of CMK-3 after and before ibuprofen loading is slightly different in surface area, scattering and functional group intensity but not significant in structure. The ibuprofen release result show that ordered mesoporous carbon can releasing ibuprofen up to 50% in simulated body fluid at pH 7.4 for 200 min. It is good information that CMK-3 in potential material for drug delivery system in the future.

5. References
[1] G. Chandrasekar, W. J. Son, and W. S. Ahn, J. Porous Mater., 2009.
[2] H. Zhou, S. Zhu, I. Honma, and K. Seki, “Chem. Phys. Lett., 2004.
Acknowledgements
The authors would like to thank Directorat General of High Education (DIKTI), Indonesia, for the financial support through a Post Doctoral Research 2019 scheme grant with number contract of grant 718/UN27.21/PN/2019 (DIKTI Number contract 092/SP2H/LT/DRPM/2019)