Green synthesis of MIL-100(Fe) metal-organic frameworks as a carrier for chloroquine delivery

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ABSTRACT

The metal-organic framework MIL-100(Fe) was synthesized by the green process using the ultrasonic method and water. By using this approach, the energy consumption was reduced by 100 times compared to the hydrothermal method. The prepared MIL-100(Fe) was characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM) and BET surface area measurements. The XRD pattern showed characteristic peaks of MIL-100 (Fe) with the main peaks at 6.3^o, 10.3^o, 11.1^o, and 20.1^o. The prepared MIL-100(Fe) was of particle size in a range of from 100 nm to 200 nm, and surface area of 950 m^2/g with a pore volume of 0.52 cm^3/g. The obtained MIL-100 (Fe) showed a high loading capacity for the chloroquine drug with a maximal capacity of 555 mg/g.

Keywords: MIL-100(Fe); Green process; Ultrasonic; Chloroquine.

1. INTRODUCTION

The energy demand for the development of industries is getting higher and higher, causing severe environmental pollution problems because the main energy sources come from the fossil fuels such as coal, gas and oils. In recent years, synthesis of nanomaterials using green approaches has attracted a great attention from scientists and goverments from all over the world for the purpose of reducing the effect of the synthesizing processes on the ecossystem [1].

Green chemistry is a field of chemistry and chemical engineering that focuses on designing products and processes which can reduce or eliminate the use of harmful and toxic substances as well as reducing the energy consumption of the process. The main purpose of using green synthesizing approaches is to minimize the use of non-renewable resources and prevent the discharge of toxic subtances into the environment [2-4].

MIL-100(Fe) is a metal-organic framework (MOF) synthesized from iron (III) salts with 1,3,5 benzentricarboxylic organic ligands, which has been commonly synthesized using traditional methods such as hydrothermal, refluxing,... [5]. With novel properties of frame structure, large surface area and porosity, MIL-100(Fe) material has been utilzied in many fields of application such as gas storage, sensing, catalysis, environmental treatment, bearing, drug delivery... [6-10].

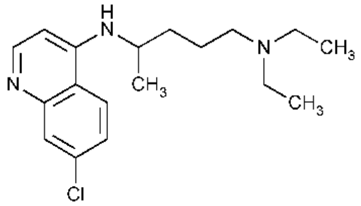


Figure 1. *The structural formula of Chloroquine.*

Chloroquine is an active drug with the chemical formula $C_{18}H_{26}ClN_3$, which commonly uses in the treatment of malaria (Figure 1) [11]. However, chloroquine in pure form tend to dilute quickly in the treatment media with low safety limit, so that it could lead to overdose shock when using with higher dose [12]. Several stratergies have been effectively employed to overcome this disadvantage such as dose interval, increasing water solubility, decreasing crystal size, and combining with other materials. Among these, increasing the solutability in water is considered as an effective way to imrpove the performance of the chloroquine. In this study, MIL-100(Fe) material was synthesized by green chemical process and employed as a carrier for the chloroquine drugs.

2. EXPERIMENTAL

2.1. Material

Iron (III) nitrate $FeCl_3.6H_2O$, 1,3,5 benzentricacboxylic (1,3,5 BTC) acid, ethanol C_2H_5OH, and Chloroquine were purchased from Sigma Aldrich. All the chemicals were used as received without any further purification.

2.2. Synthesis of the MIL-100(Fe)

Materials are synthesized according to the following methods:

Ultrasonic method: The precursors with $FeCl_3.6H_2O$: 1,3,5 BTC:H_2O ratio of 2.7 g: 1.4 g: 100 ml, respectively, was introduced into a PET plastic cup. The mixture was well-stirred for 15 minutes. Samples were then ultrasonicated in an ultrasonic homogenizer for 10 minutes with a power of 1800 W, a frequency of 20,5 kHz (sample SA). The material obtained after the reaction was filtered and washed 3 times with a mixture of alcohol and deionized water, then dried at 80 ^oC.

Hydrothermal method: Weigh each substance according to the ratio of the single component as follows: $FeCl_3.6H_2O$: 1,3,5 BTC:H_2O = 2.7 g: 1.4 g: 100 ml into a PET plastic cup. The mixture was well-stirred for 15 minutes. Mixture was then poured in a acutoclave and placed in oven at 150 ^oC for 10 hours (sample TN). The material obtained after the reaction was filtered and washed 3 times with a mixture of alcohol and deionized water, then dried at 80 ^oC.

Microwave method: Weigh each substance according to the ratio of the single component as follows: $FeCl_3.6H_2O$: 1,3,5 BTC:H_2O = 2.7 g: 1.4 g: 100 ml into a PET plastic cup. The mixture was well-stirred for 15 minutes, then put in the microwave at 2000 W power for 6 minutes. The material obtained after the reaction was filtered and washed 3 times with a mixture of alcohol and deionized water, then dried at 80 ^oC.

2.3. Characterization

The prepared MIL-100(Fe) were characterized by using X-ray difraxtion (XRD) on X'Pert Pro, scanning electron microscope (SEM) on Zeiss EVO 18. The porosity of materials was investigated by the N_2 gas adsorption isotherm method on Micromeritics TriStar II device at the Institute of Materials Science, Vietnam Academy of Science and Technology.

2.4. Loading of chloroquine by the MIL-100(Fe)

The green-synthesized MIL-100(Fe) was evaluated their capability of carrying carry chloroquine active following experiment: 0.01 g of material was added into 10 ml of samples of chloroquine solutions at different concentrations of M1 (150 mg/l), M2 (350 mg/l), M3 (550 mg/l), M4 (750 mg/l), and M5 (950 mg/l) at room temperature for 7 days. Chloroquine concentrations were determined using a UV-Vis spectrophotometer.

3. RESULTS AND DISCUSSION

3.1. MIL-100(Fe) charaterizations

The crystalinity of the MIL-100(Fe) was characterized by XRD diffraction as shown in Figure 2. It can be obvious that the peak appeared at 6.3^o, 10.3^o, 11.1^o, and 20.1^o are characteristic peaks of MIL-100(Fe) material. This result is consistent with previous reports on

MIL-100(Fe) materials [6, 9]. The diffraction peaks at 6.3^o, 11.1^o, and 20.1^o was also obsvered in the XRD patterns of the MIL-100(Fe) materials obtained from ultrasonic (SA) and microwave (VS) methods, however, the peak intensity is much lower than that of the TN sample. This can be explained by the formation of the amourphous form of the crystals due to the fast reaction time, the incomplete growth of the crystalline particles, and the small particle size when using the ultrasonic (SA) and microwave (VS) methods.

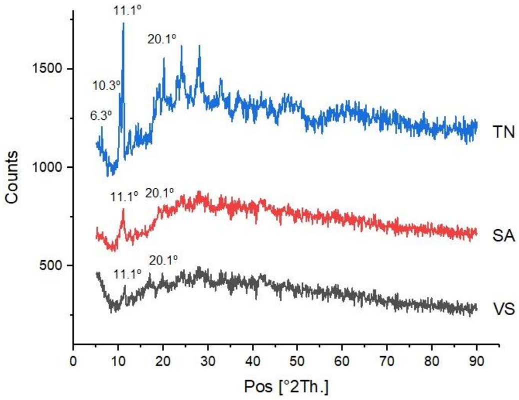
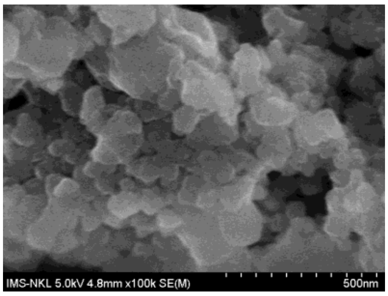


Figure 2. *X-ray difraction of material.*

The prepared MIL-100(Fe) apprears in the form of light yellow powder. The morphologies of the MIL-100(Fe) synthesized from different methods are shown in Figure 3. It can be clearly seen that the MIL-100(Fe) prepared from SA and VS methods are in particles structure with the size raning from 100 nm to 200 nm. The MIL-100(Fe) fabricated using hydrothermal methods shows clear octahedral structure with the size in range of from 400 nm to 800 nm. This is becuase the long synthesizing time (10 h) and stable synthesizing temperature (150 ^{o}C) of the hydrothermal method are the suitable conditions for the growth of MIL-100(Fe).



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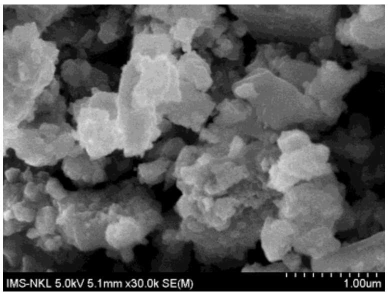

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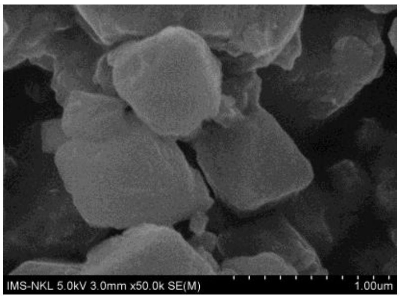

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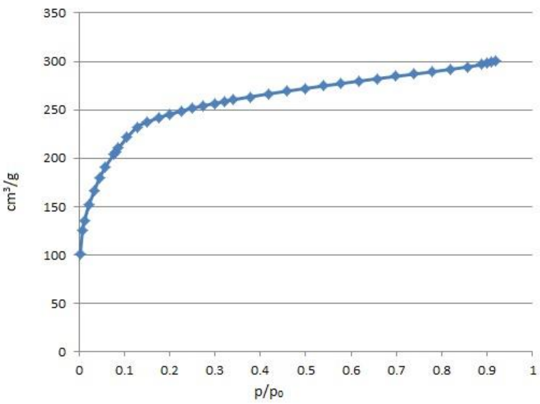
Figure 3. *SEM images of MIL-100(Fe) prepared from (a) SA, (b) CS, and (c) TN approaches.*

The porosity of the MIL-100(Fe) materials were investigated by the N_2 gas adsorption isotherm analysis. The adsorption isotherms of the three samples followed type I (according to IUPAC classification) (Figure 3), which means that the prepared MOF materials has a microcapillary form. The BET surface area and large pore volume of the MIL-100(Fe) prepared using TN method were calculated to be 1777 m^2/g and 0.79 cm^3/g, repsectively, which is highest in comparison to the MOF materials synthesized from other methods. This result is consistent with the morphologies observed in the SEM image. The specific surface areas of the MIL-100(Fe) synthesized from VS and SA methods are determined to be 93 and 950 m^2/g with pore volume of 0.33 and 0.52 cm^3/g, respectively. With such high porosity, the prepared MIL-100(Fe) materials has great potential for the adsorption application.



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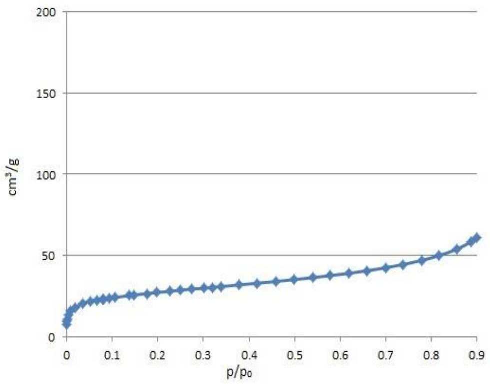

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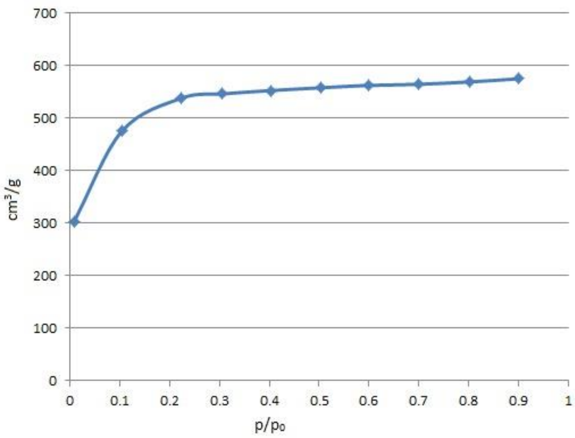

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Figure 4. *The N_2 gas isotherm adsorption curve of MIL-100(Fe) prepared from (a) SA, (b) CS, and (c) TN approaches.*

Table 1. *Porous properties of MIL-100(Fe) materials prepared from different methods.*

Sample	Surface area in BET (m^2/g)	Pore volume (cm^3/g)	Pore size (nm)
SA	950	0.52	2.16
VS	93	0.33	14.3
TN	1777	0.79	3.47

3.2. Efficiency evaluation of the MIL-100(Fe) prepared from different approaches

The green process was evaluated through energy consumption, reaction time and product yield. The results presented in table 2 show that the highest product yield of 48.71% was obtaiend from the hydrothermal method, however, the synthessizing time is longest with 600 minutes of reaction time and the energy consumption is also significantly high wiht 18 kWh. With the microwave method, product yield up to 29.28% was obtained in a short synthesizing time. However, increasing the product yield will be difficult because the temperature rises too fast, causing the solvent to evaporate during the reaction. When using the ultrasonic method, the power consumption is the lowest with only 0.18 kWh and the product efficiency is close to that of the hydrothermal method (40,57%).

Table 2. *Efficiency of material synthesized by different methods.*

TT	Method	Sample	Reaction time, t, min	Mass of sample m, g	Product yield, H, %	Reactor capacity, kW	Energy consumption, A, kWh
1	Ultrasonic	SA	10	0.852	40.57	1.8	0.18
2	Hydrothermal	TN	600	1.023	48.71	1.8	18
3	Microwave	VS	6	0.615	29.28	2.0	0.2

It can be concludes from the aforementioned results that the synthesis of MIL-100(Fe) materials using ultrasonic method can ensure both the green chemical process with fast synthesizing time, low energy consumption, and high product yield while still maintain novel properties of metal-orangic framework materials.

3.3. Chloroquine-loading capacity of the prepared MIL-100(Fe)

Langmuir isotherm adsorption model was employed to determine the maximal chloroquine adsorption capacity of the SA sample with different initial concentrations of chloroquine. The results are shown in Table 3:

Table 3. *Results on chloroquine adsorption capacity of MIL-100(Fe) prepared from SA method.*

Sample	Initial concentration C_0 (mg/l)	Concentration after adsorption C_t (mg/l)	Adsorption capacity Q (mg/g)	C_t/Q
M1	171	129	42	3.0714
M2	349	270	79	3.4177
M3	515	401	114	3.5175
M4	679	544	135	4.0296
M5	931	750	181	4.1436

Regression of experimental data was carried out to determine the constants of the Langmuir adsorption heat direction.:

$$\frac{C_t}{Q} = \frac{1}{Q_{max}} \times C_t + \frac{1}{b.Q_{max}}$$

Where C_t: Concentration of chloroquine after adsorption;

Q: Adsorption capacity;

Q_{max}: Maximum adsorption capacity;

b: Constants.

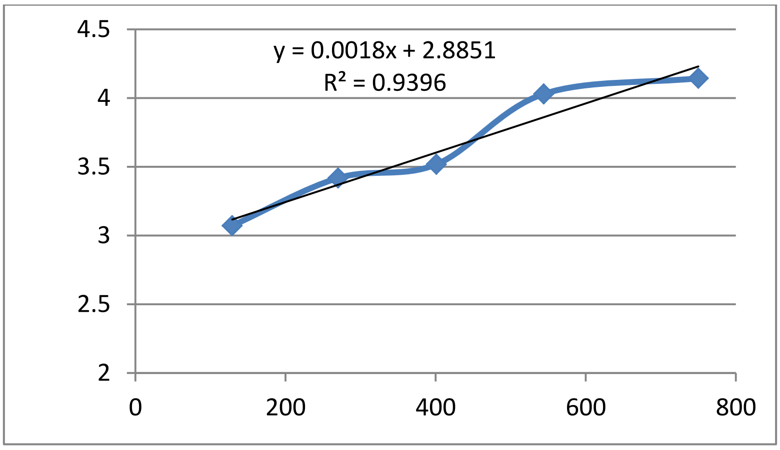

Figure 5. *The Langmuir adsoroption isotherm of the MIL-100(Fe) toward chloroquine.*

It can be seen that the Langmuir isotherm adsorption model describes quite accurately the adsorption behaviour of chloroquine on the MIL-100(Fe) material with the coefficient R^2 of 0.9396. The large adsorption capacity of the MIL-100(Fe) material for the chloroquine is ascribed to the very large specific surface area, along with the presence of the benzene ring for the materials, which are considered active sites for the bonding of chloroquine [13]. Furthermore, the presences of the N and O atoms in the MIL-100(Fe) structure enable the π -π interaction and hydrogen bonding with benzene rings, which results in high loading amount of the chloroquine drug on the MIL-100(fe) material. The maximul adsorption capacity of the MIL-100(Fe) for chloroquine is determined to be approximately 555 mg/g, which is remarlbly high in comparison to other nanomaterials used for the chloroquine loading.

4. CONCLUSION

In summary, MIL-100(Fe) metal organic framework materials were successfully synthesized from iron (III) salt and 1,3,5 benzentricarboxylic acid using hydrothermal, microwave, and ultrasonic methods. The results indicated that the ultrasonic method is considered as the greenest approach to synthesize the MIL-100(Fe) in comparison to other methods because of their short reaction time, low energy consumption, high product yield, and using non-toxic solvent. The prepared MIL-100(Fe) from ultrasonic method are octahedral shape with the size in range of from 100 nm to 200 nm and high specific surface area of 950 m^2/g. The prepared MIL-100(Fe) showed high loading capacity toward chloroquine with maximum adsorption capacity calculated from Langmuir model to be up to 555 mg/g, which has great potential for the drug delivery.

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TÓM TẮT

NGHIÊN CỨU TỔNG HỢP VẬT LIỆU MIL100(Fe) BẰNG QUY TRÌNH HÓA HỌC XANH VÀ ĐÁNH GIÁ KHẢ NĂNG MANG TẢI HOẠT CHẤT CHLOROQUINE

Vật liệu khung cơ kim MIL-100(Fe) đã được tổng hợp thành công theo phương pháp siêu âm, thủy nhiệt và vi sóng sử dụng dung môi là nước. Vật liệu thu được đã được phân tích nhiễu xạ tia X, chụp ảnh SEM, và đo diện tích bề mặt theo BET. Kết quả so sánh tính chất và hiệu suất phản ứng cho thấy, vật liệu được tổng hợp bằng siêu âm giúp giảm lượng điện năng tiêu thụ tới 100 lần so với phương pháp thủy nhiệt và có các tính chất đặc trưng của vật liệu MIL_100(Fe). Kết quả phân tích nhiễu xạ tia X cho thấy, vật liệu tổng hợp được có các peak đặc trưng của vật liệu MIL_100(Fe) với các peak chính ở 6,3^o; 10,3^o; 11,1^o; 20,1^o. Vật liệu có kích thước hạt từ 100 nm đến 200 nm, diện tích bề mặt đạt 950 m^2/g với thể tích lỗ xốp đạt 0,52 cm^3/g. Vật liệu sau khi tổng hợp đã được đánh giá khả năng mang tải hoạt chất chloroquine. Kết quả cho thấy, vật liệu có khả năng mang tải tối đa chloroquine đạt tới 555 mg/g.

Keywords: MIL-100(Fe); Green process; Ultrasonic; Chloroquine.