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Synthesis of activated spherical-like carbon (ASC) by gelatin soft templating route for inflammatory drug adsorption

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Abstract.

Synthesis spherical like-carbon have been successfully ready done this work by using gelatin as natural soft template combined with spolyoxyethylene-Polyoxypropylene block copolymer as second template and sucrose as carbon precursor. After first reaction of gelatin, block copolymer and sucrose, the mixture have catalyzed by sulfuric acid followed by hydrothermal, evaporation, carbonization and pyrolized nitrogen atmosphere reaction. The spherical like-carbon then activated by potassium hydroxide for obtain activated spherical like-carbon (ASC) followed by filtering and drying. The characterization of activated spherical like-carbon (ASC) have been done by scanning electron microscopy and fourier transform of infra red. Activated spherical like-carbon (ASC) have applied as adsorbent of ibuprofen with initial concentration 0,1 mg/g and weight of carbon its is about 20 mg adsorben. The adsorption kinetic investigated by uv-vis spectrophotometer. The morphology observation shows that activated spherical like-carbon (ASC) have spheric structure with the range size closely with 1-10 µm. The numerous carbonyl and hydroxyl functional group by FTIR observation was predicted increase as the interaction impact between ibuprofen and adsorbent. The interesting phenomenon was observed which is the increasing adsorption capacity of activated spherical like-carbon (ASC) as well equal as the increasing activation temperature.

Key Words: spheric carbon, soft template, gelatin, ibuprofen, activation temperature

I. INTRO

Carbon microspheres have attracted much attention recently due the unique pore structure and size with narrow pore size distribution and as well as volley ball- like structure. The carbon microsphere was widely applied as catalyst, adsorbent, electrode and delivering carrier due to the smooth pore structure, high adsorption capacity, high surface area, and stability. In addition, most microspheric carbon is prepared based on alkaline conditions because of simplicity and eficiency (Wang, Xiufang et al. 2016; Xie, Yunyun et al. 2017). Drug delivery system (DDS) was required high surface area and large poreso accesible for drug molecule.

According to existing research to produce carbon microspheres with high surface area can be synthesized by hard template and soft template method. In this study the microspheres carbon synthesis was carried out by soft template method or colloidal cast method, which is a method used to synthesize carbon by using carbon structure directing agents in the form of surfactants or commonly known as solgel techniques (Ulfa, Maria. 2017). Synthesis of microspheres carbon was carried out using Polyoxyethylene-Polyoxypropylene Block Copolymer as a carbon structure directing agent under acidic conditions or as a template, and gelatin was used as a co-template.

Gelatin is a soluble protein that is a gel-making material, making it suitable for soft templates in the synthesis of microspheres carbon (solgel technique) because it has hydrophobic and hydrophilic tips in its structure which are characteristics of surfactants. The source of the raw material for gelatin usually comes from natural ingredients in the form of cow bones and skin, pig skin, and fish skin. So that in its role as a co-template in the synthesis of carbon microspheres this includes safe use and low cost. (A. Bigi et al., 2002; Li-Huei Lin et al., 2006; Y.Z. Zhang et al., 2006).

Activation of carbon is usually using acid,alkaline; or salt as activators. Some examples of commonly used activators are HCl, H_2SO_4, NaOH, KOH, $ZnCl_2$, NaCl (Wang, Jiacheng et al,. 2012). In this study carbon microspheres were activated with KOH solution. KOH

solution is used as an activator because it has the advantage of being able to control the acidity of carbon powder, able to open carbon pores so that the carbon surface area will be higher, able to multiply micropore structures where the adsorbent with micropore pore size is more effective for the adsorption process, can suppress hydrocarbon impurities and impurities in carbon pores so that carbon absorption is greater, giving cavities on the surface of carbon, producing tar as fewer by-products (Jin Jin et al., 2010; Wang, Bin et al., 2016; Wang, Jiacheng. 2012; Zhou, Min et al., 2013). In this study, acid activators are not used because acid activators have a weakness which is corrosive so that it will damage and erode biological tissue if touched, the steam can cause irritation to the respiratory tract so it is less safe to use. KOH was used for the activation process in this study, because at low temperatures the activation with KOH was higher than NaOH (M.A. Lillo-Rodenas et al., 2001).

The factors that influence the activation process are activation time, activation temperature, particle size, activator ratio, and type of activator. Temperature activation affects the activation energy generated, the higher the activation temperature, the greater the energy produced. So that the activated carbon that is formed is getting better, and the activation temperature affects the final appearance of the product produced (S. Alonso et al., 2001).

Ibuprofen is a non-steroidal anti-inflammatory drug that is included in the derivative of arylacetic acid or propionic acid derivatives. Ibuprofen is an analgesic that is strong but with anti-inflammatory power that is not too strong. This drug is included in class II drugs, namely drugs with low solubility with high permeability. Ibuprofen functions to reduce pain due to inflammation. Side effects of using Ibuprofen are irritation of the digestive tract because the digestive tract quickly absorbs Ibuprofen with a half-life of 1.8-2 hours (Guindon, Josee et al., 2016; S. Albert, Kenneth et al., 1984). As time went on, the number of factories producing ibuprofen increased, resulting in higher levels of ibuprofen waste. Therefore, the high industrial waste of ibuprofen causes environmental pollution which will disrupt the ecosystem in the environment.

This research begins with the synthesis of microspheres carbon, followed by activation of microspheres carbon with KOH solution, then characterization, and then adsorption with ibuprofen. Adsorption is the process of absorption of a liquid material on the surface of a

solid. The adsorption of ibuprofen on the surface of the microspheres carbon aims to determine the adsorption capacity of the activated of the microspheres carbon in each predetermined variation. The adsorption capacity on microspheres carbon is relatively large, no studies have used microspheres for adsorption of ibuprofen. So that the use of microspheres carbon as carrier agents in the Drug Delivery System (DDS) has great potential. At the end of the study, it is expected to obtain microspheres carbon with fine pore structures, high adsorption surfaces, high bonds between adsorbents and adsorbates. So it is expected that the results of this study can be used as engineering to compile the DDS prototype.

II. EXPERIMENTAL

a. Materials

Polyoxyethylene-Polyoxypropylene Block Copolymer purchased in Sigma-Aldrich with properties related categories (3D Printing Materials for Research and Development, Amphiphilic Block Copolymers, Biochemicals and Reagents, Copolymers, Poly (ethylene glycol) and Poly (ethylene oxide), Synthetic Polymers for 3D Printing), description (Non-ionic, contains 100ppm BHT), product line (BioReagent), form (Powder), suitable for cell culture. Ethanol (Ethyl Alcohol) purchased in Sigma-Aldrich, with grade (Laboratory Reagent) properties, vapor density (1.59 (vs water)), vapor pressure (44.6 mmHg (20 ° C)), assay (≥95.0% (vol.) ≤0.005% acidity (as CH3COOH). Purchased in Sigma-Aldrich gelatin, the synonym is gelatina, testing conforms to Pharmacopeia. Sucrose purchased in Sigma-Aldrich, with synonym properties (α-D-Glc-(1→2)-β-D-Fru, α-D-Glucopyranosyl β-D-fructofuranoside, β-D-Fructofuranosyl-a-D-glucopyranoside, D(+)-Saccharose, Sugar), Related Categories (Biochemicals and Reagents, Carbohydrates, Cell Biology), assay (≥99.5% (GC)). Acetic acid purchased in Sigma-Aldrich, with properties that are related categories (Acids, Acids & Bases, Chemical Synthesis, Electronic Chemicals, Inorganic Acids, Materials Science, Micro / NanoElectronics, Synthetic Reagents), description (Nominally 95-98% H2SO4), assay (99.999%). KOH purchased in Sigma-Aldrich, with properties that are related categories (Acids & Bases, Bases, Chemical Synthesis, Inorganic Bases, Synthetic Reagents), pH (14 (56 g / l, H_2 O, 20 ° C)), specifications (Assay

(acidimetric, KOH): ≥ 85.0%). Ibuprofen purchased in Sigma-Aldrich, with properties that are related categories (Biochemicals and Reagents, Cell Biology, Cell Signaling Enzymes, Cell Signaling and Neuroscience, Cyclooxygenase, Enzyme Inhibitors, and Substrates), assays (≥98% (GC)), forms (powder). Hexane (n-Hexane) purchased in Sigma-Aldrich, with properties that are related categories (Reagent Plus Solvent Grade Products, ACS and Reagent Grade Solvents, Amber Glass Bottles), assay (≥99%), water insoluble. Aquades.

b.Microspheres Carbon Synthesis

Synthesis of microspheres carbon begins by preparing a powder of Polyoxyethylene-Polyoxypropylene Block Copolymer, and making ethanol solution with a ratio of ethanol and water with a ratio of 1.5: 11.7: 3.9. The next step is dripping ethanol into Polyoxyethylene-Polyoxypropylene Block Copolymer using the burette until the ethanol runs out, then stirring the mixture. Next add gelatin and sucrose to a ratio of 0.4 to the solution of Polyoxyethylene-Polyoxypropylene Block Copolymer while stirring and a clear solution is produced. Then, H_2SO_4 solution is made from sucrose plus aquades and droplets of concentrated H_2SO_4 solution with a ratio of 0.3: 1.5: 1.5. Furthermore, H_2SO_4 solution is dropped into a clear solution with a burette while stirring. After all the Polyoxyethylene-Polyoxypropylene Block Copolymer has been dropped, sucrose is added to the mixed solution while stirring and a clear mixture will be produced. The clear mixture is inserted into the hydrothermal reactor while in the oven, then cools it and becomes a brown mixture. Furthermore, the chocolate mixture is oven-heated in hydrothermal and oven again at 160^{o}C (partial carbonization). After that, the mixture is poured into the porcelain exchange rate and oven until it is obtained dry black solid. Black solids are carbonized in furnaces with nitrogen or argon gas, becoming fine black solids. The fine black solid is washed with distilled water, then filter with a vacuum filter and observe it. Washing is done several times until there is no white sediment, then the solid is dried in the oven overnight. The sample produced is labeled SMC.

b.Activation of SMC

Activation of the microspheres carbon was initiated by mixing SMC powder and potassium hydroxide (KOH) solution with a concentration of 10% while stirring for 30 minutes at room temperature (25^{o}C). Then the mixture of SMC with 10% KOH solution was left to stand for 24 hours with temperature variations ─9^{o}C, 29^{o}C, and 35^{o}C. After that, the mixture that has been left idle is filtered with Whatmann 42 filter paper, resulting in filtrate and solids. Then

the solid is heated in the oven to dry. The results of this activation will be used for adsorption of ibuprofen and for characterization. Characterization is done by using SEM to determine the size and morphology of the particles, and FTIR to find out the functional groups in activated SMC. The sample produced is labeled ASMC (─ 9oC); ASMC (29oC); ASMC (35oC).

b. Adsorption of Ibuprofen

Adsorption of ibuprofen was started by dissolving ibuprofen powder with hexane solvent until it obtained a solution of ibuprofen with a concentration of 100 ppm. Then take 50 ml of the 100 ppm ibuprofen solution and put it in the beaker. Add 20 mg of ASMC to the glass cup containing a solution of ibuprofen, while sterilizing at room temperature (25^{o}C). Then take 3 mL of sample solution every 5 minutes' intervals 15 times and take a UV-Vis spectrophotometer at a wavelength of 272 nm. So that the UV-Vis graph will appear from the sample, namely 100 ppm ibuprofen solution.

c. Characterization of ASMC

The characterization of ASMC was carried out through surface area analysis techniques with scanning electron microscope (SEM), and functional group analysis techniques with fourier transform infrared (FTIR). SEM analysis using a JEOL JSM-700 microscope at 15.0 kV. FTIR analysis using Bruker Vertex 70 spectroscop with wavelengths from 4000-500 cm-1. Whereas to measure absorbance in adsorbed samples, an UV-Vis spectrophotometer was performed with the U-2000 model from Hitachi Japan at a wavelength of 272 nm.

III. RESULT AND DISCUSSION

a.Activation of Microspheres Carbon (SMC)

ASMC produced after activation with KOH solution at −9°C; 29°C; 35°C will be used for adsorption with 100 ppm ibuprofen solution, and for characterization using surface analysis techniques with SEM and functional group analysis techniques with FTIR.

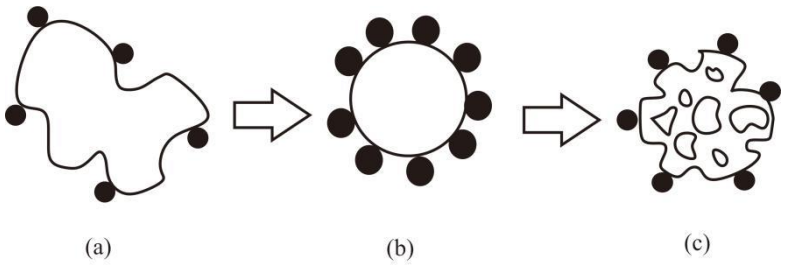


Figure 1. Illustration of structural changes (a) ASMC-(−9°C), (b) ASMC (29oC), (c) ASMC (35oC)

From Fig 1 it can be seen that the activation process at temperatures of −9°C and 35°C causes damage to the carbon structure, but more severe damage occurs to the activation of carbon at a temperature of −9°C. While the activation of carbon at 29°C does not cause carbon structure desctruction. The resulting ASMC is surrounded by potassium aggregates, water particles (H_2O), impurities, and other particles.

Table 1. Table of influence of SMC activation temperature on mass before activation and mass after activation

Sampel	Activation Mass	
	Before (g)	After (g)
ASMC(−9°C)	0,30	0,74
ASMC(29°C)	0,30	0,82
ASMC(35°C)	0,30	0,75

From the table above, the results show that there is an increase in ASMC mass. The highest increase in mass of ASMC occurs at 29°C activation, this is estimated because ASMC at 29°C has the right energy to activate SMC, potassium aggregates; water particles (H_2O); impurity; and the other particles attached to the surface of the SMC are the most numerous and evenly distributed compared to ASMC at temperatures of −9°C and 35°C. Whereas the

mass increase in ASMC temperature −9°C and 35°C only shows a very small difference and the mass increase is not as much as ASMC (29oC), this is estimated because ASMC-(−9°C) and ASMC (35oC) carbon structure damage so that the aggregate potassium; water particles (H_2O); impurity; and other particles attached to the SMC surface are only a little or not as much as ASMC (29oC). Potassium aggregates that are attached or trapped on the surface of the SMC can occur because the size of the SMC pores is less than 2 nm (micropore), whereas it is estimated that the average radius of the element K is 0.23 nm.

a.Adsorption of Ibuprofen

The adsorption process of ibuprofen is done by mixing ibuprofen and SMC solution while stirring at room temperature (25ºC). Then take 3 mL of sample solution every 5 minutes at the interval of 15 times. The sample solution that has been taken will be analyzed using a uv-vis spectrophotometer at a wavelength of 272 nm. From the results of the analysis obtained absorbance values for each temperature variation ─9ºC; 29ºC; 25ºC. Then the absorbance data is converted into concentration with the help of the equation obtained from the standard solution curve, the standard solution curve equation obtained is 0.0257x + 0.0199 with R^2=0.9813.

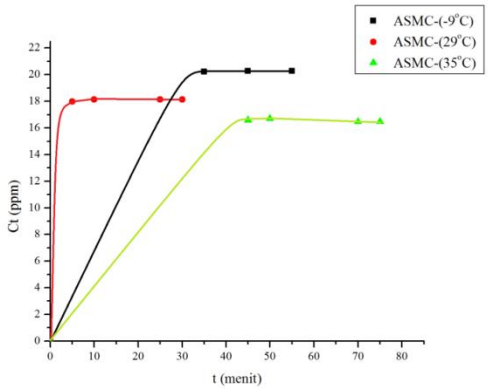


Figure 2. Graph of adsorption performance from ASMC (─ 9oC), ASMC (29oC), ASMC (35oC)

From the graph above it can be seen that ASMC (─ 9oC) has the highest equilibrium concentration of 20.22 ppm, while ASMC (35oC) has the lowest equilibrium concentration of 16.58 ppm. The higher the temperature of the carbon activation of the microsphere produces the lower the equilibrium concentration. But ASMC (29oC) reaches the equilibrium concentration at the fastest time, namely in the 5th minute, while ASMC (─ 9oC) and ASMC (35oC) require a long time to reach equilibrium concentrations which are 35 and 45 minutes respectively. This is expected to occur because the temperature of 29ºC is the right

temperature for activation, so the right energy is generated to activate it, so that the resulting adsorption surface is high with more regular carbon pores.

Table 2. Table of effect of SMC activation temperature on maximum adsorption capacity (q_{max})

Sampel	q_{max} (mg/g)
ASMC (— 9oC)	56.96
ASMC (29oC)	58.47
ASMC (35oC)	59.50

The table above shows that the higher the activation temperature produces the higher adsorption capacity (q_{max}). It is estimated that because the higher the activation temperature will produce higher energy, so that the resulting q_{max} is higher too.

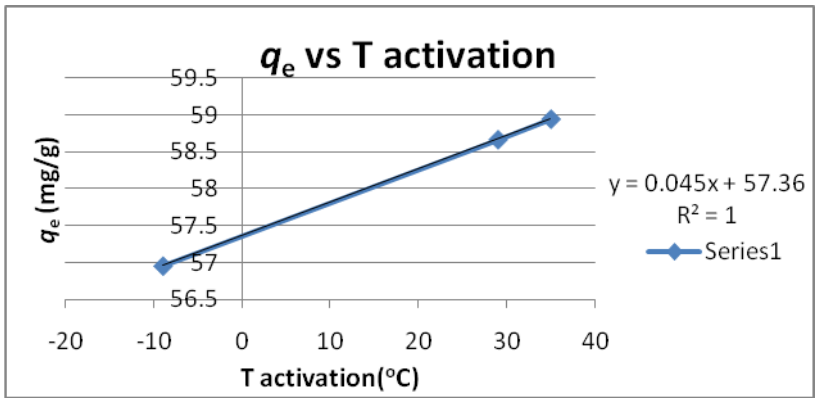


Figure 3. Graph of the relationship between adsorption capacity at equilibrium (q_e) in mg/g and the activation temperature of SMC in ^oC

From the graph shows that there is a relationship between adsorption capacity when balanced with the SMC activation temperature, which is the higher the activation temperature, the higher the adsorption capacity when balanced. The relationship between the two is shown by

a graph which produces R^2=1. Because the activation temperature affects the amount of damage to the carbon structure produced. The energy produced is higher along with the higher activation temperature, so that the resulting bond gets stronger. The impact velocity that occurs between carbon molecules at each temperature varies, so the adsorption capacity produced will also be different. Where, the higher the activation temperature will result in a greater impact speed with greater intensity, and will cause the adsorption capacity of the ibuprofen molecule to increase.

a. Characterization Results

i. *Fourier transform infrared* (FTIR) Characterization Results

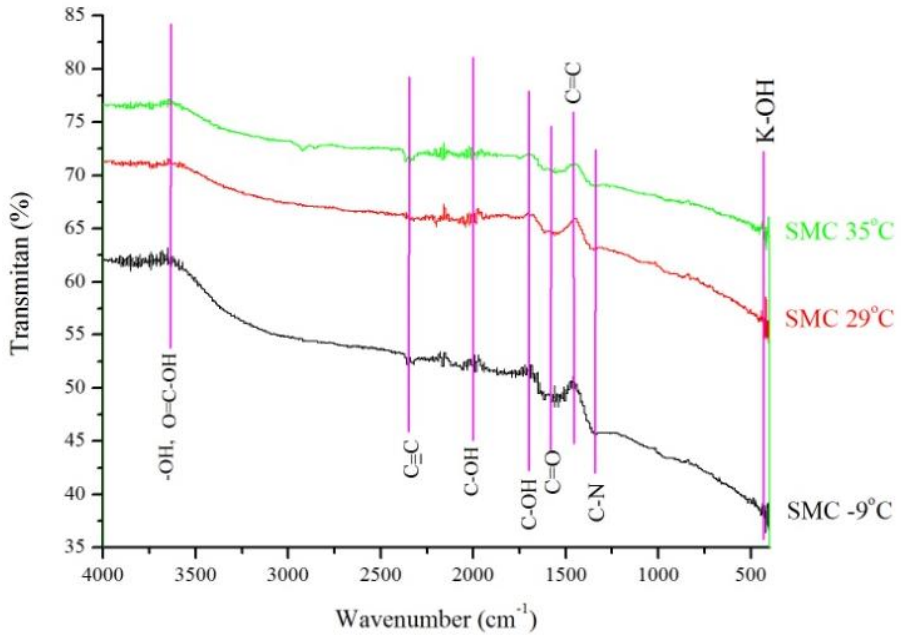
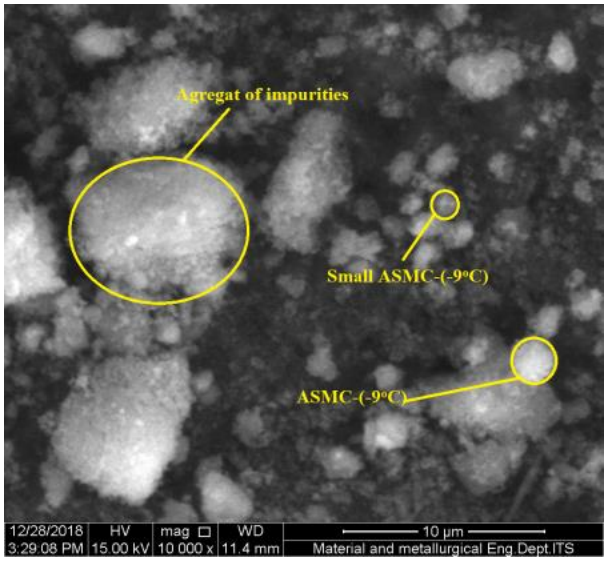


Figure 4. Graph of results of characterization with FTIR from ASMC

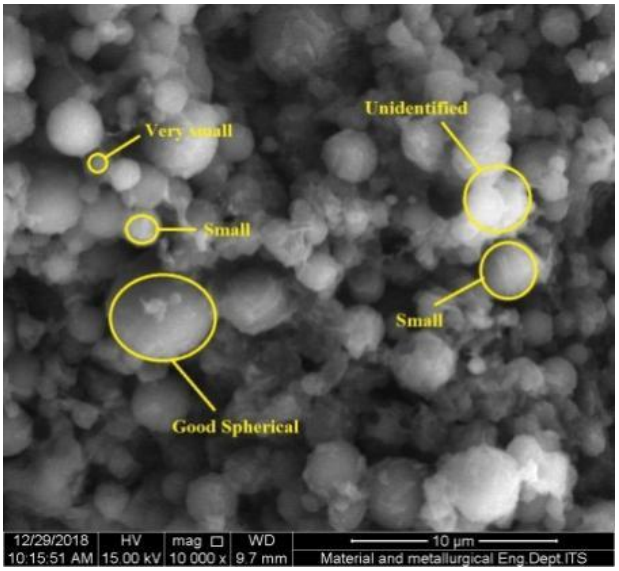
According to research conducted by Chin-San Wu (2007) in the range of wavelengths between 3700-2800 cm^{-1}, it shows a group of functions –OH. According to Min Li's (2011) experiment at 1100-3570 cm^{-1} shows the functional group O=C–OH. Whereas in the Xiaoming Sun (2004) experiment at 1620 cm^{-1} showed double bonds C=C and 1710 cm^{-1} were C=O, and in experiments conducted by Abdel-Naseer (2009) double bonds C=C appeared at length wave 1660-1430 cm^{-1}. In the research conducted by J Rumanos, the C–OH group appeared at wavelengths between 3429 cm^{-1} to 1630 cm^{-1}. Then in the K.Y.Foo (2011) study at 2357 cm^{-1} C≡C bonds appeared. And according to R.G Snyder (1960) K–OH groups appear at wavelengths of 4000-300 cm^{-1}. According to Xuefei Li (2009), the adsorption peak at 1335 cm^{-1} appeared C–N.

In this study, FTIR results were obtained which showed that K–OH groups appeared at wavelengths of 432.50-492.52 cm^{-1}. At wavelength 1558.92-1556.28 cm^{-1} C=C group appears, then C–OH group appears at a wavelength of 2040.44-1694.17 cm^{-1}. Then at 2337.27-2200.80 cm^{-1}. In addition, at a wavelength of about 3500 cm^{-1}, the –OH group and O=C–OH appear. The C≡C bond appears at 2500-2250 cm^{-1}. The C=O bond appears at 1750-1500 cm^{-1}. And the C–N group appears at 1500-1250 cm^{-1}. From the results of the FTIR above, the higher the activation temperature results in the –OH group; O=C–OH; C–OH; C=O; and C–N decreases. Whereas for the C≡C group more and more along with the higher activation temperature. The C–N group tends not to change as the activation temperature changes, the C–N group at each temperature is relatively the same. But most K–OH groups are found in ASMC (29oC), thus indicating that at the activation temperature of 29^{o}C the K–OH group that envelops carbon plays a role in helping the adsorption process and at 29^{o}C the right temperature for carbon activation.

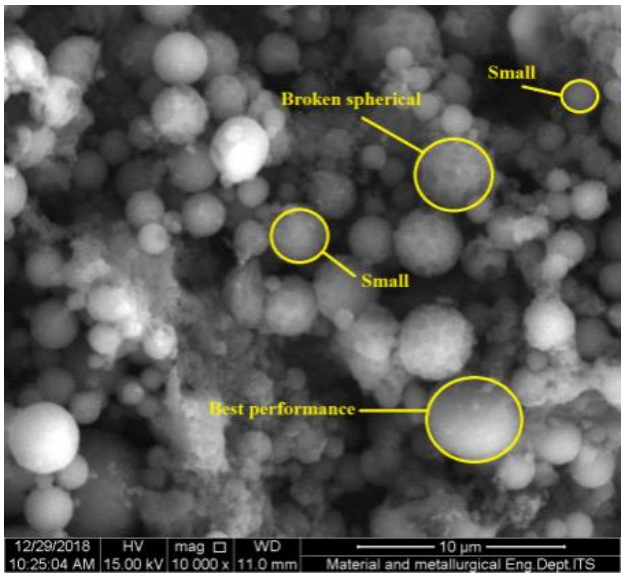
ii. Characterization of scanning electron microscope (SEM)



(a)



(b)



(c)

Figure 5. Results of characterization with SEM from (a) ASMC (─ 9oC), (b) ASMC (29oC), (c) ASMC (35oC)

From the results of the characterization with SEM, the ASMC structure damage occurs at activation with a temperature of −9°C and 35°C, it can be seen that the ASMC-(−9oC) has the most damaged structure not rounded again, whereas ASMC (35oC) occurs damage to structures but not as severe as that of ASMC-(−9°C). ASMC (35oC) is damaged but is still round in shape with a non-smooth surface, but like a rounded surface, the surface is hollow and uneven. The damaged surface is covered in very little potassium aggregate; water particles (H_2O); impurity; and other particles. In some parts severe damage is seen but not significant compared to ASMC-(−9°C). In ASMC (29oC) there is nothing significant structural destruction which is the structure of ASMC (29oC) still looks round with a smooth surface covered with potassium aggregates; water particles (H_2O); impurity; and other particles. The ASMC-(−9°C) sample not completely covered by impurities.

Table 3. Table number of ASMC structures that are damaged and not damaged after being activated at −9ºC, 29ºC, 35ºC

Sampel	∑ Damaged (%)	∑ Undamaged (%)
ASMC (─ 9oC)	85 %	3 µm = 5 % 1 µm = 10 %
ASMC (29oC)	2 %	5 µm = 3 % 3 µm = 13 % 2 µm = 22 % 1 µm = 45 % 0,5 µm = 8 % 0,1 µm = 7 %
ASMC (35oC)	20 %	4 µm = 15 % 3 µm = 21 % 2 µm = 35 % 1 µm = 9 %

From the table above, it can be seen that the greatest damage to the ASMC structure occurs at the activation temperature of −9ºC, and the smallest damage occurs at 29ºC activation temperature, while at 35ºC the activation temperature also breaks down the structure but is still relatively small. In ASMC (29oC) it produces a structure with a size between 0.1-3µm but is dominated by a size of 1µm, the size is smaller than ASMC-(−9ºC) and ASMC (35oC). From the table, it is known that ASMC-(−9ºC) produces 85% of the damaged structure, so the number of undamaged ASMC is very small and predominantly 1µm in size. Whereas in ASMC (35oC) the number of undamaged structures measuring between 4-1µm is dominated by 2µm size.

CONCLUSION

From this research, it can be concluded that the synthesis of microspheres carbon with the soft template method and activated with KOH at 29^{o}C produces ASMC which has a high surface area and adsorption capacity. FTIR results show that clusters that appear on ASMC include –OH; O=C–OH; C–OH; C=O; C–N; C≡C; C–N; K–OH. Then from the SEM results it shows that ASMC-(–9^{o}C) and ASMC (35oC) damage to carbon structure, where in ASMC-(–9^{o}C) carbon is the most damaged. Damage to the carbon structure is at least at ASMC (29oC), so that the temperature of 29^{o}C is the right temperature to do SMC activation. The amount of q_{max} is directly proportional to the higher activation temperature. Therefore, the results of this study can be used as an adsorbent in the control of ibuprofen waste in the environment and can be used as a basis for making drug delivery system (DDS) prototypes. But to deepen its use in DDS, further research is needed.

Acknowledgements

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