Characteristics Testing of Microcrystalline Cellulose from Nata de Coco Compared to Avicel pH 101 and Avicel pH 102

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***Abstract*—Microcrystalline cellulose is an imported raw material in Indonesia, which used widely as an excipient in tablet production. One of the alternative materials to produce microcrystalline cellulose is from *nata de coco*. This research aimed to know the characteristic of microcrystalline cellulose from *nata de coco* compared to avicel pH 101 and avicel pH 102. *Nata de coco* were alkalinated, dried and hydrolyzed to get microcrystalline cellulose. Independent variables in this research are microcrystalline cellulose from *nata de coco*, avicel pH 101 and avicel pH 102. While the dependent variables are flow properties, compactibility, compressibility, water absorption, tap density, bulk density, loss of drying, infrared absorption spectra, and SEM images. Data analyzed using one way ANAVA with CI 95% and using software SPSS for windows. The result showed that data from characteristic test microcrystalline cellulose from *nata de coco* is different in flow properties, compactibility, compressibility, tap density, bulk density, and loss of drying from avicel pH 101 and avicel pH 102, but having the same water absorption. Infrared spectrum data showed that microcrystalline cellulose from *nata de coco* is similar to avicel pH 101 and avicel pH 102. The SEM result showed that microcrystalline cellulose from *nata de coco* having bigger particle size (66.67–266.67 µm) than avicel pH 101 (13.33–166.67 µm) and avicel pH 102 (13.33–200 µm).**

Keywords: Avicel pH 101; Avicel pH 102; Nata de coco

I. INTRODUCTION

Indonesia is one of the countries with high biodiversity. But until today, 96% of medicines raw materials were imported from other countries[1]. One of the imported raw materials used widely as excipient (filler-binder) in tablet production is microcrystalline cellulose. In tablet production, microcrystalline cellulose is the first choice for excipient because having good compactibility and rapid disintegration time. Nevertheless, the pricing of good characteristic raw materials are so high, and limit its application in small and medium industries. It's making the growth of Indonesian pharmaceutical industry is low.

Microcrystalline cellulose is a modification of natural cellulose that can be obtained from various sources both from plant and fermentation products. One of the alternatives is producing microcrystalline cellulose from *nata de coco*[2]. *Nata de coco* is the product of coconut water fermented by *Acetobacter xylinum*. The main content of *nata de coco* is cellulose[3].

Microcrystalline cellulose from *nata de coco* need to be test its characteristics compared to standard microcrystalline cellulose used as tablet excipient, avicel pH 101 and avicel pH 102. The basic testing are flow properties, water absorption, compactibility, compressibility, loss of drying, tap density, bulk density, and infrared spectrum. This research result expected being a basic for further research, either formula optimization or process. Additionally, microcrystalline cellulose from *nata de coco* expected to be used directly as excipient in pharmaceutical industry; especially tablet production so could minimize the production costs through reduction of imported raw materials in production process.

II. MATERIALS AND METHODS

A. Materials

Materials used are *nata de coco*, avicel pH 101, avicel pH 102, NaOH, HCl, and aquadest. Equipments used are powder grinding machine, percolator, stainless steel pan, water bath, electrical balance, glassware, fan, dwell angle test tools (Erweka GT), digital stopwatch, stokes Monsanto hardness tester, fluidity measurement (Erweka GT), friabillator abrasive tester (Erweka TA-20), Tap density test tools (Erweka SVM 22), vacuum cleaner, balanced weighing, drying cabinet, filter, single punch tablet printing machine, room humidity controlling equipment, infrared spectroscopy, and scanning electron microscope.

B. Methods

Preparation of Microcrystalline Cellulose from Nata de Coco

Nata de Coco were dried and grinded into powder named cellulose powder. It was boiled in hot water, and then separated its residue to boil with sodium hydroxide 2%. The residue got from the boiling process was washed with aquadest until the pH 6-7 before soaked into 18% sodium hydroxide. The residue washed using aquadest again until pH 6-7 and dried using oven resulting α-cellulose powder. α-cellulose powder hydrolyzed using chloride acid 2,5 N by boiling it for 10-15 minutes. The residue neutralized by aquadest, then being dried and grinded mechanically until resulting microcrystalline cellulose.

Characteristic Testing

1. Fluidity testing using funnel method through measuring the angle of stationary[4]
2. Compactibility and compressibility tested into microcrystalline powder that has been printed into tablets with punch scale 6 (up) and 10 (down). The compactibility testing used hardness tester, while compressibility tested using compressibility test equipment.
3. Water absorption tested by water absorption testing equipment that being connected with electrical balance then measured its rate of water absorption through dividing the reduction of water in the ampoule on the electrical balance with water absorption time which is counted 20 minutes.
4. Tap density tested using tap density equipment and counted its percentage of tap density by dividing difference volume with initial volume
5. Bulk density tested using 100 ml volume measuring glass to get the value of mixture weight in grams divided by mixture volume in milliliters.
6. Loss of drying tested by dried *nata de coco,* avicel pH 101 and avicel pH 102 in the oven at 105^0 C temperature for 5 hours.
7. Physicochemistry of the powder tested using infrared spectroscopy
8. Particle size of microcrystalline cellulose observed using scanning electron microscope.

Data Analysis

Data analyzed using one way ANAVA with CI 95% by SPSS for windows. Independent variables were microcrystalline cellulose from *nata de coco,* avicel pH 101 and avicel pH 102. Dependent variables were fluidity, compactibilitiy, compressibility, water absorption, tap density, bulk density, loss of drying, infrared absorption spectrums, and scanning electron microscope figure. Controlled variable was the treatment.

III. RESULT AND DISCUSSION

This research aimed to know the characteristics of microcrystalline cellulose from *nata de coco* compared to Avicel pH 101 and Avicel pH 102. Avicel is microcrystalline cellulose that usually being used for tablet filler and also can use for tablet binder. Additionally, Avicel also can be used as crusher material[5]. Avicel has a good fluidity and direct compression properties. Avicel could produce hard, low (good) compressibility, and low friability tablet, also long stability time tablet[6].

Dwell angle is a fluidity characteristic which related tightly into cohesiveness between particles built up granules. Dwell angle itself is an angle formed between the surfaces of granules stack with horizontal plane. Granules will free flowing if the dwelling angle formed were 30º - 40°[4]. The size of dwelling angle being affected by gravitation and frictions between particles, if the gravitation and the frictions are low so the particles will be easier to flow. The flatter the cone produced, the lower the angle, and the better of powder fluidity[6]. Based on dwelling angle test result, it can be seen that microcrystalline cellulose from *nata de coco* (31.67°± 0.58) having the best fluidity characteristic. All of the samples were having characteristic of free flowing because the dwelling angle weren't more than 40º. Statistical analysis of fluidity data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results ($P > 0.05$). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample ($P < 0.05$, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against avicel pH 102; avicel pH 101

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Table I. The characteristic test result of microcrystalline cellulose obtained from avicel pH 101, avicel pH 102, and *nata de coco*

Test Sample	Fluidity/ Dwell Angle (^{0})	Compactibility/ Hardness (kg)	Compess-ibility/ thickness (mm)	Water Absorption ability (grams/ minutes)	Tap density (%)	Bulk density (grams/ml)	Loss of Drying (%)
Nata de Coco	31.67° ± 0.58	1.93 ± 0.10	3.54 ± 0.02	0.06 ± 0.00	16 ± 4.58	0.43 ± 0.00	23.91 ± 0.08
Avicel pH 101	40° ± 0	2.57 ± 0.12	3.37 ± 0.01	0.08 ± 0.01	25.67 ± 1.53	0.33 ± 0.01	4.23 ± 0.19
Avicel pH 102	35° ± 1	5.15 ± 0.09	3.38 ± 0.01	0.07 ± 0.01	25.67 ± 1.15	0.35 ± 0.00	4.78 ± 0.12

against *nata de coco*; and avicel pH 102 against *nata de coco.*

Compactibility is a parameter to know the hardness and the friability of a tablet. A tablet must have a good hardness so can resist the shocks between the transport and the storage process until being used by patients. The bigger compression given, the harder a tablet will be. Based on compactibility data, showed that avicel pH 102 having the best compactibility (5.15 kg ± 0.09) while *nata de coco* microcrystalline cellulose powder having the worst compactibility (1.93 kg ± 0.10). Statistical analysis of compactibility data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample (P < 0.05, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against avicel pH 102, pH 101 against *nata de coco*; and avicel pH 102 against *nata de coco*.

Tablet thickness calculated into the materials volume inserting into the punch, the diameters of punch, and pressure of the punch used for compressing filler materials. Various tablet thickness affected by punch size and the materials used rather than the pressure used[7]. One of the factors affecting tablet compressibility is material density. Material density is proportionate with punch pressure. The higher material density, the bigger punch pressure[8]. Based on compressibility test result, could be seen that Avicel pH 101 having the best compressibility characteristic (3.37 mm ± 0.01) and the worst compressibility characteristic was the microcrystalline cellulose from *nata de coco* (3.54 mm ± 0.02). Statistical analysis of compressibility data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample (P < 0.05, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against *nata de coco*; and avicel pH 102 against *nata de coco.*

Water absorption ability related to tablet disintegration, which cannot be happen if water doesn't absorb in the tablet, where it dependent to the compression and water absorption ability from the material used. Water could penetrate into the tablet pores because of the capillary action. Cruncher materials in the tablet started its functions through expansion process, chemical reaction and enzymatic reaction after water absorb into the tablet. It can be concluded that the higher water absorption ability, the faster tablet absorbed. Based on water absorption ability result, showed that Avicel pH 101 having the best water absorption ability (0.08 grams/minute ± 0.01) while *nata de coco* microcrystalline cellulose having the worst water absorption ability (0.06 grams/minute ± 0.01). Statistical analysis of water absorption ability data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were no significant differences in the three test sample (P > 0.05, CI 95%).

Tap density showed reduction of granules/ powders volume because of tapping/ vibrating. The smaller tap density percentage of the granules/ powders, the better its fluidity. Granules or powders with tap density below 20% having good fluidity[9]. Based on tap density test result, it can be seen that avicel pH 101 and avicel pH 102 having biggest tap density index (25.67%) while microcrystalline cellulose both from *nata de coco* having the lowest tap density index (16%). Statistical analysis of tap density data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample (P < 0.05, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against *nata de coco*; and avicel pH 102 against *nata de coco*.

Bulk density will affect compression ratio that will be affected to tablet thickness and also impacted on fluidity. Sphere particles having a higher bulk density compared into non sphere particle. Smaller granules could form bigger mass than bigger granules[4]. Bulk density test result showed that microcrystalline cellulose from *nata de coco* having the biggest bulk density (0.43 grams/ml ± 0.00) and avicel pH 101 having the lowest bulk density (0.33 grams/ml ± 0.01). Statistical analysis of bulk density data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample (P < 0.05, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against *nata de coco;* and avicel pH 102 against *nata de coco.*

Loss of drying is a measurement for wasting products after drying process at 105^{0}C for 30 minutes or until constant, stated in percentage[10]. The loss of drying ability test showed that microcrystalline cellulose from *nata de coco* having the biggest loss of drying ability (23.91 grams/ml ± 0.08) while avicel pH 101 having the lowest loss of drying (4.23 grams/ml ± 0.19). Statistical analysis of loss of drying data using Kolmogorov-Smirnov test obtained normally distributed and homogeneous data with significant results (P> 0.05). Statistical tests One-Way ANOVA showed that there were significant differences in the three test sample (P < 0.05, CI 95%). LSD test results showed that there were significant differences between the test sample of microcrystalline cellulose from avicel pH 101 against avicel pH 102, avicel pH 101 against *nata de coco*; and avicel pH 102 against *nata de coco.*

The complete fluidity, compactibility, compressibility, tap density, bulk density, and loss of drying test result of microcrystalline cellulose obtained from avicel pH 101, avicel pH 102, and *nata de coco* showed in table 1.

The result of infrared spectroscopy showed that microcrystalline cellulose powder both from avicel pH 101 and avicel pH 102 having main spectrum in 3337, 2897, 1427, 1366 and 1030/cm wavelength and having hydroxyl group, hydrogen bonding, C-H alkenes, CO ether and alcohol bonding. The infrared spectrum of *nata de coco* microcrystalline cellulose powder showed that the main spectrum were in 3344, 2897, 1427, 1107, and 1030/cm wavelength and having hydroxyl group, hydrogen bonding, C-H alkenes, CO ether and alcohol bonding. Infrared spectrum of avicel pH 101 showed that microcrystalline cellulose from *nata de coco* having the same properties as avicel pH 101 and avicel pH 102. They have hydroxyl groups, hydrogen bonding, C-H alkenes, CO ether bonding, and alcohol as seen in the infrared spectrum wavelength. It can be inferred that microcrystalline cellulose obtained from *nata de coco* having similar infrared spectrum with avicel pH 101 and avicel pH 102. It can be concluded that microcrystalline cellulose isolation from *nata de coco* giving pure result because of having similar infrared spectrum compared both to avicel pH 101 and avicel pH 102.

The particle size and shape of microcrystalline cellulose from avicel pH 101, avicel pH 102, and *nata de coco* showed in figure 1, figure 2, and figure 3. Scanning electron microscope result showed that there are differences of microcrystalline cellulose particle size from the samples.

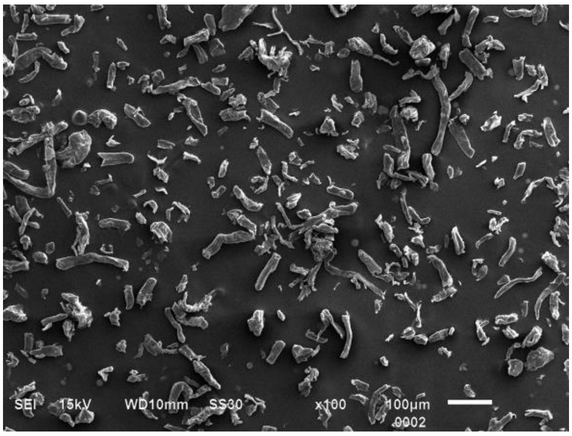

Fig 1. The Scanning Electrone Microscope Result of microcrystalline cellulose obtained from avicel pH 101

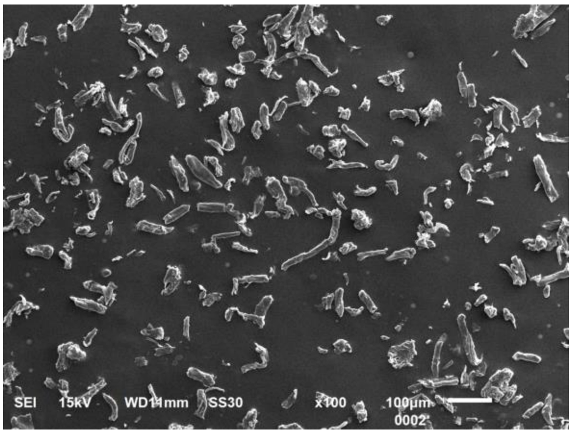

Fig 2. The Scanning Electrone Microscope Result of microcrystalline cellulose obtained from avicel pH 102

Microcrystalline cellulose powder from avicel pH 101 particle size were ranged from 13.33 until 166.67 µm with irregular shape and uneven surface texture and forming sharp and blunt angles. The microcrystalline cellulose powder particle size from avicel pH 102 ranged from 13.33 until 200 µm with irregular shape and uneven surface texture and forming sharp and blunt angles. While the particle size of microcrystalline powder from *nata de coco* was ranged from 66.67 until 266.67 µm. The powder have irregular shape, the surface texture were uneven with blunt angles.

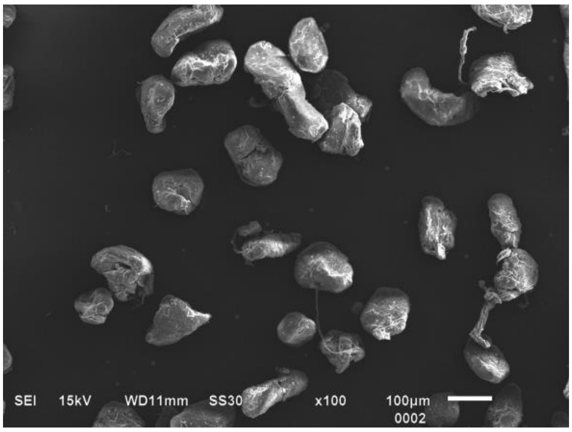

Fig 3. The Scanning Electrone Microscope Result of microcrystalline cellulose obtained from *nata de coco*

Scanning electron microscope analysis held for knowing particle size and shape of the microcrystalline cellulose. Particle shape of microcrystalline cellulose from *nata de coco* was different from avicel. It didn't have sharp form; but shape, surface, and the angles were the same. Based on that data, it can be seen that microcrystalline cellulose from *nata de coco* having bigger particle size than Avicel pH 101 and Avicel pH 102.

IV. CONCLUSIONS

1. Based on characteristic test data of fluidity, compactibility, compressibility, tap density, bulk density, and loss of drying; microcrystalline cellulose from *nata de coco* was different from Avicel pH 101 and Avicel pH 102, but having the same water absorption ability.
2. Based on infrared spectrum interpretation showed that microcrystalline cellulose from *nata de coco* was similar to Avicel pH 101 and Avicel pH 102.
3. Based on scanning electrone microscope result showed that microcrystallone cellulose from *nata de coco* having bigger particle size (66.67 – 266.67 µm) than avicel pH 101 (13.33 – 166.67 µm) and avicel pH 102 (13.33 – 200 µm).

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