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Research Article

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Microcrystal Cellulose from Sugarcane Bagasse (*Saccharum Officinarum* L.): Tablet Filler Excipient

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ABSTRACT

Microcrystal cellulose is a result from alpha cellulose isolation. Woody plants are generally the source for microcrystal cellulose production. One of the natural ingredients that can be used to make microcrystalline cellulose is sugarcane bagasse (Saccharum officinarum L.).

Sugarcane bagasse contains 37.65% cellulose which can be isolated by delignification steps using base solution, bleaching process, and alpha cellulose hydrolysis with high temperature heating using dilute acid solution. Microcrystal cellulose yield from sugarcane bagasse was 26.03% and fulfilled the characteristic based on literature. Microcrystal cellulose has a potential to be used as tablet filler ingredient which fulfill tablet physical property test.

Keywords: Microcrystal Cellulose; Sugarcane Bagasse; Filler Ingredient; Tablet

INTRODUCTION

Indonesia is a country with rich natural resources. The diversity of natural resources is directly correlated with chemical diversity which has enormous potential for drug development [1]. Cane is one of the plants which have that potential. In Indonesia, sugarcane is widely cultivated on the islands of Java and Sumatra. Sugarcane bagasse contains 45.96% cellulose [2]. Cellulose from sugarcane bagasse which goes through isolation process can be used for microcrystal cellulose production [3]

In pharmaceutics field, microcrystal cellulose is used as tablet filler ingredients. The benefit of using microcrystal cellulose is that the cohesiveness of tablets from a compression mixture. Microcrystal cellulose also has the ability to increase flow properties of the print life of the tablet.
That characteristic of microcrystal cellulose is very helpful in tablet printing process using direct pressing method which needs quality and consistency increase from the starting material including excipient [4]

The purpose of this study is to produce microcrystal cellulose from sugarcane bagasse and to characterize microcrystal cellulose from sugarcane bagasse.

EXPERIMENTAL AND STATISTICAL STUDY

Instruments

The tools used in this study were digital scales (Kenko), beaker cups, electric stoves, measuring cups, stirring rods, filter paper, ovens

Materials

Materials used in this study were sugarcane bagasse from iced sugarcane drink trader around Harapan Bangsa campus, acetic acid, sodium hydroxide, sodium hypochlorite, chloride acid.

Research method

This research was done through some steps, including:

Sugarcane (raw material) preparation

Sugarcane was obtained from iced sugarcane drink trader around Harapan Bangsa University campus in Purwokerto, Central Java. Sugarcane bagasse which was obtained then sorted and washed repeatedly until cleaned with flowing water, and then it was cut to smaller sizes.

Furthermore, sugarcane bagasse then dried with oven in 50°C for 72 hours until dried sugarcane bagasse was obtained. The purpose of this preparation was to facilitate the isolation of cellulose contained by minimizing the size, increasing contact surface area, and breaking chemical chains in long molecular chains so it's expected to get optimal yield.

Alpha cellulose isolation

Isolation of α-cellulose from plant fiber was done through alkali heating method. Sugarcane bagasse was boiled using acetic acid 0.1 N with sample to solvent ratio of 1:20; this process is called pre-hydrolysis [5]. Pre-hydrolysis was done in an hour under 105^{o}C. After that, sample was separated from its solvent by filtering and squeezing and then sample was rinsed off repeatedly until the pH was neutral [6]. This stage aims to soften the material and accelerate the breaking of the pentose (hemicellulose) bond [7]. Isolation stage then continued by alkali heating using sodium hydroxide 25% b/v in 105^{o}C and boiled for one hour. Sample to sodium hydroxide ratio was 1:20 [8]. In this process, pulp or cellulose porridge was made where α-cellulose was isolated as residue.

Alpha-cellulose is a compound that is insoluble in NaOH or strong bases, this character was used to degrade lignin polymer which then would be dissolved in water. In this process a dark brown pulp is formed which settles in the sodium hydroxide solution [9]. Plant fiber was then got re-separated from its solvent through filtering and squeezing, sugarcane bagasse then rinsed until the pH became neutral again. The pulp obtained then repeatedly washed until pH 6-7 was reached. The next stage was bleaching.

The purpose of this stage was to remove lignin and carbohydrate residue which was not completely separated in pulp. The bleaching process made the pulp color brighter or whiter. This process was done by soaking the plant fiber in NaClO solution with sample to solvent ratio of 1:8 [10]. At the time of immersion, the sample which was originally floating in a brownish-white solution then turned yellowish white and slowly turned completely white and descended to the bottom of the surface. This happened because oxidized product becomes a material which could be easily dissolved in water. Solution was filtered and the residue was rinsed repeatedly using aquades until the pH back to neutral. The pulp was then dried in 50^{o}C oven for 12-24 hours [11]. Dried pulp which was obtained is called α-cellulose [5].

Microcrystal cellulose manufacturing

Oven-dried pulp in the form of α-cellulose underwent partial hydrolysis process or de-polymerization becoming microcrystal cellulose through long cellulose chain hydrolysis cut process by soaking in HCl 2,5 N solution which was reacted in 105 ^{o}C temperature for 15 minutes, sample to solvent ratio was 1:20. [12]Along the hydrolysis process, partial separation happened to cellulose micro-fibril sequence where the amorphous form will break up and leave the crystalline form, which is a region of cellulose molecules arranged in an orderly fashion [13]. The purpose of this process was to make α-cellulose, which is a long-chained cellulose with high polymerization degree of 600-1500, hydrolyzed, causing the polymer to be cut into smaller size (micro) with smaller polymerization degree n ≈ 220, resulting in microcrystal cellulose[14].

Microcrystal cellulose residue obtained then rinsed with aquades until neutral pH's obtained and filtered by filter paper. Then the filtering, drying, and sieving stages are carried out using spray dry technology as stated in the Handbook of Pharmaceutical Excipients [15]

Microcrystal cellulose characterization

Microcrystal cellulose powder resulted from sugarcane bagasse isolation was characterized and compared with literature from Handbook of Pharmaceutical Excipient. The tests included:

Water content

Water content testing is done by using a moisture balance tool. Microcrystalline cellulose is weighed 10 grams and inserted in the specimen available in the moisture balance tool.

pH determination

pH determination was done using digital pH meter by dispersing 15% of microcrystal cellulose into aquades, digital pH meter was then inserted into the solution and the pH was read on the device [16].

Permanganat numbers

Based on SNI 0494:2008 0.1 gram of microcrystal cellulose was put into beaker cup, added with 70 mL aquadest, and dissolved using a sonicator and then 2.5 mL H_2SO_4. 4N and 2.5 mL $KMnO_4$ 0.1 N was added. After five minutes, 1 mL of KI 10% was added, continued by titration using $Na_2S_2O_3$ 0.1 N solution and 0.2% startch/amylum was used as indicator. The above treatment was carried out on blanks without using isolated microcrystalline cellulose.

Microcrystal cellulose as filler ingredient

Microcrysstal cellulose from sugarcane bagasse was used as material for theophylline tablet filler which was made in 3 formulas, using the comparison of Avicel PH 101 and Avicel PH 102. Avicel PH is the trade name for microcrystal cellulose that has been circulating in the market [17].

RESULTS AND DISCUSSION

Yield inspection result

Microcrystalline cellulose can be obtained through the process of isolating alpha cellulose from pulp. The yield resulted from making microcrystalline cellulose was as follows:

Table 1: Microcrystal cellulose yield

Sugarcane bagasse (gram)	Microcrystal cellulose (gram)	Microcrystal cellulose yield (%)
250	65,075	26,03

Result shown in Table 1 above stated that yield resulted from microcrystal cellulose was 26,03%. This result is smaller than previous research [18] which resulted in 28,6% yield.

Microcrystal cellulose characteristic test result

Excipients used in pharmaceutical preparations must meet specified specifications. Microcrystal cellulose from sugarcane bagasse test result can be seen in Table 2.

Table 2: Microcrystal cellulose characterization

Characterization	Microcrystal cellulose	Specification (Rowe, 2009)
Water content (%)	4.95	<5
pH	6,9	5-7,5
Powder qualitty		
a. Qualitative identification		
- Color change	Violet Blue	Violet Blue
- Shape	Crystal	Crystal
- Color	White	White
b. Organoleptic		
- Smell	Odorless	Odorless
- Taste	Tasteless	Tasteless
c. Solubility		
- Water	Insoluble	Insoluble
- Alcohol 96%	Insoluble	Insoluble
- HCl 2N	Insoluble	Insoluble
- NaOH 1N	Barely soluble	Barely soluble
- Ether	Insoluble	Insoluble
White Degree	White	White
Permanganat numbers (%)	4,052	< 6

Microcrystal cellulose physical properties evaluation result

Flow rate test result

Flow rate result test is one of the tests used to determine the flow nature of a material. As much as 100 grams of sample was flowed into flow and granulate tester device. Microcrystal cellulose, Avicel® PH 101, and Avicel® PH 102 flow rate test results can be seen in Figure 1.

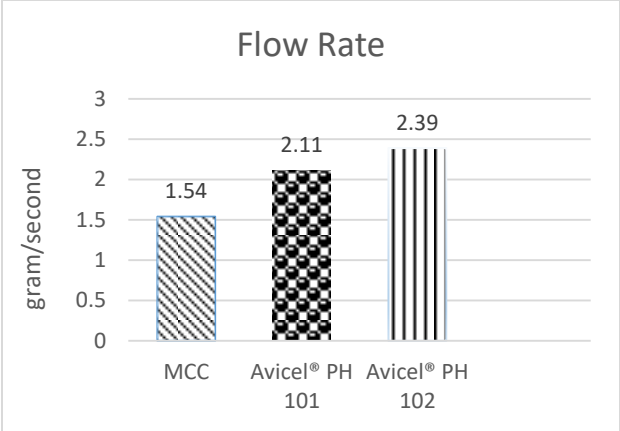


Figure 1: Microcrystal cellulose, Avicel® PH 101 and Avicel® PH 102 flow rates

Resting angle test result

The smaller the resting angle that is formed, the better the flow will be. Microcrystal cellulose has a resting angle that is less able to flow. The best flow nature is seen in material which has resting angle of <20 (Aulton, 1988).

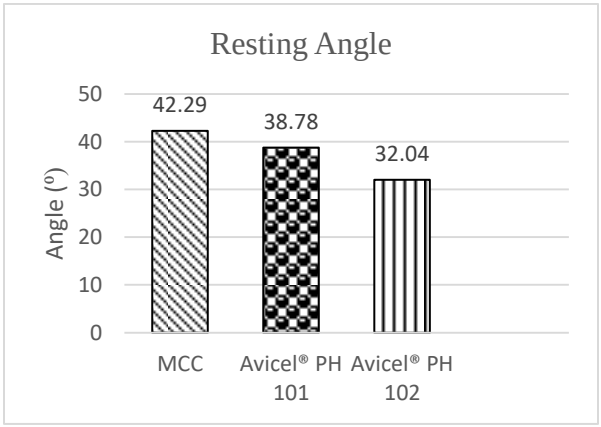


Figure 2: Resting angles of microcrystal cellulose, Avicel® PH 101 and Avicel® PH 102

Based on Figure 2, it can be seen that resting angle of microcrystal cellulose resulted from isolation was 42.29 and is bigger than both Avicel® PH 101 and Avicel® PH 102. This happened because microcrystal cellulose particle size's smaller than Avicel® PH 101 and Avicel® PH 102. The small particle size can affect the cohesion between particles which affect powder's flow [19].

Hausner factor

Hausner factor (Hf) is the ratio between incompressible specific gravity (ρm) with real specific gravity (ρn).

$$Hf = \frac{\rho m}{\rho n}$$

The closer the result of Hf values to 1, the better the flow characteristics of powder for tablet printing. If the Hf value is much greater than 1, the flow characteristics will be more difficult because there will be variations in the mass of the tablets to be printed in figure 3.

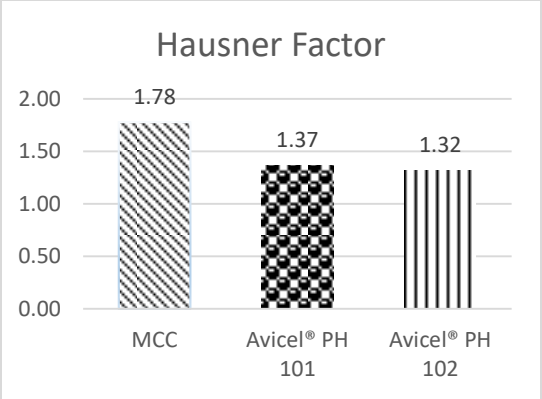
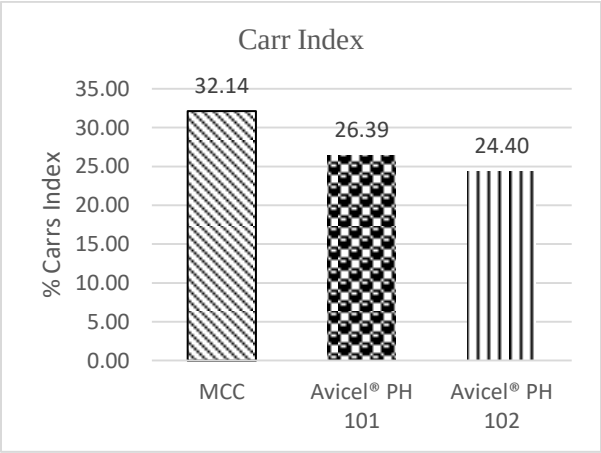


Figure 3: Hausner factor of microcrystal cellulose, Avicel® PH 101 and Avicel® PH

Compressibility test result

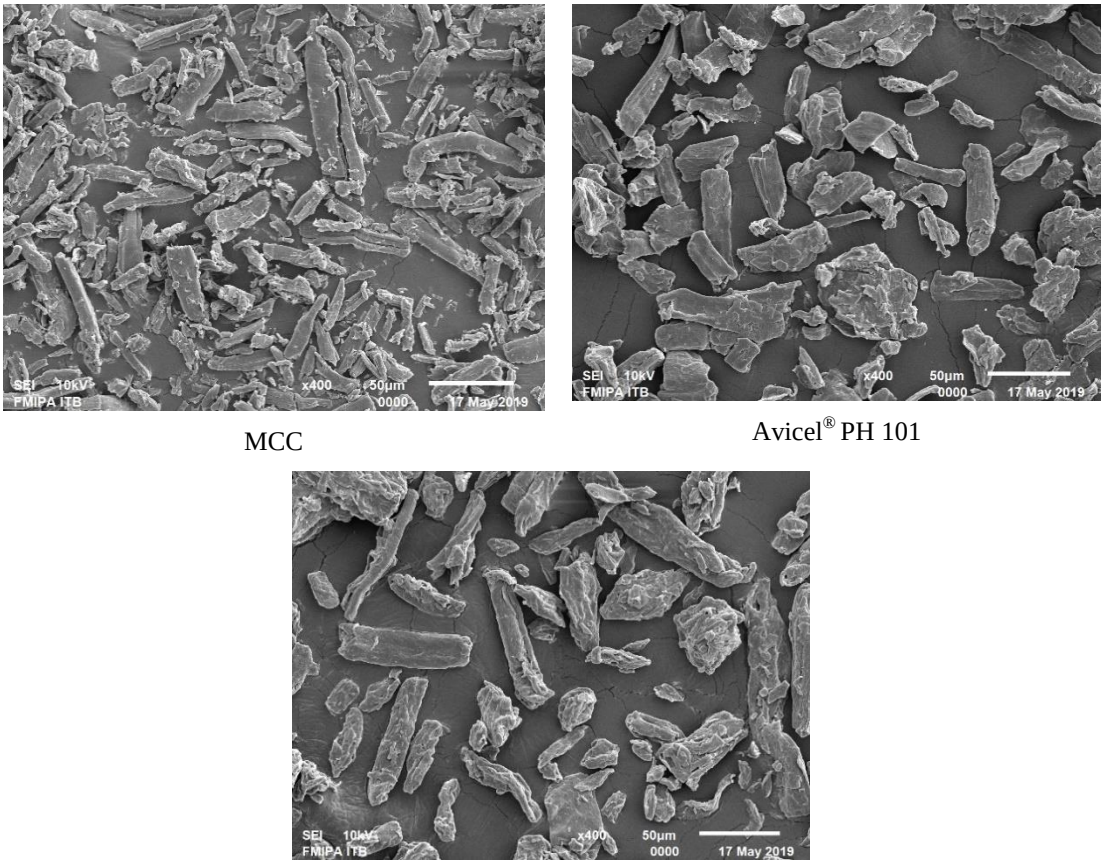
Compressibility testing is performed to determine the physical characteristics of microcrystalline cellulose. Compressibility of microcrystalline cellulose is done by calculating the real density and incompressible density. The greater the percentage of compressibility from the value of 21%, the worse the powder will get because if the powder is very tight (high compressibility), it will be difficult to flow so that the flow rate is getting worse in Figure 4.



Figurer 4: Carr Index of Microcrystal Cellulose, Avicel® PH 101, and Avicel® PH 102

Morphology and surface observation of microcrystalline cellulose particles and print mass with Scanning Electron Microscopy (SEM)

Microscopic testing to determine the morphological and surface characteristics of the MCC used SEM instruments with magnifications of 400 xs and 1,000 xs. The results of the microcrystalline cellulose characterization using SEM can be seen in Figure 5 and Figure 6.

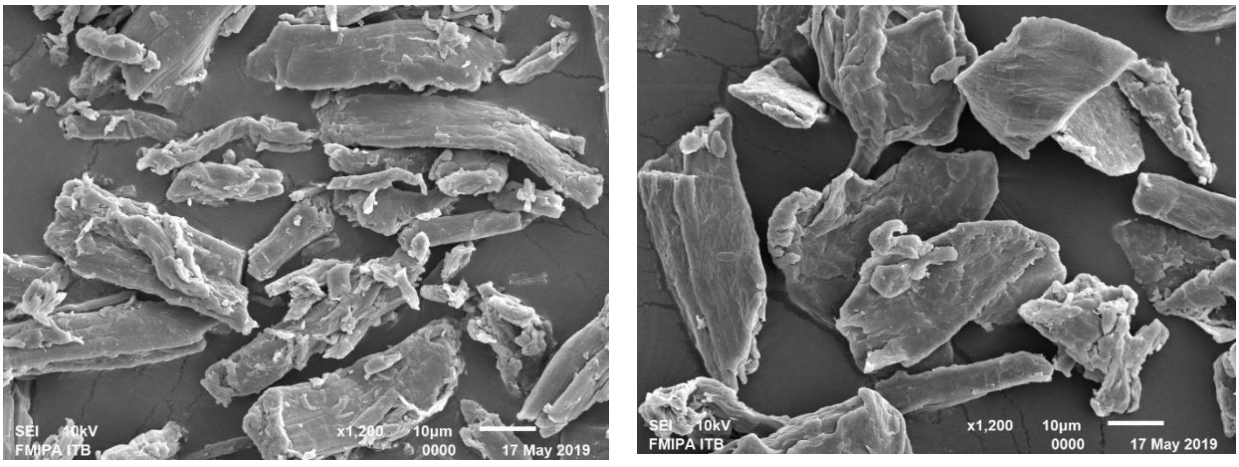


MCC Avicel® PH 101

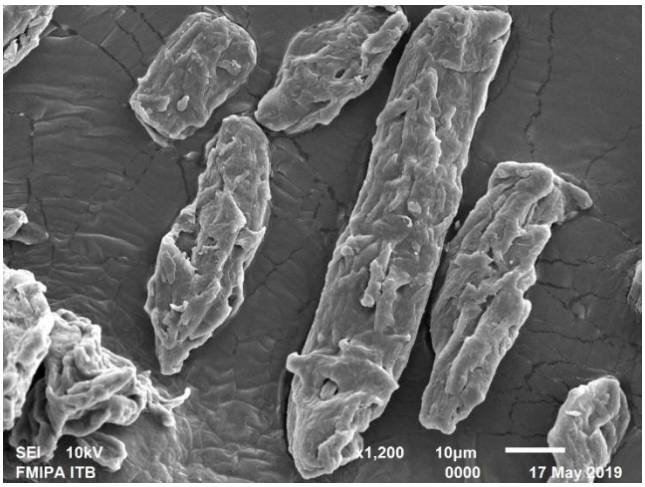
Avicel® PH 102

Figure 5: Scanning Electron Microscopy (SEM) 400x magnification

Based on Figure 5, SEM observations of MCC with magnifications 200 times of the actual size shows MCC has estimated particle size from 12.95 to 185.2 µm with irregular shapes and uneven surface textures that form sharp and blunt angles. Whereas Avicel® PH 102 has particle sizes ranging from 40.24 to 288.6 µm with irregular shapes and uneven surface textures and forming sharp and blunt angles.



MCC Avicel® PH 101



Avicel® PH 102

Figure 6: Scanning Electron Microscopy (SEM) 1200x magnification

Theophylline tablet physical characteristic test includes uniformity in weight, hardness, fragility and time of destruction. The results of heophylline tablets physical properties test with microcrystalline cellulose as fillers can be seen in Table 3

Table 3: Evaluation Result of Theophylline Tablets with Microcrystal Cellulose as Filler

Formula	Weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (kg)	Fragility (%)	Time of destruction
F1	303,97 ± 8,53	12,06 ± 0,01	4,95 ± 0,07	6,15 ± 0,59	0,75	10 minutes 23 seconds
F2	306,67 ± 10,93	12,06 ± 0,02	5,05 ± 0,23	7,00 ± 0,86	0,40	9 minutes 20 seconds
F3	305,40 ± 10,72	12,07 ± 0,01	5,10 ± 0,09	6,55 ± 1,00	0,30	8 minutes 55 seconds

Based on Table 3, F1 was tablet with microcrystal cellulose from sugarcan bagasse as filler, F2 used Avicel PH 101 and F3 used Avicel PH 102.

The weight uniformity requirements for tablets with an average weight of more than 300 mg, namely column A 5% and column B 10%, showed that no more than 2 tablets deviated in column A and none of the tablets deviated in column B [9]. All three formulas fulfilled the requirement.

Based on the results of the hardness testing that has been done, it can be concluded that all theophylline tablets made meet the requirements of 4-8 newton hardness tablets [8].

The fragility of tablets was tested using a friability tester. Based on the results of tests that have been carried out it can be concluded that all theophylline tablets made meet the fragility requirements. Tablet fragility is the weight difference before it was approved from the initial tablet. The use of microcrystalline cellulose as a filler increases the percentage of fragility tablets produced, but is still in accordance with the requirements of the nature of the tablet that is not allowed to reduce more than 1% (Ansel, 2005).Destruction time test is carried out using a disintegrant

tester. Based on the results of tests that have been carried out it can be concluded that all theophylline tablets meet the requirements of the disintegrated time test.

CONCLUSION

Based on the research that has been done, it can be concluded that the microcrystal cellulose from sugarcane bagasse meets the standards based on the literature with a 26.03% microcrystal cellulose yield. Microcrystal cellulose has the potential as tablet filler that meets the test requirements for physical characteristics of the tablet.

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