CHAPTER IV

RESULTS AND DISCUSSION

1. Isolation of microcrystalline cellulose (MCC) from durian fruit-hulls

1.1 Laboratory-scale experiments

A preliminary test in laboratory-scale production was conducted to isolate MCC from durian fruit-hulls using the procedure of Sitthipairojsakul (2002), with the objective in obtaining similar quality of cellulose product.

The isolation of MCC from the fiber of durian fruit-hulls after polysaccharide gel (PG) extraction was processed through several steps. The first step was alkali hydrolysis (soda process) which is a method used in chemical pulping process to separates cellulose from lignin, hemicellulose and other extractives (structurally unrelated polysaccharides). Thirty grams of fiber residue was hydrolyzed in 300 mL of 1.5% concentration of sodium hydroxide (NaOH) solution by autoclaving at 121°C 15 lb/in^2 for 30 minutes. Solid fiber residue was collected by filtering through nylon sheet and washed with deionized water until pH of filtrate equals to 7 and appeared colorless. However, color of product turned dark after alkali hydrolysis, which was due to impurities. The percentage yield of product obtained in this step was 56.5% of initial fiber weight. Including in the first step was bleaching process in sodium hypochlorite solution (25 g chlorine/L) 20 volume of solid weight at room temperature for 4 hours to improve brightness and eliminate lignin content. In this study, sodium hypochlorite (NaOCl) was successibly used for bleaching instead of calcium hypochlorite ($Ca(OCl)_2$) because it was commonly available and the cost was also cheaper than calcium hypochlorite. After bleaching, filtered and washed the solid fiber with deionized water until the filtrate was free from residual chloride ion which was measured by reading the score of silver chloride (AgCl) precipitate. Yellow-white product of fiber residue was obtained from first bleching step, and the yield of product was 48.1% of initial fiber weight before alkali hydrolysis. The bleaching treatment was not only improve brightness, but also converted the remaining insoluble lignin to water

soluble material which was subsequently removed by washing with water (Callihan, 1975). Furthermore, Popa and Spiridon (1998) reported that mild oxidizing agents such as chlorine, bromine, or iodine readily convert the aldehyde end groups from the plants polysaccharides to aldonic acid end groups. Under alkali conditions, glycosidic bond may be cleaved by β–alkoxy elimination.

The second step was acid hydrolysis. Yellow-white solid fiber was hydrolyzed in 20 volume of solid weight of 1.0 Molar of hydrochloric acid (HCl) by autoclaving at 121°C 15 lb/in^2 for 30 minutes. The solid fiber was filtered and washed with deionized water until pH of filtrate equals to 7, and the brown product of 36.4% yield of initial fiber weight before alkali hydrolysis was obtained. The purpose of this step was to remove the non-cellulosic substances and substantially all inorganic impurities remained in the fiber residue, and to partially depolymerize the fiber in amorphous region, resulted in leveled-off degree of polymerization (DP) of the cellulose crystallites. After acid hydrolysis, the product of acid hydrolysis was then bleached again in sodium hypochlorite solution (18 g chlorine/L) for 4 hours to improve the solid brightness. After second bleaching, the solid fiber was filtered and washed with deionized water until no residual chloride ion detected in the filtrate. The white solid fiber of 33.5% yield of initial fiber weight before alkali hydrolysis was obtained after this treatment.

The third step of MCC isolation was washing to eliminate cationic impurities and to obtain purified cellulose product for pharmaceutical application. The isolated fiber was washed in 20 volume of 0.5 Molar sodium chloride (NaCl) solution and stirred occasionally for 3 hours, filtered and washed until filtrate until no residual chloride ion detected in the filtrate. The white solid fiber was then washed in 20 volume of 0.1 Molar hydrochloric acid and stirred occasionally for 2 hours, filtered and washed with excess deionized water until pH of the filtrate became neutral. After all chemical treatment processes, the solid fiber product was dried in hot air oven at 60°C, and the 31.0% yield of initial fiber weight before alkali hydrolysis was obtained.

The last step was size reduction, dried cellulose fiber product from the third step was milled using ball mill apparatus and then passed through 60 mesh sieve The 29.5% yield of white solid powder of initial fiber weight before alkali hydrolysis, was obtained. The percentage yields of cellulose products obtained from each step of isolation process are summarized in Table 6 and Figure 4. Brown fiber residue before

entering the isolation process and cellulose product obtained from the final step of isolation were shown in Figure 5 and 6, respectively.

Table 6 Steps of isolation process and percentage yield of MCC product calculated in relation to the total fiber residue after PG extraction of dried fruit-hulls of durian.

Treatment	Process yield (±SD) (%)		
	30-g batch (n = 3)	300-g batch (n = 3)	3000-g batch* (n = 2)
Total fiber residue after PF extraction	100	100	100
Alkali hydrolysis	56.5 (±2.7)	61.9 (±4.23)	66.7
Bleaching 1	48.1 (±2.84)	51.9 (±5.41)	54.9
Acid hydrolysis	36.4 (±2.21)	41.2 (±2.25)	45.0
Bleaching 2	33.5 (±2.0)	38.8 (±1.97)	37.9
Treatment in 0.5 M NaCl followed by in 0.1 M HCl	31.0 (±1.83)	37.1 (±1.72)	33.0
Ball milling and sieve sizing	29.5 (±0.97)	32.9 (±2.34)	27.4

* Average results from 2-repeated batch isolation.

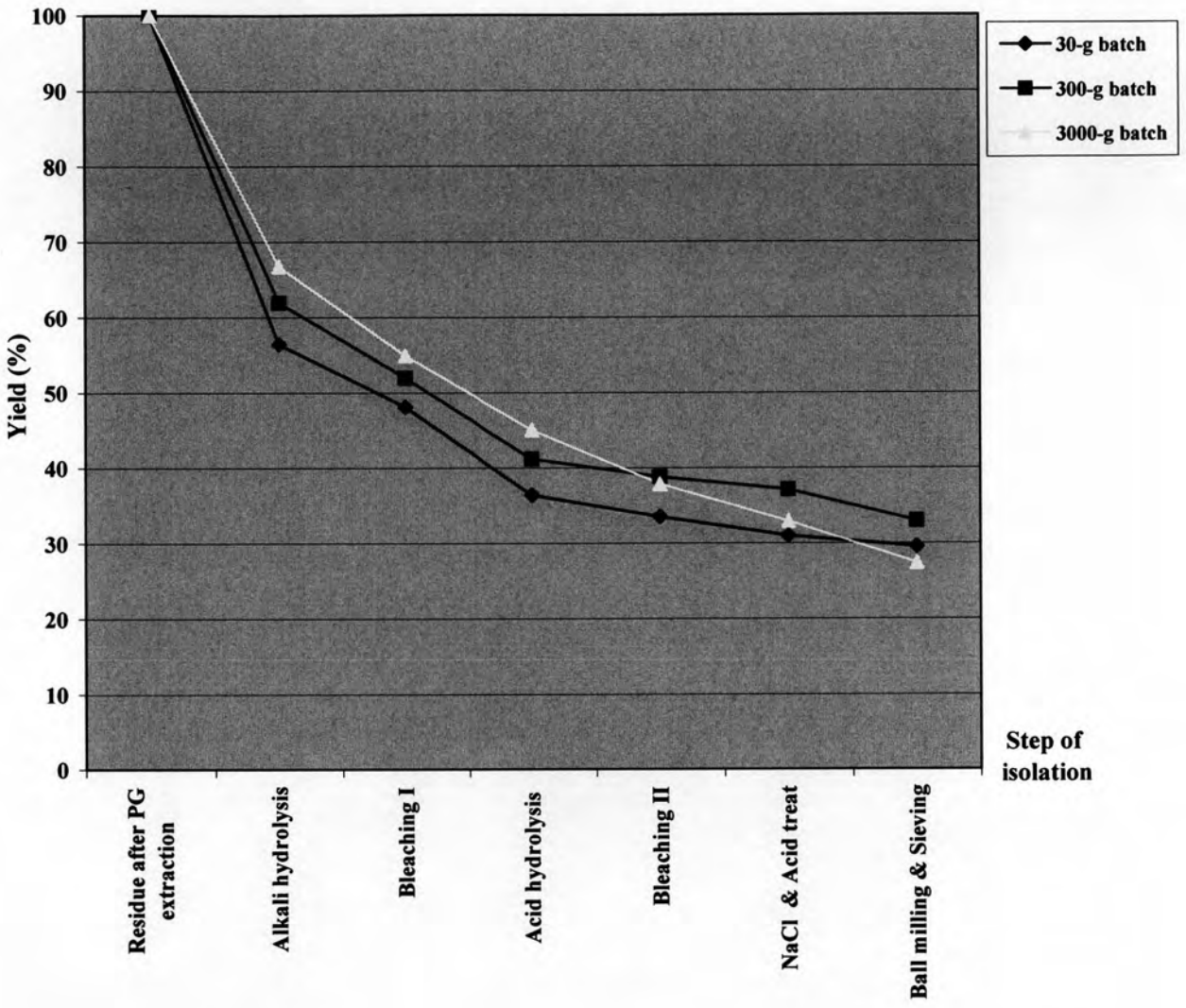


Figure 4 Graphical representation for the steps of isolation process and percentage yield of MCC product calculate in relations to the total initial fiber residue after PG extraction of dried fruit-hulls of durian.

Figure 5 Fiber residue of durian fruit hulls after polysaccharide gel (PG) extraction, a starting material for the isolation of microcrystalline cellulose (MCC).

Figure 6 MCC was isolated and dried in hot air oven, milled and passed through 60-mesh sieve. A fine-white powder was obtained.

Physicochemical characterization of final cellulose product obtained from 30-g batch isolation compared to commercial microcrystalline cellulose (Avicel PH101®) using scanning electron microscopy, laser light scattering particle size analyzer, infrared spectrophotometry, powder X-ray diffractometry, differential scanning calorimetry and thermogravimetry (as results shown in Figures 14-19, respectively), were found to be very similar. Prepared cellulose also complied with the pharmaceutical requirements of microcrystalline cellulose stated in the USP26/NFXXI which includes identification, pH, loss on drying, residue on ignition and water soluble substance. Thus, it could be concluded that microcrystalline cellulose from durian fruit-hulls was successfully produced using the isolation procedure of 30-g batch isolation described above, and would be used as a model to verify performance in the scaling-up to pilot-scale experiments.

1.2 Pilot-scale experiments

The scale-up process was performed to increase the product of microcrystalline cellulose derived from durian fruit-hulls with the desired and consistent properties, for future use in pharmaceutical formulations. Several conditions for isolation were optimized with respected to laboratory scale.

Once an isolation of MCC from durian fruit-hulls was accomplished successfully in a laboratory-scale experiment, the values of the operating variables and the physical properties were known or could be measured. This isolation system was then examined in a number of digestion and mixing vessels of increasing scale (scale 300-g, 3000-g) where the process conditions were very similar to those used in the laboratory-scale.

For the optimum design of a production-scale (prototype), we must translate the data on a small scale (model) to the larger scale. The fundamental requirement for scale-up is that the model and prototype should be similar to each other. Two kinds of conditions must be satisfied to ensure similarity between model and prototype. They are:

(1) Geometric similarity of the physical boundaries:

The model and the prototype equipment must be the same shape, and all linear dimensions of the model must be related to the corresponding dimensions of the prototype by a constant scale factor.

(2) Dynamic similarity of the flow fields:

The ratio of flow velocities of corresponding fluid particles is the same in model and prototype as well as the ratio of all forces acting on corresponding fluid particles. When dynamic similarity of two flow fields with geometrically similar flow patterns. The first requirement is obvious and easy to accomplished, but the second is difficult to understand and also to accomplished and needed highly advanced experimental design which were not done in this experiment.

1.2.1 300-g batch isolation

The first pilot-scale process was performed using initial weight 300 g of durian fruit-hulls fiber residue. The study was performed 3 times to ensure reproducibility. Pilot plant scale-up was based on geometric similarity for the size of isolation tank (Table 7). But for ball mill apparatus, size of 1 L was used in the process due to the limitation of equipment available. In addition, similarity factors which were time and temperature for the digestion of raw fibers, mixer velocity and after-treatment end point detection concerning pH and residual chloride ion (as shown in Table 5), were used to keep the constant condition between laboratory-scale and pilot-scale. The isolation process consisted of four main steps as same as the model's (30-g batch) which were:

(1) Alkali hydrolysis and bleaching
(2) Acid hydrolysis and bleaching
(3) Washing with sodium chloride treatment followed by washing with dilute acid
(4) Dried and reduced particle size by milling and sieve sizing

Percentage yield of MCC obtained from 300 g of raw fiber was 32.90% (Table 6 and Figure 4). Physicochemical characterization of MCC product compared to commercial MCC (Avicel PH101®) using scanning electron microscopy, laser light scattering particle size analyzer, infrared spectrophotometry, powder X-ray diffractometry, differential scanning calorimetry and thermogravimetry (Figures 14-19, respectively), were similar to the results of laboratory scale experiment (30-g batch) as will be discussed in detail in the later sections. MCC produced also complied with the pharmaceutical requirements stated in the USP26/NFXXI which includes identification, pH, loss on drying, residue on ignition and water soluble substance.

When the 300-g batch isolation was successfully scaled-up, the second pilot-scale process was then performed using initial weight 3000 g of durian fruit-hulls fiber residue

1.2.2 3000-g batch isolation

The second pilot-scale using initial weight 3000 g of durian fruit-hulls fiber residue was performed with the same principle of first pilot-scale. The study was performed 2 times to ensure reproducibility.

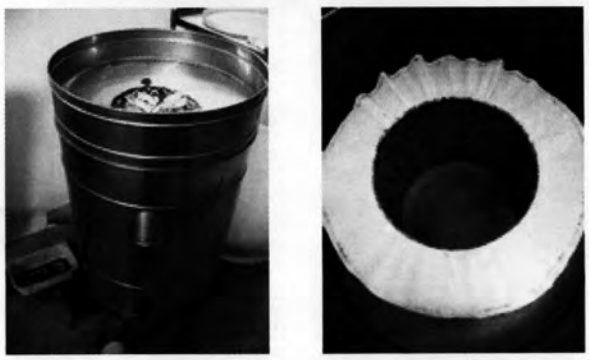
In the step of alkali and acid hydrolysis, plastic tank was replaced by Teflon coated stainless steel tank 40 L because the moist heat generated in the autoclave could not effectively penetrated through the wall of plastic tank. In case of isolation tank, the sizes used complied with concept of geometric similarity. Percentage yield of MCC obtained from 3000 g of raw fiber was 27.40% (Table 6 and Figure 4), lower than percentage yield obtained from 30-g and 3000-g batch isolation due to the equipment and process changes (Table 7). For every washing process in 30-g and 300-g batch isolation, the filtrate was removed from the solid fiber by filtering and squeezing through nylon sheet. This method was thought to be not practical for 3000-g batch isolation because of large volume of fiber residue. Thus, centrifugal separator was selected and used to separate the solid fiber from the filtrate, which helps to save time and labor use in the isolation process.

Physicochemical characterization of MCC product compared to commercial MCC (Avicel PH101®) using scanning electron microscopy, laser light scattering particle size analyzer, infrared spectrophotometry, powder X-ray diffractometry, differential scanning calorimetry and thermogravimetry (Figures 14-19, respectively), were found to be similar to the results of 30-g batch and f300-g batch as will be discussed in detail in the later sections. MCC produced also complied with the pharmaceutical requirements stated in the USP26/NFXXI which includes identification, pH, loss on drying, residue on ignition and water soluble substance. Pictures of the isolation process of pilot-scale batch 3000-g were shown in Figure 7-13.

Table 7 Equipment and process changes in the isolation process of MCC from durian fruit-hulls during scale-up.

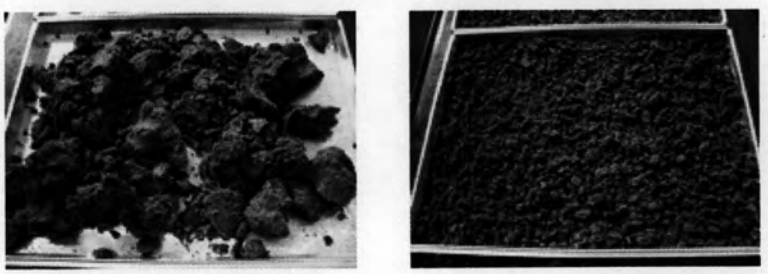
Treatment	30-g batch	300-g batch	3000-g batch
Equipment changed:			
Alkali hydrolysis/ Acid hydrolysis	Plastic beaker 1 L	Plastic tank 10 L	Teflon coated stainless steel tank 40 L
Bleaching 1/ Bleaching 2	Plastic beaker 1 L	Plastic tank 10 L	Plastic tank 100 L
Treatment in 0.5 M NaCl / in 0.1 M HCl	Plastic beaker 1 L	Plastic tank 10 L	Plastic tank 100 L
Ball milling	Ball mill 1 L	Ball mill 1 L	Ball mill 50 L
Process changed:			
Washing process	Filtered through nylon sheet	Filtered through nylon sheet	Used centrifugal separator

Autoclave in 1.5% sodium hydroxide solution at 121°C, 15 lb/in^2 for 30 minutes.



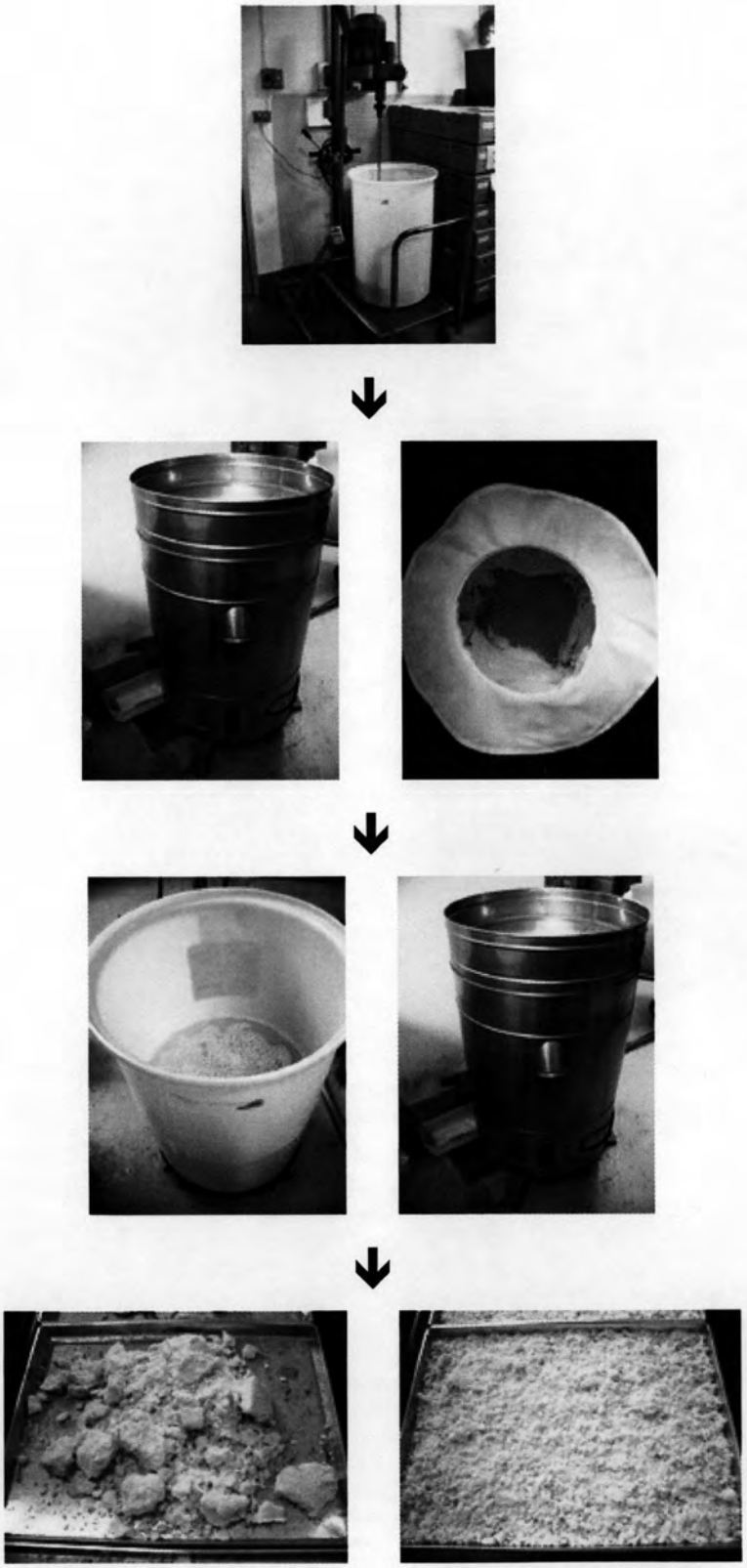
Centrifuge to separate fiber residue.

Wash the residue with deionized water. Repeat centrifugation and wash until pH of water is equivalent to 7.



Fiber residue after alkali hydrolysis.

Figure 7 Alkali hydrolysis for 3000-g batch isolation.



Stir in sodium hypochlorite solution (25 g chlorine/L) for 4 hours.

Centrifuge to separate fiber residue.

Wash the residue with deionized water. Repeat centrifugation and wash until no residual chloride ion.

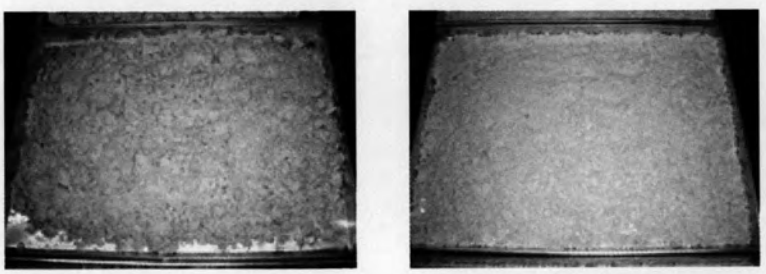
Fiber residue after first bleaching.

Figure 8 First bleaching for 3000-g batch isolation.

Autoclave in 1.0 M hydrochloric acid solution at 121°C, 15 lb/in^2 for 30 minutes.

Centrifuge to separate fiber residue.

Wash the residue with deionized water. Repeat centrifugation and wash until pH of water is equivalent to 7.



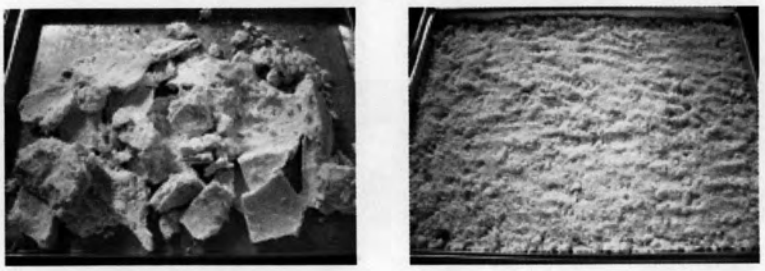
Fiber residue after acid hydrolysis.

Figure 9 Acid hydrolysis for 3000-g batch isolation.

Stir in sodium hypochlorite solution (18 g chlorine/L) for 4 hours.

Centrifuge to separate fiber residue.

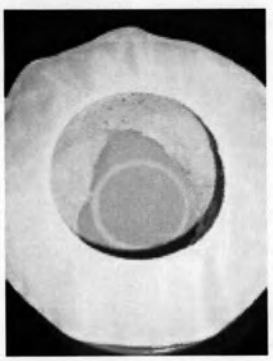
Wash the residue with deionized water. Repeat centrifugation and wash until no residual chloride ion.



Fiber residue after second bleaching.

Figure 10 Second bleaching for 3000-g batch isolation.

Stir in 0.5 M sodium chloride solution for 3 hours.



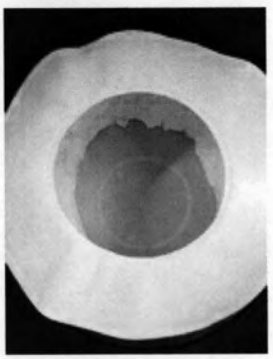
Centrifuge to separate fiber residue.

Wash the residue with deionized water. Repeat centrifugation and wash until no residual chloride ion.

Fiber residue after sodium chloride treatment.

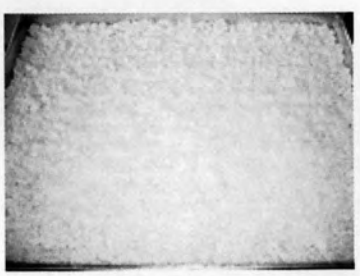
Figure 11 Sodium chloride treatment for 3000-g batch isolation.

Stir in 0.1 M hydrochloric acid solution for 2 hours.



Centrifuge to separate fiber residue.

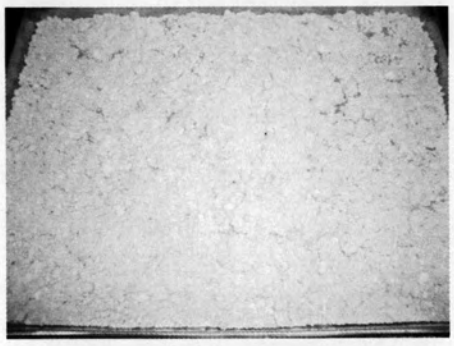
Wash the residue with deionized water. Repeat centrifugation and wash until pH of water is equivalent to 7.



Fiber residue after acid treatment.

Figure 12 Acid treatment for 3000-g batch isolation.

Dry in hot air oven for 2 hours.



Fiber residue after drying.

Mill in ball mill apparatus.

Sieve sizing.

Figure 13 Drying and size reduction for 3000-g batch isolation.

2. Physicochemical characterization of prepared microcrystalline cellulose (MCC)

2.1 Particle morphology

Determination of particle morphology performed by scanning electron microscope is shown in Figure 14. Figure 14 (a-c) were MCC prepared from durian fruit-hulls batch size 30, 300, and 3000 gram, respectively, compared to (d) commercial MCC (Avicel PH101®). A commercial MCC went though physicochemical modification during the manufacturing process which dramatically improved its basic properties of cellulose for direct compression. The commercial preparation was done by initial acid hydrolysis of wood cellulose removing the amorphous portions. After that it was spray dried resulting in aggregates with many surfaces for bonding (Wallace et al., 1983). From Figure 14 it can be seen that commercial MCC sample showed typical elongated shape of MCC crystals while the prepared MCC showed irregular-flat aggregated crystals which may resulted from the impaction force of ceramic ball during milling process.

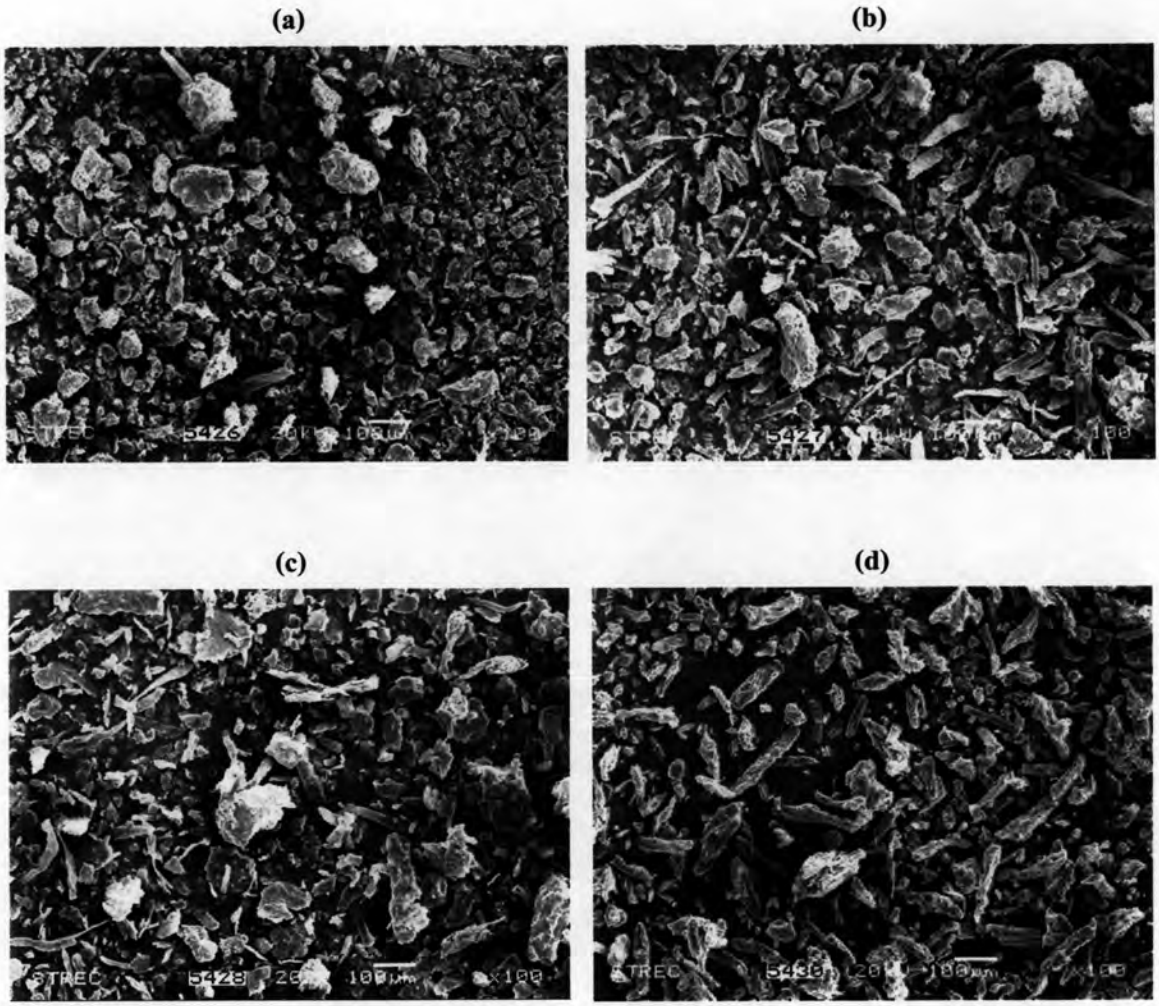


Figure 14 Scanning electron photomicrographs of MCC powder prepared from durian fruit-hulls (x100); (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®).

2.2 Particle size distribution

From Figure 15 the results showed that prepared MCC 30-g, 300-g, 3000-g batch isolation and Avicel PH101® had the size range of 0.724-239.683 μm, 1.259-416.869 μm, 0.832-239.883 μm and 3.311-363.078 μm, respectively. Both prepared and commercial MCC samples have a nearly narrow and almost normal particle size distribution although the prepared MCC showed the presence of minute lower particle size than Avicel PH101® due to different drying and particle size reduction processes. However, prepared MCC from every isolation batch showed nearly identical particle size distributions, signifying scale-up reproducibility.

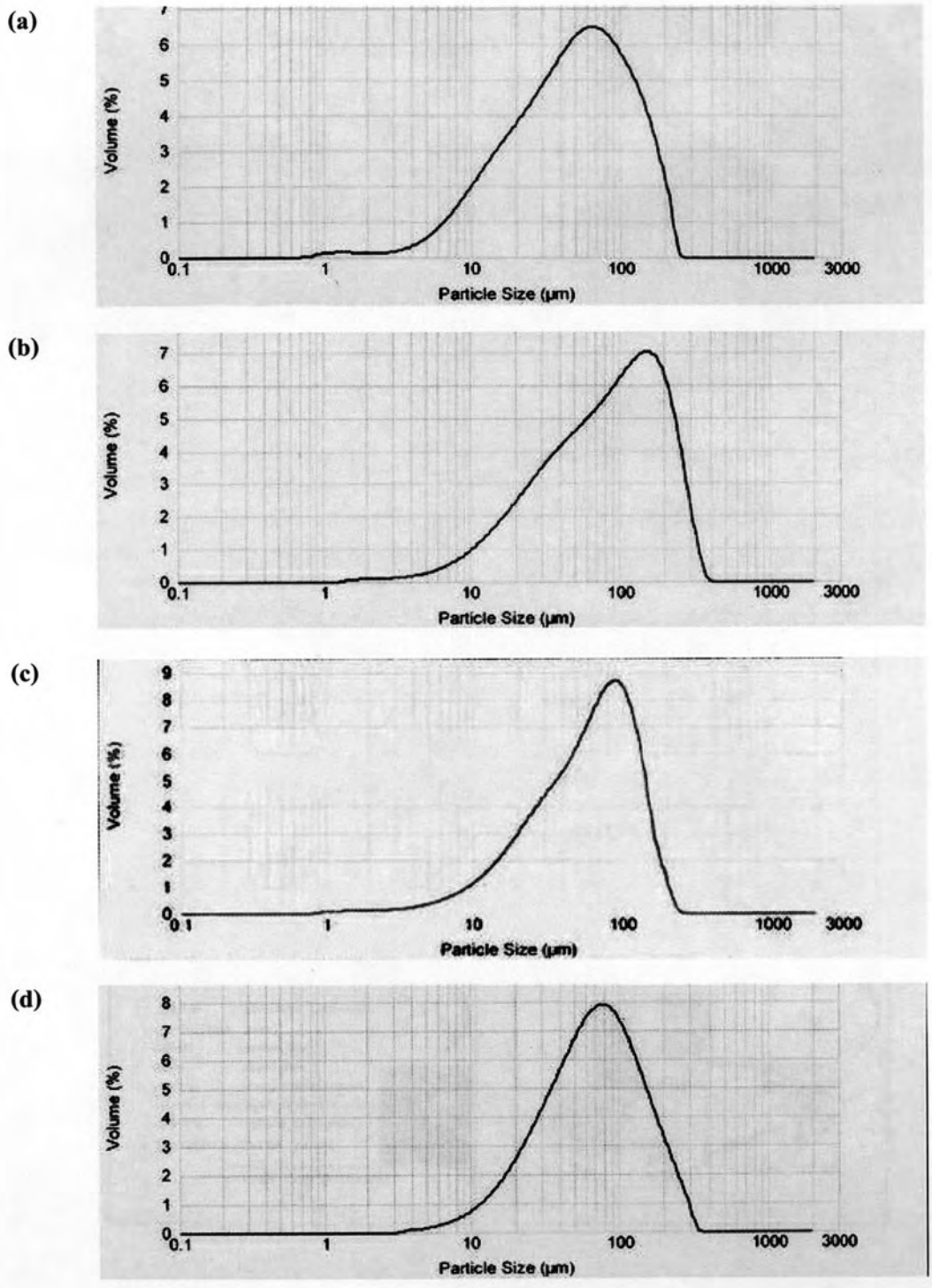


Figure 15 Particle size distribution profiles of MCC prepared from durian fruit-hulls; (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®).

Table 8 Volume weighted mean diameter, d(0.1), d(0.5), d(0.9) and particle size range of MCC prepared from durian fruit-hulls of various batch size in comparison to MCC (Avicel PH101® and Vivapur Type 101®).

	Prepared MCC batch size 30 g	Prepared MCC batch size 300 g	Prepared MCC batch size 3000 g	Avicel PH101®	Vivapur Type 101® *
d(0.1)	17.790	18.940	16.324	21.734	< 30
d(0.5)	60.196	85.483	61.750	67.725	40 - 70
d(0.9)	121.313	217.666	131.982	167.827	> 80
Volume weighted mean diameter (μm)	63.549	103.691	68.881	82.924	-
Particle size range (μm)	0.724 – 239.683	1.259 – 416.869	0.832 – 239.883	3.311 - 363.078	-

*From specification bulk pharmaceutical excipients (BPE)

2.3 Infrared spectrophotometry

The IR spectra of polysaccharide fiber from durian fruit-hulls obtained from various batch size and Avicel PH101® using KBr technique are quite similar. The results given in Figure 16 show a sharp band at 900 cm^{-1}, which is characteristic of β–glycosidic linkages between the sugar units (Sun, Fang and Tomkinson, 2000). This result confirmed that glucose residues linked together were the backbone of the macromolecule by forming β-glycosidic bonds.

The intermediate portion of the spectrum, 1,300-900 cm^{-1} is usually referred to as the 'finger print' region (Silverstein, Bassler and Morril, 1974). The absorption in this region is frequently complex, with the band originating in interaction vibration modes. Silverstein et al. (1974) suggested that this portion of the spectrum is extremely valuable when examined in reference to the other regions. Absorption in this intermediate region is probably unique for every molecular species. Figure 16 illustrates that all of prepared MCC, Avicel PH101® gave very similar pattern in this region. For this reason, the prepared MCC and Avicel PH101® should have the same functional groups within the structure.

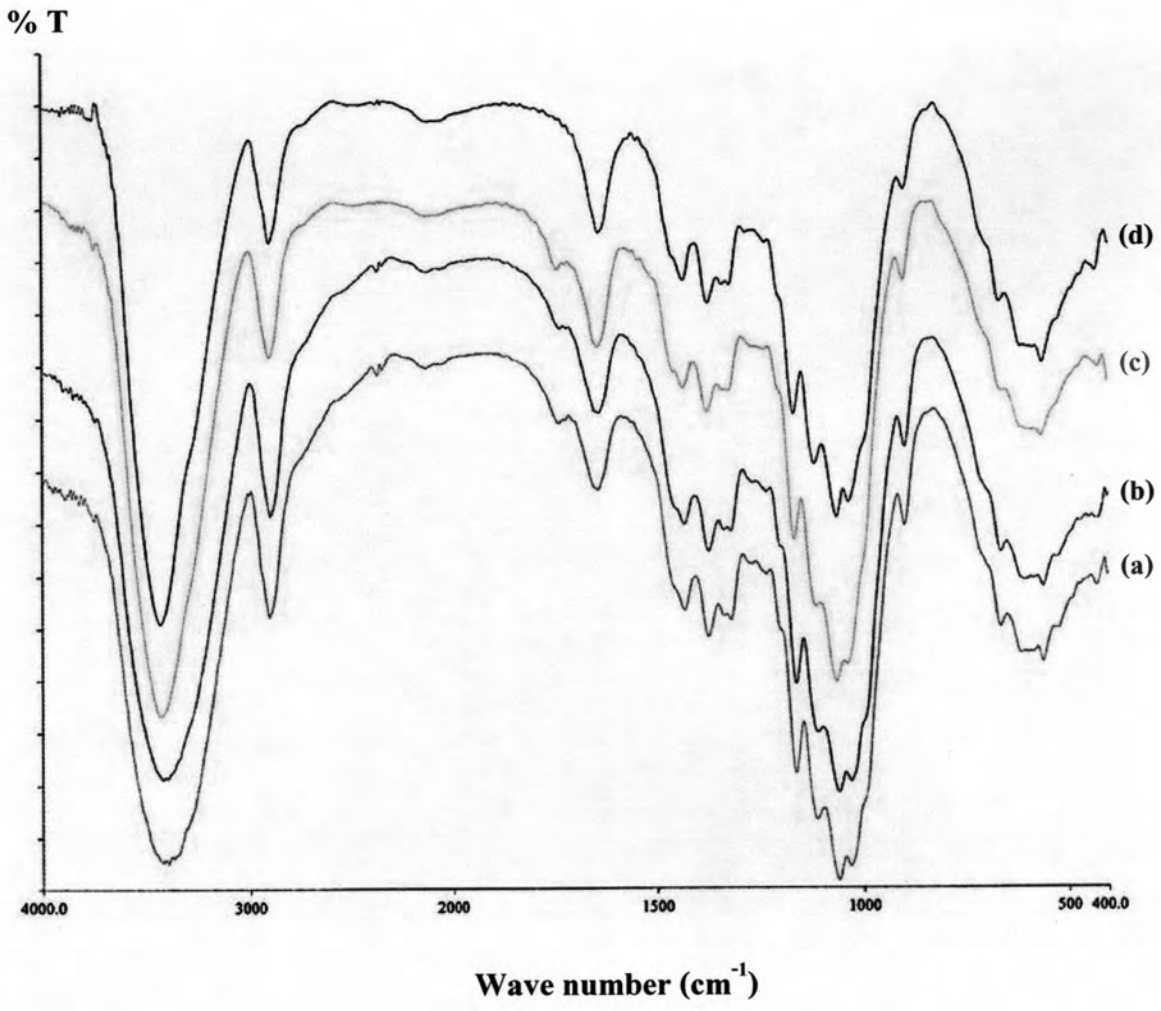


Figure 16 IR spectra of MCC prepared from durian fruit-hulls; (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®).

2.4 Powder X-ray diffractometry

Cellulose materials from various sources and treatments differ considerably in their degree of crystallinity. The powder X-ray diffraction pattern of samples, MCC isolated from durian fruit-hulls of various batch size (30, 300 and 3000 g) and commercial MCC (Avicel PH101®), in this study were quite similar as illustrated in Figure 17 which indicated that they had similar degree of crystallinity and solid state structure. The standard MCC (Avicel PH101®) was the most crystalline whereas prepared MCC from 3000-g batch isolation was the lowest, but not much differ from other batch isolation. The peaks shown at 15, 16 and 22^{O} 2θ are charactistics of cellulose I (Atalla, 1984).

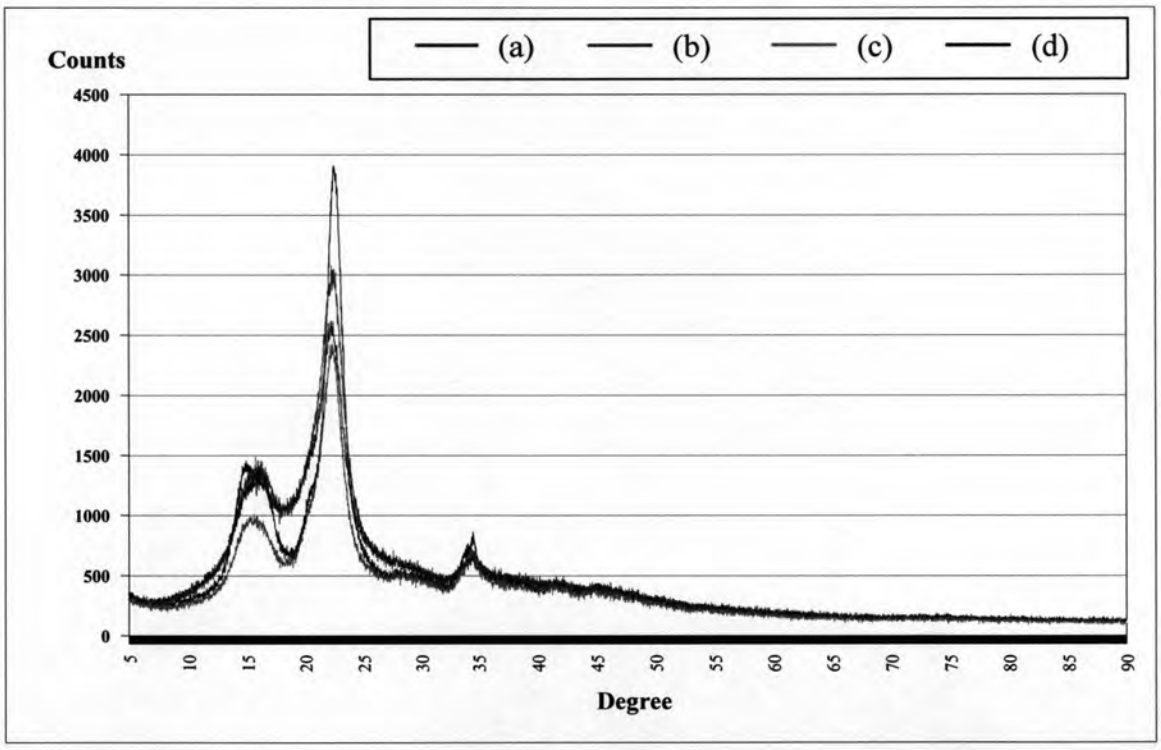


Figure 17 Powder X-ray diffraction patterns of MCC prepared from durian fruit-hulls; (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®).

2.5 Thermal analysis

One exothermic and two endothermic peaks are observed in the DSC thermograms (Figure 18). The first endothermic reaction resulted from dehydration. At temperature below 140°C the water evolution occured and every samples showed very similar peak profiles. At higher temperature, between 300 and 380°C, the exothermic reaction resulted from thermal decomposition and combustion of organic matter components. This event showed distinct and contrasting thermal stability between samples. The second endothermic peak was much sharper for the commercial MCC and appeared at higher temperature, which indicated slightly higher crystallinity or higher thermal stability than prepared MCC. The degradation routes were confirmed using a thermogravimetry (TG), as illustrated in Figure 19. At temperature below 150°C, the masses of all samples were loss corresponding to loss of water (moisture contents of 4.83%, 3.91%, 4.59% and 4.50%, for batch isolation 30-g, 300-g, 3000-g and Avicel PH101®, respectively). At higher temperature, between 260-380°C, the thermal decomposition took place resulted in rapid mass loss. Some differences were also observed, the thermal decomposition initiated near 220°C for all prepared MCC from various batch isolation and near 270°C for Avicel PH101®. Higher temperature for thermal decomposition and lower residual mass after the major weight loss were related to higher crystallinity and, hence, thermal stability of the commercial cellulose (Uesu et al., 2000).

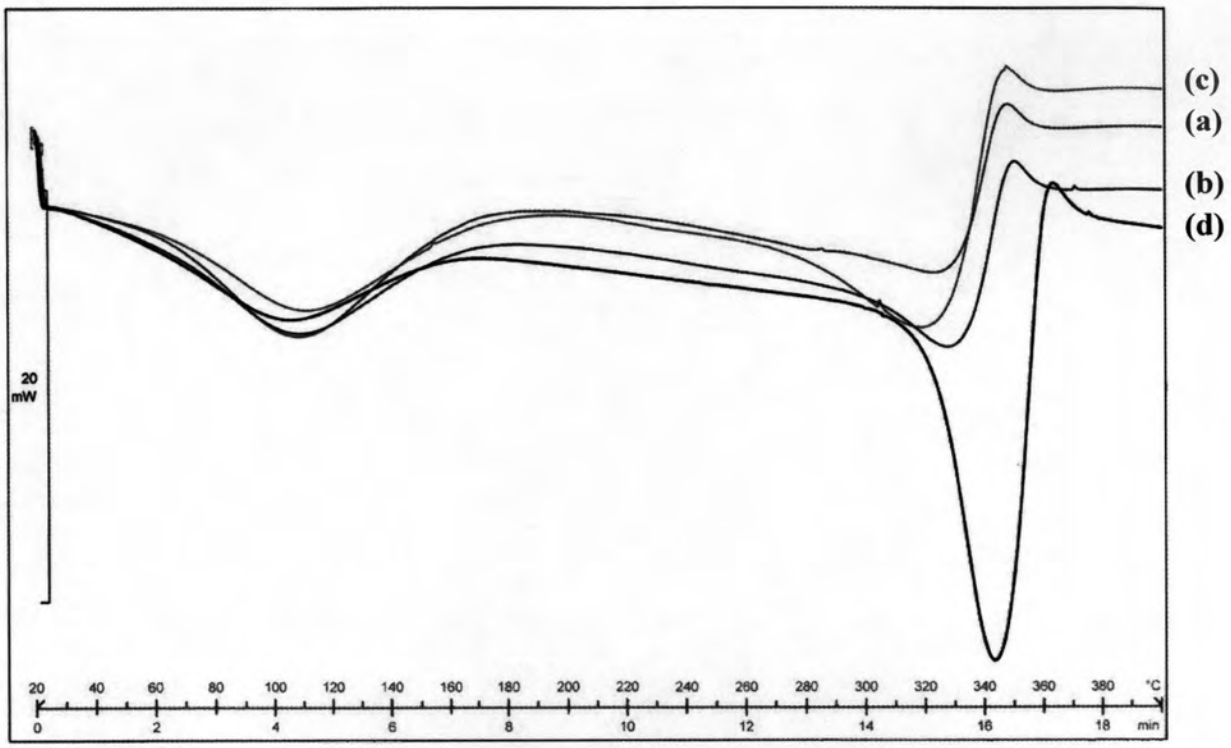


Figure 18 Differential scanning calorimetry (DSC) thermograms of MCC prepared from durian fruit-hulls; (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®) at a scanning rate of 10°C /min.

The mass loss that the MCC samples underwent from room temperature to 400°C are shown in Figure 19. Some differences are also observed: the thermal decomposition initiate near 270°C for the commercial MCC and approximately near 220°C for the prepared MCC.

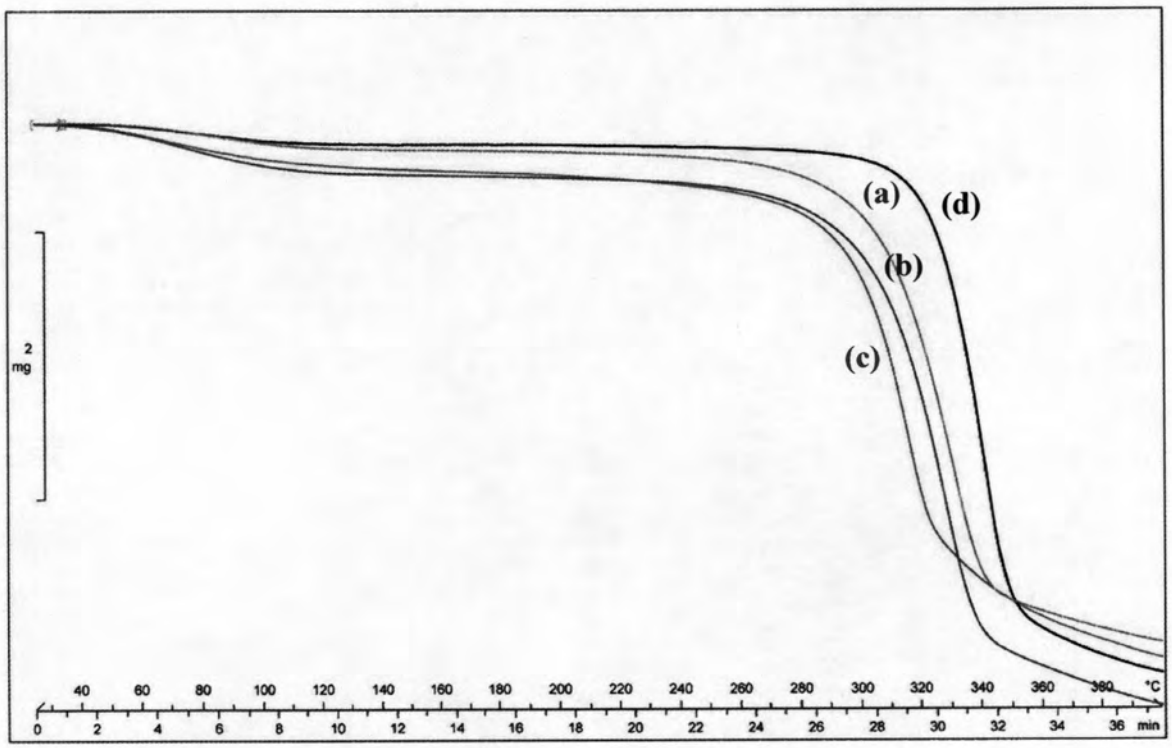


Figure 19 Thermogravimetric (TG) profiles of MCC prepared from durian fruit-hulls; (a) 30-g batch isolation, (b) 300-g batch isolation, (c) 3000-g batch isolation, (d) commercial MCC (Avicel PH101®) at a scanning rate of 10°C/min.

3. Pharmaceutical properties of prepared microcrystalline cellulose (MCC)

MCCs isolated from durian fruit-hulls of various batch size (30-g, 300-g and 3000-g batch isolation) were investigated for its pharmaceutical properties according to the USP26/NFXXI and were found to complied. Identification of all MCC samples appeared a white, opaque, bubble-free dispersion which did not form supernatant liquid at the surface. Mean values of pH, loss on drying, residue on ignition and water soluble substances of prepared MCC were 5.2, 4.83%, 0.05% and 0.12%, respectively. In case of residue on ignition and water soluble substance, the values of all prepared MCC were more than that of Avicel PH101®. MCC was also examined for its typical bulk properties including bulk density, tapped density, compressibility and flow ability. The results showed the values of bulk density, tapped density and compressibility were 0.33 g/mL, 0.50 g/mL and 33.07%, respectively, which were comparable to Avicel PH101®. However, flow ability investigated using a glass funnel with 0.9 cm orifice diameter (largest orifice available) indicated that none of all samples exhibited satisfactory flow. The results are summarized in Table 9.

In case of bulk density, Podezeck and Revesz (1993) described that a suitable bulk density was found to be 0.25-0.50 g/mL. The results in Table 10 indicated that MCC showed bulk density within the given limits. Usually, bulk density is very important factor when the formulator considers the size of high-dose capsule product or a low-dose formulation in which there are large differences in drug and excipient densities. Tapped density and compressibility showed that MCC has a potential to be used as an excipient in direct compression technique. However, one of the most important properties of a direct compressible tablet excipient, along with compressibility, is flowability of the powder. In this test found that all samples did not flow at all using a glass funnel with 0.9 cm orifice diameter.

Table 9 Pharmaceutical properties of MCC prepared from durian fruit-hulls of various batch size investigated according to USP26/NFXXI in comparison to commercial MCC (Avicel PH101®).

Properties	Prepared MCC from various batch isolation			Commercial MCC (Avicel PH101®)	Acceptable limit
	30-g batch (±SD)	300-g batch (±SD)	3000-g batch (±SD)		
Identification	Passed	Passed	Passed	Passed	Passed
pH (n =3)	5.2 (±0.05)	5.2 (±0.02)	5.3 (±0.03)	6.0 (±0.01)	5.0-7.0
Loss on drying (%) (n =3)	4.83 (±0.03)	3.91 (±0.12)	4.59 (±0.24)	4.50 (±0.09)	≤ 7.0%
Residue on ignition (%) (n =3)	0.05 (±0.01)	0.04 (±0.01)	0.05 (±0.01)	0.02 (±0.01)	≤ 0.05%
Water soluble substance (%) (n =3)	0.12 (±0.01)	0.12 (±0.01)	0.19 (±0.01)	0.10 (±0.01)	≤ 0.24%
Bulk density (g/mL) (n =3)	0.33 (±0.00)	0.28 (±0.00)	0.35 (±0.00)	0.31 (±0.02)	-
Tapped density (g/mL) (n =3)	0.50 (±0.00)	0.41 (±0.01)	0.50 (±0.00)	0.42 (±0.00)	-
Compressibility (%) (n =3)	33.07 (±0.16)	31.21 (±1.23)	29.60 (±0.18)	25.68 (±4.25)	-
Flow ability (g/s) (n =3)	0 (±0.00)	0 (±0.00)	0 (±0.00)	0 (±0.00)	-

4. Evaluation of tablet characteristic of polysaccharide fiber from durian fruit-hulls

Tablets prepared from 100% MCC isolated from durian fruit-hulls 3000-g batch isolation by direct compression technique using round flat-faced punch with 10 mm in diameter and compressed with a hydraulic press for 3 seconds under force 500 lb/in^2. The tablets were evaluated for weight variation, thickness, hardness, friability and disintegration time in comparison to tablets made from commercial MCC (Avicel PH101®).

Table 10 Evaluation of tablets composed of 100% MCC from durian fruit-hulls 3000-g batch isolation in comparison with tablets prepared from commercial MCC (Avicel PH101®).

Tablet evaluation	Prepared MCC from 3000-g batch isolation (±SD)	Commercial MCC (Avicel PH101®) (±SD)
Weight (mg) (n = 20)	249.3 (± 0.46)	249.4 (± 0.49)
Thickness (mm) (n = 20)	2.76 (± 0.05)	2.80 (± 0.05)
Hardness (kp) (n = 20)	10.57 (± 0.35)	15.71 (± 0.42)
Friability (%) (n = 20)	0.02	0.01
Disintegration time (min) (n = 6)	8 min 16 sec	1 min

From Table 10, the results showed that directly compressed tablets of prepared MCC and commercial MCC (Avicel PH101®) have approximately the same weight 249.3 ± 0.46 and 249.4 ± 0.49 g, respectively, thickness 2.76 ± 0.05 and 2.80 ± 0.05 mm, respectively. But for hardness, the results of prepared MCC was 10.57 ± 0.35 kp when of Avicel PH101® was 15.71 ± 0.42 kp, which were different. The percentage

weight loss during friability test of both tablets from prepared MCC and tablet from Avicel PH101® were less than 1.0% (0.02% and 0.01%, respectively), which were in acceptable friability limit.

The results indicated in Table 10 revealed that disintegration of tablets made from prepared MCC was poorer than commercial MCC. Disintegration time of tablets made from prepared MCC was 8 min 16 sec, slower than the commercial MCC which disintegrated by 1 min. Possible explanation might be because the former was not spray dried to give agglomerates of particles of uniform size and intact pores as the commercial product. Rather, prepared MCC consisting mainly of flat irregular shaped particles due to compaction during ball milling which resulted in less pores and high binding property. This difference in the disintegration properties between all MCCs could be attributed to the liquid-penetration capability. This behavior was thought to be caused by a difference in the widening of the pores during penetration. (Bhimte and Tayade, 2007). The mechanism of disintegration of MCC may be explained that when water was absorbed into the tablet matrix it will pass through capillary pores, thus, destroying the H-bond between molecule of glucose and the adjacent unit and then disintegrated (Lerk, Bolhuis, and de Boer, 1979; Nyqvist and Nicklasson, 1983). It has often been indicated that differences in the characteristics of MCC among manufacturers are due to the kinds of pulp used as raw materials and their manufacturing conditions, which eventually affect the compactability (Suzuki and Nakagami, 1999).

5. Unit cost analysis

Unit cost calculated for the MCC prepared from durian fruit-hulls is summarized in Table 11. To analyse the unit cost of prepared MCC, data was collected from every step of 3000-g batch isolation. Total cost was calculated from the sum of direct material cost, direct labor cost, electrical cost, depreciation cost and other expenses. The total cost of 3000-g batch isolation process in this study was 2,435.59 baht, which comprised of direct material cost 951.43 baht (39.06%), direct labor cost 860 baht (35.31%), electrical cost 76.43 baht (3.14%), depreciation cost 431.74 baht (17.73%) and other expenses 115.98 baht (4.76%), when the MCC product obtained was 822 g. Rank of all

costs from highest to lowest were; direct material cost 39.06%, direct labor cost 35.31%, depreciation cost 17.73%, other expenses 4.76% and electrical cost 3.14%, respectively. When calculated as cost per unit weight (1 kilogram), the unit cost of prepared MCC from 3000-g batch isolation was 2,963.00 baht per kilogram, which was considered to be higher than of commercial MCC (Avicel PH101®) used in Thai pharmaceutical industry due to process, equipment and facility limitations.

Table 11 Unit cost calculated for the MCC from durian fruit-hulls 3000-g batch isolation.

Cost categories		**Cost calculated**	
Material cost	=	951.43	bath
Labor cost	=	860.00	bath
Electrical power cost	=	76.43	bath
Depreciation cost	=	431.74	bath
Other expenses (5% of sum of the above)	=	115.98	bath
Total cost	=	**2,435.59**	**bath**
MCC product obtained from 3000-g batch isolation	=	822.00	g
Hence, unit cost of MCC prepared from 3000-g batch isolation	=	**2,963.00**	**baht/kg**

** When calculated unit cost, the currency exchange rates were 39.56 baht/USD (bank selling price) and 39.31 bath/USD (bank buying price). And the benzene prices were 26.44 baht/L (benzene 95) and 25.64 baht/L (benzene 91).*

6. Plant designing for industrial-scale

A statement of goals is an essential first step in establishing the design parameters for a new facility. This will assist the designer - as well as the owner - in measuring how the ultimate design responds to the owner's needs. While functional and cost issues are typically enunciated as project goals, this step can be used to broaden the concepts governing the design of the facility. The lack of strategic information refer to business needs, image, and quality level is often a source misunderstanding by designers and can result in inappropriate design features. Combining these with the more traditional goals associated with facility work will lead to a be understanding of all the reasons for undertaking the project (Zawistowski and Rago, 1994).

From the model of pilot-scale 3000-g batch isolation, the production scheme for industrial MCC isolation from durian fruit-hulls with starting weight of raw fiber 30 kilograms, was designed (see flowsheet of MCC isolation in Figure 20). The main equipments needed for this production-scale are:

- 5 plastic tanks (100-L size)
- 5 agitators (speed up to 1250 rpm)
- 2 hot air ovens (600-L size)
- 1 hammer mill
- 2 autoclaves (600-L size)
- 2 centrifugal separators (10-L size)
- 1 set of agitator and plastic tank (100-L size) with 2 releasing valves
- 1 ball mill apparatus (50-L size)
- 1 sieve shakers (60-mesh)

The isolation process was similar to 3000-g batch isolation but different in the number of equipments and some process was modified. In washing process, one plastic tank with agitator was positioned above the centrifugal separators, which help continuous agitating of the solid fiber suspension during every washing process. The 2 releasing valves are used for continuous feeding of the fiber suspension from washing tank down to the centrifugal separators with the appropriate rate to maintain the balance of centrifuge during centrifugation.

The processes above are meant to illustrate the need for a systematic, well considered, approach to the initial design of an industrial plant facility. Careful

collection and recording of the data and criteria which form the basis for the design of any building is especially important in the early stages. Misunderstandings and misinterpretations that persist beyond schematic design can result in escalating costs, missed deadlines and unsatisfactory results. Establishing the ground rules through a formalized process will significantly improve the prospects of achieving the goals.

Figure 20 Flowsheet for the MCC isolation process.