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Encapsulation of Gemor Bark Extract Using Cetyltrimethylammonium bromide-Modified Nanocellulose

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Abstract

Gemor (*Nothaphoebe coriacea*) is one of the plants of Non-Timber Forest Product typical of wetlands with secondary metabolite compounds such as alkaloids, steroids, flavonoids, triterpenoids, and phenolics. Besides being used as an insecticide, gemor bark also has antioxidant activities, anti-influenza, antivirus, antiherpes, and anti-inflammatory. This study aimed to encapsulate gemor bark extract using cetyltrimethylammonium bromide (CTAB)-modified nanocellulose to increase the effectiveness of its use. The result showed that gemor bark extract had an IC_{50} value of 39.97 ppm. In comparison, encapsulated gemor bark extract (Gemor-Nc-4 mM CTAB) had an excellent antioxidant activity with an IC_{50} value of 98.41 ppm and encapsulation efficiency of 53.70 %.

1. Introduction

Gemor (*Nothaphoebe coriacea*) is known as a plant of Non-Timber Forest Product [1]. Gemor bark contains secondary metabolite compounds such as alkaloids, steroids, flavonoids, triterpenoids, and phenolic [2]. Gemor has the potential to have medicinal properties from its leaves, twigs, and barks. Phenolic compounds in gemor bark can be used as inhibitors of viral activities such as anti-influenza, antivirus, and antiherpes. Gemor bark has anti-inflammatory activity with a maximum inhibitory value of 71.667% [3].

Bioactive compounds become unstable in several environmental conditions and processing [4]. Furthermore, most bioactive compounds also have low solubility [5]. Bioactive compounds such as phenolics are very susceptible to oxidizing environments, such as light, oxygen, moisture due to unsaturated bonds in molecules [6]. Therefore, encapsulation can support the delivery of bioactive compounds and has a controlled release at various time intervals. This method increases the protection, safety, and effectiveness of the compound [7]. Ching *et al.* [8] reported that the drug loading capacity of curcumin encapsulated with nanocellulose in surfactant medium (Tween-80) gave an increase from 0.1 mg/g to 7.73 mg/g as the surfactant concentration increased.

Nanocellulose is a natural polymer that can be used as a coating material. Nanocellulose is the most appropriate feedstock for nanocarrier supply. It is because the most abundant natural polymer has unique and nanostructured properties such as low density, hardness, and abrasiveness, the ability for structural and chemical modification, high biocompatibility, and biodegradability in nature [9]. Cetyltrimethylammonium bromide (CTAB) is quaternary ammonium with the C_{16} alkyl chains, a hydrophobic cationic surfactant. A modification of nanocellulose using CTAB can increase the hydrophobicity of nanocellulose [10]. It makes nanocellulose more compatible with the molecules in bioactive compounds [11]. Therefore, this study aimed to encapsulate gemor bark extract using CTAB-modified nanocellulose at various concentrations to control the release of gemor bark extract and increase the effectiveness of its use.

2. Methodology

The methodology included materials, nanocellulose synthesis, modification of nanocellulose using CTAB,

encapsulation of gemor bark extract using CTAB-modified nanocellulose, encapsulation efficiency, and antioxidant activity.

2.1. Materials

Organic solutions included ethanol 96%, distilled water, methanol pro analysis, 2,2-diphenyl-1-picrylhydrazyl, sulfuric acid 96%, microcrystalline cellulose (Avicel PH 101), cetyl trimethyl ammonium bromide (biochemical A0805), gemor bark extract from Pojon village Central Kalimantan.

2.2. Synthesis of nanocellulose

The synthesis of nanocellulose was carried out by the acid hydrolysis method. Microcrystalline cellulose (MCC) was hydrolyzed at 45 ℃ for 2 hours using sulfuric acid 50% with the ratio of MCC and sulfuric acid were 1:20. Hydrolysis was stopped by adding 250 mL distilled water. The colloid suspension was centrifuged at 4000 rpm for 25 minutes. Then, the suspension was dialyzed for seven days to neutralize and remove sulfate ions. A neutral colloid suspension formed was sonicated for 30 minutes to homogenize nanocellulose [12].

2.3. Modification of nanocellulose using CTAB

Nanocellulose and cationic surfactant (CTAB) in equal amounts were added to the Erlenmeyer flask. Nanocellulose of 0.4% was mixed with 1, 2, 4 mM CTAB. The mixtures were heated at 60 ℃ for 3 hours and stirred for 24 hours [10].

2.4. Encapsulation of gemor bark extract using CTAB-modified nanocellulose

About 0.2% gemor bark extract of 40 mL was added to CTAB-modified nanocellulose of 20 mL (at various concentration 1, 2, 4 mM). The mixtures were stirred for 2 hours and stored in the refrigerator for 24 hours. The encapsulated gemor bark extract was centrifuged at 2000 rpm for 15 minutes and dried in the oven at 60 ℃ [13].

2.5. Encapsulation efficiency

Determination of gemor bark extract contents was carried out by measuring the standard curve of the gemor bark extract solution. The measured solution content was the gemor bark extract before and after encapsulation. The absorbance of the solutions was measured using spectrophotometer UV-Vis at 430 nm. The encapsulation efficiency can be calculated by the following equation.

$$EE\ (\%) = \frac{E1-E2}{E1} \times 100\%$$

EE is encapsulation efficiency, E_1 (ppm) is gemor bark extract content before encapsulation, and E_2 (ppm) is gemor bark extract content after encapsulated [14].

2.6. Antioxidant activity analysis

Antioxidant activity of the sample was carried out using 2,2- diphenyl-1-picrylhydrazyl (DPPH). A stock sample solution of 500 ppm was prepared using methanol solvent, then 1 mL of 1 mM DPPH solution was added to 3 mL of samples at various concentrations (50, 60, 70, and 80 ppm). The mixtures were homogenized and incubated for 30 minutes at room temperature. Furthermore, the absorbance was measured using a UV-Vis spectrophotometer at 515 nm, and the measurement was carried out in triple [15].

3. Result and Discussion

3.1. Synthesis of nanocellulose

The synthesis nanocellulose process used acid hydrolysis as a standard method. It is a fast and easy method to produce nanocellulose that can provide a high crystallinity index of nanocellulose. Strong acids such as H_2SO_4 and HCl break glycosidic bonds in cellulose [12]. This could happen because sulfuric acid could strongly isolate nanocellulose by making the nanocellulose dispersed as a stable colloid system due to the esterification of the hydroxyl group by sulfate ions [16]. The reaction mechanism of acid hydrolysis of nanocellulose can be seen in Figure 1.

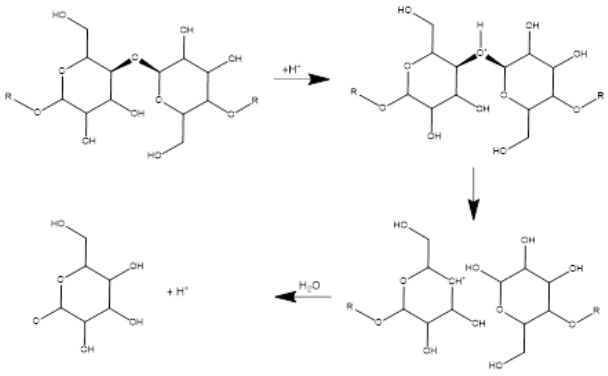

Figure 1. Mechanism of Acid Hydrolysis of Cellulose [17]

Figure 2 and 3 show that the typical peaks of cellulose were still visible in synthesized nanocellulose. Therefore, the data proved that the method used to synthesis nanocellulose did not damage the basic structure of cellulose.

FTIR spectrum of nanocellulose showed that the synthesized nanocellulose had several unique cellulose functional groups. A peak at 897.2 cm^{-1} corresponded to glycosidic bonds with glucose of cellulose structure and a peak at 1160 cm^{-1} was corresponded to stretching vibration of C-O-C asymmetric bonds of cellulose. Moreover, the peaks at 1336-1362 cm^{-1} were associated with bending vibration of C-H and C-O of polysaccharide groups. A small band located at 1429 cm^{-1} was assigned to the bending vibration of CH_2 symmetric bonds [18]. The absorbance peak at 1643 cm^{-1} corresponded to the bending vibration of the O-H bond of cellulose and showed the water adsorbed in nanocellulose [10]. The intense peaks at 2899 cm^{-1} and 3334 cm^{-1} showed the stretching vibration of C-H and O-H bonds of cellulose [10] [12].

Material characterization using a Particle Size Analyzer (PSA) was used to identify the particle size of the nanocellulose from microcrystalline cellulose. Table 1 and Figure 4 show that the distribution of nanocellulose particles was dominated by the size of a particle at 44.94 nm, although several sizes of particles, such as 46 nm and 166 nm, were also formed.

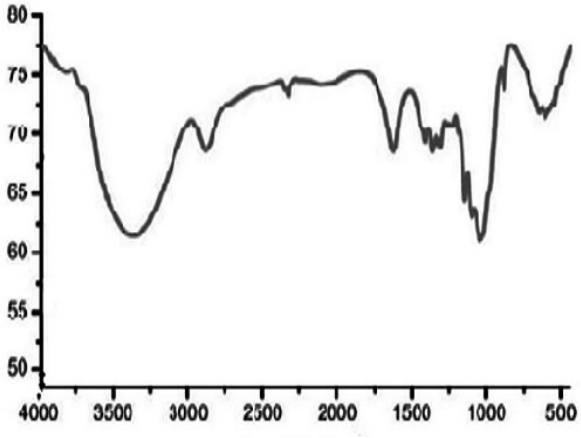

Figure 2. FTIR Spectrum of Cellulose [19]

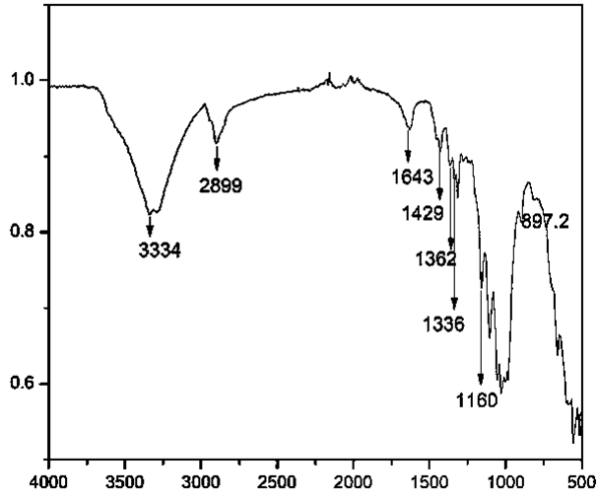

Figure 3. FTIR Spectrum of Nanocellulose

Phanthong *et al.* [20] reported that nanocellulose generally has a diameter of less than 100 nm and a length of several micrometers. Therefore, in this study, nanocellulose was successfully synthesized. The polydispersity index of nanocellulose particle distribution was 1.0. Polydispersity index indicated the uniformity of nanocellulose. Putri *et al.* [21] stated that if the PD index value is less than 0.3, the particle size distribution is getting narrower which has a good homogeneity of the sample size. This showed that the size uniformity of the nanocellulose particles in this study was still very small.

Table 1. Diameter of nanocellulose particles

Peak	Size (nm)	Number (%)
1	46.10	0.1
2	166	0.7
3	44.94	99.3

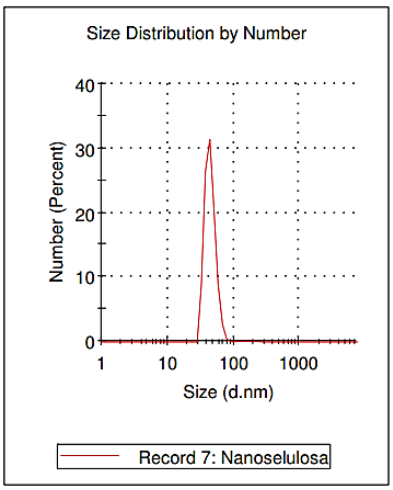

Figure 4. Particle Size Distribution of Nanocellulose through PSA Analysis

3.2. Modification of nanocellulose using CTAB

Modifying nanocellulose was carried out to provide amphiphilic properties, which can be used as a coating material for bioactive compounds. Natural bioactive compounds have a low solubility in water [22]. The surface modification of materials using CTAB can increase the hydrophobicity of nanocellulose. Nanocellulose and CTAB interact electrostatically, which the cationic charged head of CTAB interacts non-covalently with the negatively charged of nanocellulose surfaces [10].

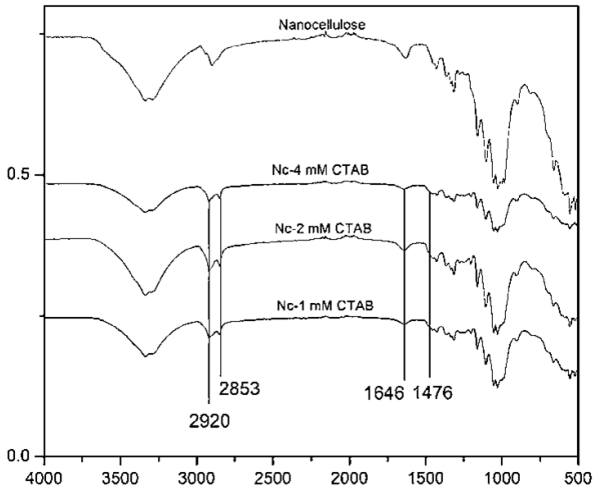

Figure 5. Spectra FTIR of Nc-1 mM-CTAB, Nc-2 mM-CTAB, Nc-4 mM CTAB, and nanocellulose

The FTIR spectrum of the nanocellulose and modified nanocellulose with various CTAB concentrations were measured at a wavenumber of 4000-500 cm^{-1}. According to the FTIR spectrum in Figure 5, it was indicated that nanocellulose was successfully modified by CTAB surfactant. A peak centered at 1476 cm^{-1} observed in spectra of the modified nanocellulose indicated the presence of symmetric N^+-CH_3 stretching band of CTAB surfactant [11]. Additionally, a peak centered at 1646 cm^{-1} was observed and assigned to the characteristic asymmetric N^+-CH_3 stretching band of CTAB [23]. The absorbance peaks at 2920 cm^{-1} and 2853 cm^{-1} corresponded to the stretching vibration of -CH_2

symmetric and asymmetric bonds from the long alkyl chain of CTAB [24].

3.3. Encapsulation of gemor bark extract using CTAB-modified nanocellulose

Gemor bark extract will bind to nanocellulose-CTAB through hydrogen bonds, as well as van der Waals interactions on the nanocellulose side. It will interact electrostatically on the hydrophobic part of nanocellulose-CTAB [10, 25].

The FTIR spectrum is used to identify the chemical groups of gemor bark extract before and after the encapsulation process (Figure 6 and 7). The spectrum corresponding to gemor extract presented a band at 1062 cm^{-1} representing the vibration of C-O bonds of gemor bark extract [26]. The peak at 1234 cm^{-1} corresponded with the bending vibration of O-H bonds [26]. The peak at 3269 cm^{-1} corresponded with the stretching vibration of O-H bonds from phenolic compounds of gemor bark extract [27]. Additionally, a peak at 1372 cm^{-1} and a sharp peak at 2918 cm^{-1} were assigned to bending vibration of C-H bonds and stretching vibration of C-H bond in an aromatic chain of gemor bark extract [26, 27]. The peak at 1515 cm^{-1} and 1599 cm^{-1} were stretching vibrations of C=C bonds of the aromatic chain [27], and a peak at 2851 cm^{-1} corresponded to stretching vibration of CH_2 symmetric bonds [28].

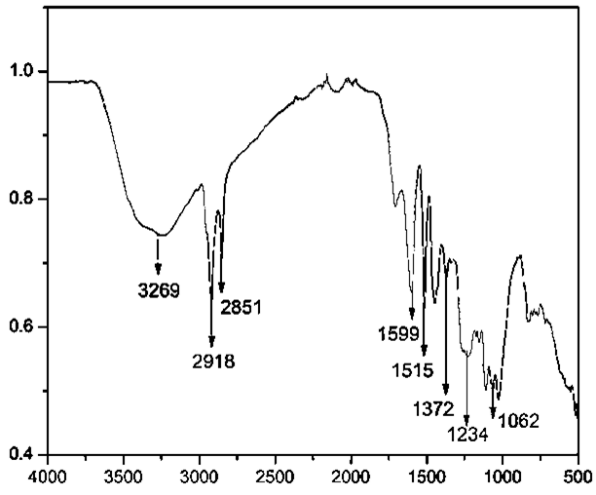

Figure 6. Spectra FTIR of gemor bark extract

Figure 7 shows the FTIR spectrum of the encapsulated gemor bark extract with CTAB-modified nanocellulose. FTIR spectra of gemor-Nc showed an increase and shift of the peak at 3291 cm^{-1}, which was indicated the formation of hydrogen bonds between the nanocellulose and gemor bark extract [11]. FTIR spectrums of gemor-Nc-1 mM CTAB, gemor-Nc-2 mM CTAB, and gemor-Nc-4 mM CTAB peaks of 2989 and 2863 cm^{-1} were corresponded to stretching vibration of CH_2 symmetric and asymmetric of the long alkyl chain of CTAB [24]. A peak at 1493 cm^{-1} corresponded to the stretching vibration of N^+-CH_3 from surfactant CTAB [11]. Furthermore, the existence of typical absorption peaks of gemor bark extract at 1548 cm^{-1} and 1619 cm^{-1} assigned to stretching vibration of aromatic chain indicated that encapsulation using Nc-CTAB did not change the basic structure of the gemor bark extract. The characteristic appearance spectra of Nc-CTAB and gemor bark extract in Figure 7 showed that Nc-CTAB and gemor bark extract

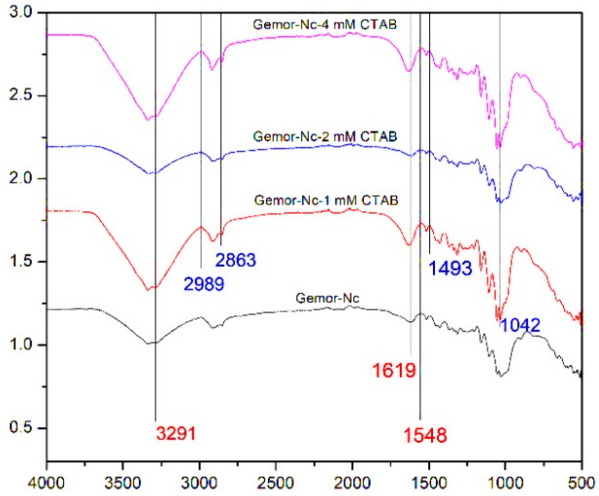

Figure 7. Spectra FTIR of gemor-Nc, gemor-Nc-1 mM CTAB, gemor-Nc-2 mM CTAB, and gemor-Nc-4 mM CTAB

3.4. Encapsulation efficiency

Table 2 shows the encapsulation efficiency (%) of gemor bark extract. Gemor-Nc-4 mM CTAB showed the highest encapsulation efficiency of the sample. It indicated that the higher the CTAB concentration added, the better encapsulation efficiency of gemor bark extract. The addition of CTAB concentration caused more hydrophobic parts to form in the nanocellulose so that the hydrophobic interaction of Nc-CTAB with gemor bark extract was also more robust.

Zainuddin *et al.* [10] reported that bioactive compounds have a benzene chain interaction with the hydrophobic part of Nc-CTAB via the electrostatic and hydrophobic interaction. It means that many bioactive compounds contain a benzene ring in the chain, which causes some of these compounds to be more hydrophobic. Thus, by modifying nanocellulose using CTAB, the bioactive components that tend to be hydrophobic contained in gemor bark extract will interact with the CTAB-modified cellulose chain through electrostatic interactions on the ring portion of the bioactive compounds.

Therefore, the efficiency of the encapsulation of bioactive compounds in Nc-CTAB depends on the hydrophobicity of the surface. The more hydrophobic the Nc-CTAB surface, the more bioactive compounds that can be bounded.

Table 2. Encapsulation efficiency of gemor bark extract

Sample	Encapsulation Efficiency (%)
Gemor-Nc	17.5
Gemor-Nc-1 mM CTAB	48
Gemor-Nc-2 mM CTAB	48.9
Gemor-Nc-4 mM CTAB	53.7

Gemor bark extract is insoluble in water, forming an aggregate when dissolved in water. Wang *et al.* [11]

reported that nanocellulose has a large surface area and hydrogen bonds, creating a smaller structure of encapsulated bioactive compounds (gemor bark extract). Hydrophilic nanocellulose formed a relatively stable gemor-Nc system, reducing aggregation in the resulting gemor encapsulation. CTAB was added to provide a hydrophobicity of nanocellulose, which made nanocellulose more compatible with the molecule of gemor bark extract. This made it easier for the nanocellulose to encapsulate the bioactive molecules through their hydrophobic parts, increasing the particle size and stability of the gemor bark extract.

3.5. Antioxidant activity

The antioxidant activity of gemor bark extract shown in Table 3 indicates that gemor bark extract could prevent 50% free radical activity at a concentration of 39.97 ppm. In addition, Table 3 shows that gemor-Nc, gemor-Nc-1 mM CTAB, and gemor-Nc-2 mM CTAB have moderate antioxidant activity, while gemor-Nc-4 mM CTAB shows good antioxidant activity.

Muttakin *et al.* [29] stated that bioactive compounds have potent antioxidants when the IC_{50} value is less than 50 ppm, then IC_{50} value in the range of 50-100 ppm indicates the powerful antioxidant activity, while the range of 100-150 ppm indicates the moderate antioxidant activity. The better antioxidant activity at gemor-Nc-4mM CTAB was due to the high content of active compounds encapsulated in Nc-4mM CTAB. However, the antioxidant activity of unencapsulated gemor bark extract tended to be higher than gemor-Nc-4 mM CTAB. This activity became lower than unencapsulated gemor bark extract because it was influenced by the amount of active substance encapsulated in Nc-CTAB. The number of bioactive compounds in encapsulated gemor bark extract tended to be less than gemor bark extract at the same concentration. It can be seen by the percentage of encapsulation efficiency, which the largest percentage of encapsulated active substance in the encapsulation efficiency was 53.7%.

The result indicated that there were still some percentages of gemor bark extract that were not encapsulated, so the number of bioactive components that can be encapsulated affects its antioxidant ability. Therefore, the antioxidant activity correlated with the encapsulation efficiency of gemor bark extract. Kurniasih *et al.* [30] reported that the increase in antioxidant activity is associated with the number of active compounds encapsulated.

Table 3. Antioxidant activity of encapsulation of gemor bark extract

Sample	IC_{50} (ppm)
Gemor Bark Extract	39.97
Gemor-Nc	106.41
Gemor-Nc-1 mM CTAB	133.55
Gemor-Nc-2 mM CTAB	145.15
Gemor-Nc-4 mM CTAB	98.41

4. Conclusion

FTIR spectra showed that gemor bark extract was successfully encapsulated by CTAB-modified nanocellulose with the highest encapsulation efficiency at gemor-Nc-4 mM CTAB, namely 53.7%. It showed that the encapsulation efficiency of encapsulated gemor bark extract was affected by the increase in the concentration of added CTAB. Gemor-Nc-4 mM CTAB had a vigorous antioxidant activity with the IC_{50} value of 98.41 ppm, while gemor bark extract had an antioxidant activity of 39.97 ppm. The lower IC_{50} value of gemor-Nc-4 mM CTAB than unencapsulated gemor bark extract because antioxidant activity was influenced by the encapsulation efficiency of gemor bark extract.

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