Synthesis and Characterization of Chitosan Membrane as a Matrix in Drug Delivery of Curcumin

Budi Hastuti* and Alfiah Assy’adha

1Department of Chemistry Education, Faculty of Teacher Training and Education, Universitas Sebelas Maret

*Corresponding author: budi hastuti@staff.uns.ac.id

Abstract. This study aims to find out how to synthesize the chitosan membrane contained curcumin and its characteristics. The characterization of chitosan membrane was determined use FTIR for functional group analysis, XRD for crystallinity and SEM to show the surface of morphology and cross-section on the chitosan membrane. Curcumin encapsulated into the chitosan membrane was performed by using UV-Vis spectrophotometry at λ 426 nm. The results of this study indicate that the chitosan membrane synthesized was obtained homogeneous clear yellow membrane sheets. The characterization of FTIR instrument obtained that chitosan membrane have peaks at wavenumber of 3425.58 cm\(^{-1}\) that show OH groups and 1627.92 cm\(^{-1}\) which show the presence of amine groups. While XRD characterization show chitosan membrane was semi-crystalline which was shown by a high peak intensity with angles 2\(^{\theta}\) 4.1604 and 2\(^{\theta}\) 3.8711. According to the SEM photo shows a smooth and even surface morphology. The optimum time for encapsulation of curcumin into the chitosan membrane is 60 minutes with % EE of 14%.

1. Introduction

Indonesia is a country that has rich in spices. So in ancient times when the Dutch colonized Indonesia aimed at mastering various types of spices. Spices are biological resources that are used by humans for various purposes in daily life. The benefits of spices, among others, as a food flavour enhancer, food flavouring and also as an herbal treatment. Research conducted by Hakim (2015) in Kopen, Banyuwangi, there are 27 types of spices used by the people there. Types of spices used for food flavoring: galangal, ginger, turmeric, chili, and lemongrass. The spices besides food seasonings are also used for herbal medicines [1].

Herbal medicine is a medicine made from natural ingredients using traditional processing without a mixture of chemicals. Usually herbal medicine is formed of powder, capsules, liquid (herbal medicine). One type of spice that is often used as medicine is turmeric. Turmeric (Curcuma domestica VAL.) is a plant that contains mainly curcuminoids and essential oils. Based on the results of research at the Research Institute for Medicinal Plants and Spices (Balittro) found that the content of curcumin in the turmeric rhizome averaged 19.92% [2]. Curcuminoids contain curcumin compounds and their offspring. The content of curcumin in turmeric is very useful for medicines.

Curcumin is an ingredient found in curcuminoids in the turmeric rhizome. The nature of curcumin as an anticancer, antitumor, antioxidant, anti-inflammatory, antimutagen and others [3]. In the field of pharmacology, curcumin is often used as a slow-release drug that is mixed in a particular matrix. Drug release is a process of release of the drug from the used ingredients. In the drug release process, the
drug delivery system should ideally deliver on a controlled drug or controlled level for the desired duration. This is done to ensure the level of safety and patient needs [4]. Compounds that can be used as drugs must have certain characteristics such as absorption, distribution, metabolism, excretion, and toxicity (ADMET) [5]. However, curcumin also has the disadvantage that the level of solubility is low in the water so that it will limit its activity pharmacologically [6]. Therefore, needed a curcumin delivery matrix. This curcumin delivery matrix utilizes natural polymers.

The application of natural polysaccharides polymers is increased during recent years because of their unique biological and physical properties as carriers of drugs that can be used effectively [7]. Chitosan is a natural polymer which consist of polysaccharides that have an abundance second after cellulose and have a structure similar to cellulose. Some of polymers cellulose derivates are widely used in controlled release preparations as matrix in drug delivery systems [8]. Chitosan is a polysaccharide containing d-glucosamine and N-acetyl-D-glucosamine. Chitosan produced from the deacetylation of chitin which can form gels, films, microparticles, nanoparticles, and beads. Because of this ability, it can be used for matrix or drug release membrane [9].

Chitosan has unique properties that are biodegradable, biocompatible, and non-toxic [10]. Chitosan has polycationic properties by having amino and hydroxyl groups. The presence of chitosan active groups, namely amino and hydroxyl groups can bind toward molecules such as proteins and drugs. Chitosan can be used as a membrane material for slow-release preparations with superior properties.

Based on the background above, this research is intended to develop natural polymers as slow-release matrix drugs by making chitosan membranes. This membrane utilizes natural polymers that have unique properties that can interact with curcumin. Curcumin is encapsulated in chitosan membrane which is used as a drug delivery agent and used as a slow release which is suitable for overcoming the therapeutic problems needed.

2. Materials and Instrumentation

2.1. Materials
Chitosan (technical) powder, curcumin pro-analyst, the solutions used were of the type of pro-analyst namely glacial acetic acid 2% and 70% ethanol solution, and distilled water.

2.2. Instrumentation
The FTIR was used to see the functional groups of the membrane, SEM was used to determine the surface morphology of the membrane, to see the crystallinity use XRD, and UV-vis spectrophotometry to determine the concentration contained in the chitosan membrane.

3. Experiment Method

3.1. Preparation of chitosan membrane
0.5-gram chitosan powder dissolved in 25 ml of 2% acetic acid solution, stirred by using a magnetic stirrer for ± 1 hour. After the mixture is homogeneous then printed with printed media made from polypropylene and dried on the temperature of 50°C for ± 24 hours.

3.2. Determination of the maximum wavelength of curcumin solution and the calibration curve of curcumin solution
100 ppm of curcumin solution in 50 ml of 70% ethanol is varied to 10 ppm, 20 ppm, 30 ppm, 40 ppm, 50 ppm, 60 ppm, 70 ppm, 80 ppm, and 90 ppm. Finding the maximum wavelength of a curcumin solution by testing a 100-ppm curcumin solution at a wavelength of 300-600 nm. The results obtained wavelength of curcumin is 426 nm. After that, determine the absorbance of curcumin solution from 10 ppm to 100 ppm by using the λ maximum.
3.3. The loading of curcumin in the chitosan membrane

50 mg chitosan membrane put into a 25 ml solution of 100 ppm curcumin solution. Then, the curcumin solution stirred using a magnetic stirrer and was taken 1 ml of the solution every 5, 10, 15, 30, 45, 60, and 120 minutes. Next, the concentration of curcumin solution determined using a UV-vis spectrophotometry at 426 nm.

3.4. Characterization of chitosan membrane

3.4.1. Functional group analysis with Fourier Transform Infrared (FTIR) spectrophotometer. The functional group of the membrane was tested with FTIR. Samples analyzed in the form of chitosan membrane powder to characterize of functional groups in the chitosan membrane.

3.4.2. Structure Analysis of Surface by using SEM. Characterization SEM was carried out at the PPGL Research and Testing Laboratory. The analyzed sample is a 2×2 cm membrane size. The results obtained in the form of images from the front surface.

3.4.3. Analysis of crystallinity using XRD. The XRD testing was carried out at the UII Research and Testing Laboratory. Samples analyzed in the form of chitosan membrane powder that has been crushed first.

4. Result

This study has been synthesized chitosan membrane. Chitosan used in the form of brownish-yellow powder and a bit rough. While the chitosan membrane produced in the form of a clear yellow layer is presented in Figure 1.

![Figure 1](image-url)

Figure 1. (a) chitosan powder and (b) chitosan membrane.

Chitosan membranes characterized using the FTIR (Fourier Transform Infrared) instrument to determine the functional groups contained in the chitosan membrane. Based on the FTIR spectra of the chitosan membrane in Figure 2 showed that it has a wide absorption at 3425.58 cm⁻¹ that indicates the vibration stretching -OH group. The band at 1627.92 cm⁻¹ indicates the presence of a -COOH group and the band on 1519.91 cm⁻¹ indicate of –NH₃ group.
Figure 2. Results of FTIR spectroscopy of the chitosan membrane.

The results of chitosan membrane characterized by using SEM image to show the surface morphology of the membrane. In figure 3 it is showed the photo SEM of the chitosan membrane with a magnification of 500x. It can be seen that the chitosan surface has a smooth and flat surface.

Figure 3. The SEM image surface of chitosan membrane with a magnification of 500x

Chitosan membrane that has been made is also analyzed in terms of crystallinity using XRD. Based on the XRD results shown in Figure 4, it provides information that the chitosan membrane has semi-crystalline properties. The characteristic diffractogram image of chitosan membrane has angles of 2θ on 15° and 21°.
Drug release is influenced by several factors, one of the most important factors being the loading time of the drug into the drug delivery matrix. The loading time determines the optimal time for the drug compound to be held in the pore of the drug delivery matrix so that the optimal drug concentration can be found in the drug delivery matrix. Loading is done by immersing 50 mg of chitosan membrane in 25 ml of 100 ppm curcumin solution. The immersion time are 5, 10, 15, 30, 45, 60 and 120 minutes. Based on research conducted by Dash et al (2010) this loading has the purpose of trapping curcumin into the chitosan membrane as a conduit and stored until the release process is carried out [11]. Calculation of the percentage of Curcumin Efficiency of Encapsulation contained in the chitosan membrane using the following formula:

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\%EE = \frac{[\text{Curcumin total}] - [\text{Curcumin loaded}]}{[\text{Curcumin total}]} \times 100 \%
\]  

(1)
In Figure 5 above the graph shows % EE during the chitosan membrane loading of curcumin with various time variations. The optimum % EE yield of chitosan membrane loading against 100 ppm curcumin is 14% at 60 minutes. The efficiency pattern of the encapsulation of curcumin load over time shows that curcumin was initially inserted into the membrane increasing gradually. After reaching the optimal loading time, at 60 minutes with % EE is 14%, the loading of curcumin decreases, this shows that the loading of curcumin by the chitosan membrane has been saturated.

5. Conclusion
The results of this study indicate that the chitosan membrane synthesis obtained homogeneous clear yellow membrane sheets. Characterization of chitosan FTIR was obtained characteristic peaks on wave number 3425.58 cm\(^{-1}\) that shows OH groups and 1519.91 cm\(^{-1}\) which shows the presence of amine groups. While the XRD characterization of chitosan shows semi-crystalline which is shown by diffractogram image that has a high peak intensity with angles 2θ on 15° and 21°. According to the SEM image, it shows that chitosan has a smooth and even surface morphology. The optimum time for encapsulation of curcumin into the chitosan membrane is 60 minutes, with % EE of 14%.

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References
[1] Hakim, Luchman, Jati Batoro, Kurniasih Sukenti 2015 *J-PAL.* 6 133-142
[2] Rukmana, Rahmat 1997 *Kunyit* (Jogjakarta: Kanisius)
[3] Chattopadhyay I, Biswas K, Bandopadhyay and Banwjee RK 2004 *Current Science* 87 44-53
[4] Singyhi G and Singh M 2011 *J. Pharm. Res.* 11 77-84
[5] Akhtar F, Rizvi M M A, and Kar S K 2012 *Biotech.* 30 310-320
[6] Sahu A, Bora U, Kasoju N and Goswami P 2008 *Acta Biomat.* 4 1752-1761
[7] Saheb M, Fereydouni N, Nemati S, Barreto G, Johnston T P, Sahebkar A 2019 *Journal of Cellular Physiology* 50 1-16
[8] Herdini, Darusman L K, Sugita P 2010 *Makara, Sains,* 14 57-62
[9] Safdar R, Omar A A , Arunagiri A, Regupathi I, and Thanabalan M 2019 *Journal of Drug Delivery Science and Technology* 49 642–659
[10] Kaban J, Bangun H , Dawolo A K, Daniel 2006 *Jurnal Sains Kimia* 10 10–16
[11] Dash S, Murthy P, N Nath L, Chodury P 2015 *ActaPolo.Pharm. Res.* 67 217-223