Synthesis and Characterization of Pectin-Chitosan as Candidate Materials for Slow Release System

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Abstract. The polyelectrolyte complex (PEC) is a complex formed between opposite charge particles which have recently attracted attention for their potential for drug delivery applications. In this study, PEC from pectin (anionic species) and chitosan (cationic species) was studied. Pectin and chitosan solutions in 2% v/v acetic acid were mixed in the ratio pectin : chitosan of 1:1. The difference in characteristics of PEC pectin-chitosan (Pec-Chi) with its original polymer is indicated by functional group analysis using FTIR. Morphology characterization of films were investigated by XRD. The results showed that Pec-Chi adsorbent had better stability and resistance to the acidic environment. Characterization using FTIR showed that the adsorbent has functional groups of amines, carboxyl and hydrogen. Furthermore, XRD data show that the adsorbent was a not crystalline.

1. Introduction
The use of natural polymers in the design of drug delivery system has received attention in recent years, due to their excellent bioavailability and biodegradability. As the oral route is the most common route for drug administration, the use of polymers in controlling the release of drug has become the most important tool in the formulation where the drug is incorporated in the polymers. Related to this, understanding factors that influence drug release kinetics during the process of adsorption, distribution, metabolism and excretion (ADME) is very important, in order to produce better pharmacological action [1]. Furthermore, in vitro drug dissolution studies become a very important part in the development of drug technology because it is a beginning in examining the effectiveness of drug release.

Research on drug release from its matrices such as natural polysaccharides as matrices in drug delivery systems have been extensively investigated in their application [2]. Chitosan and its derivatives is an example of a polysaccharide which have been studied in drug delivery systems in various forms [3]. Chitosan is biocompatible, biodegradable and non-toxic so that it can be used as a matrix in controlled curcumin release systems [4]. Chitosan is a cationic (positively charged) polymer derived from poly-N-acetyl-D-glucosamine which is biodegradable, biocompatible, non-toxic and is often used extensively in the biomedical field [5]. The positive charge of chitosan is very important in the drug delivery system because it plays a role in interactions with the drugs it delivers. The interaction of chitosan with drugs can increase solubility, stability and bioavailability of encapsulated drugs in it [6].
The use of chitosan as an ingredient in controlled drug release matrices has the disadvantage that the mechanical strength of chitosan membranes is very low that the membrane is fragile. In addition, chitosan has low hydrophilicity properties so it is necessary to modify chitosan physically and chemically to increase the mechanical strength and hydrophilicity of the membrane. One of them is by adding anionic polysaccharide which has a higher hydrophilicity than chitosan. Pectin can improve mechanical properties and increase the hydrophilicity of chitosan membranes. Pectin is soluble in water because it has a carboxyl group [7]. Pectin is biodegradable and non-toxic so it is widely used in the pharmaceutical industry for drug delivery in the form of tablets, gels and film membranes. Chen et al. (2010) make chitosan-pectin composites to increase membrane strength so that they can control hydrophilicity and disintegration [8]. The research proves that chitosan-pectin composite membrane shows the right balance between the hydrophilic group and hydrophob which is the nature of a film. Chitosan pectin membranes have greater hydrophilicity and water absorption compared to pure membranes (chitosan or pectin only). Therefore, chitosan-pectin composite membranes is expected as biocompatible, biodegradable and non-toxic material, that thus suitable to be applied as drug release agent.

2. Materials and method

2.1. Material
Chitosan purchased from CV Ocean Fresh Bandung, pectin from apple waste purchased from UD Organic Yogyakarta, HCl (E-Merck), isopropanol (E-Merck), chloroacetic acid (E-Merck), NaOH (E-Merck), acetic acid (E-Merck), and aquadest.

2.2. Preparation of the membrane.

2.2.1 Synthesis of carboxymethyl chitosan (CMC) by grafting chitosan with chloroacetate. 3 g chitosan powder was dissolved in 80 mL of isopropanol then was added with drops of 40% NaOH as much as 28 mL. Chitosan and isopropanol were stirred for 30 minutes. Then chloroacetic acid is added with the mole ratio of chloroacetic acid : chitosan is 10 : 1. The mixture is filtered and washed with aquabides and ethanol. The filtered chitosan deposit is dried and ovened at 60°C for 3 hours. Functional group characterization was performed using FTIR spectroscopy.

2.2.2 Synthesis of Pectin-CMC adsorbent. 0.2 g CMC powder was dissolved in 10 mL of 5% acetic acid. 0.2 g pectin powder was dissolved in 10 mL of 5% acetic acid. Both solutions were mixed, stirred for 2 hours then printed in petridish and dried. After drying the membrane is removed from the mold by adding 10 mL 1 M NaOH. The membrane that has been separated from the mold is washed with distilled water and then dried. Functional group characterization was performed using FTIR spectroscopy, characterization using XRD and surface analysis using SEM.

3. Results and discussion
The synthesis of PEC pectin-carboxymethyl chitosan membrane as an intermediate delivery material for this drug was initially carried out by grafting chitosan with a monocloroacetic group so that carboxymethyl chitosan was formed. After that it is composited with a pectin group, so that PEC Pectin-Carboxymethyl chitosan (CMC) membrane will form, which is a membrane that is more stable and more soluble in water. Thus PEC Pectin-Chitosan has the potential to be used as a slow release material for drugs.

Chitosan has low hydrophilicity properties so it is necessary to modify chitosan physically and chemically to increase the mechanical strength and hydrophilicity of the membrane. The addition of pectin which is anionic polysaccharide which has a higher hydrophilicity than chitosan can improve the mechanical properties and increase the hydrofility of the chitosan membrane. Thus the chitosan-pectin
composite membrane increases the hydrophilicity and absorption of water in the composite membrane, so that it has the potential as a drug disintegration.

3.1. Functional group analysis uses FTIR

In order to prove that the –COOH group is the dominant active group in pectin, the –NH₂ group is the active group that is dominant in chitosan while the active group which is dominant in CMC is the –NH₂ and –COOH groups. Furthermore, PEC Pectin-CMC membrane was tested for functional groups using an infrared spectrophotometer. FTIR spectra are presented in Figure 1.

![Figure 1. FTIR spectra of A. chitosan, B. CMC, C. Pectin and D. Pectin-CMC compounds.](image)

In Figure 1, it appears that in chitosan spectra, CMC has a wave number of 1597 cm⁻¹ as –NH absorption (amine) and 3464 cm⁻¹ as –OH absorption. In the pectin spectra there is a wavenumber 1627 cm⁻¹ as –COOH absorption and at wavenumber 1751 cm⁻¹ as C=O ester. Pectin-CMC spectra show wave number 1420 cm⁻¹ as vibration absorption peak –NH (amine), 1635 cm⁻¹ as –COOH absorption, and 1735 cm⁻¹ represents stretching vibration absorption –C=O ester, 2940 cm⁻¹ is stretching vibration absorption of the O-CH₃, and 3464 cm⁻¹ groups is the absorption of –OH groups.

3.2. Analysis of crystallinity with XRD

Analysis with XRD spectrometry was intended to determine the crystallinity of chitosan, pectin, chitosan after chloroacetate and CMC grafting after being added to pectin. The diffractogram of chitosan, CMC, pectin and Pectin-CMC is shown in Figure 2.
Figure 2. Diffractogram of XRD from chitosan, CMC, Pectin and Pectin-CMC.

The diffractogram of chitosan, CMC and Pectin-CMC showed a widening peak at 2θ = 10°, and 2θ = 20°. Peak 2θ = 10°, and 2θ = 20° in CMC decreased compared to the initial chitosan. This shows that there is a decrease in the degree of crystallinity due to the grafting process. The transplantation process changes the side groups by replacing hydrogen atoms with acetic acid groups so that the hydrogen bonds are weakened. Decreased crystallinity of chitosan by chloroacetate grafting was also shown by Abreu and Campana-Filho (2005). The process of combining CMC compounds with Pectin caused a change in diffractogram, non-crystalline and pectin CMC which was crystalline after being combined to form semi-crystalline Pectin-CMC compounds. The decrease in crystallinity is also shown by Pectin-CMC compounds, this indicates that PEC Pectin-CMC to absorb moisture in it is useful for preparation of hydrogels.

4. Conclusion
The PEC Pectin-CMC membrane synthesized in this study can be applied as a drug release matrix. From the FTIR test results showed that the PEC Pectin-CMC membrane had carbonyl group (C=O), amine group (–NH₂) and hydroxyl group (–OH). The XRD test showed that the membrane showed a decrease in crystallinity, which showed that the membrane could be applied as a matrix of slow release drug.

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