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EFFECT OF POLYCAPROLACTONE ON CHARACTERISTICS AND MORPHOLOGY OF ALGINATE/CHITOSAN/LOVASTATIN COMPOSITE FILMS

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ABSTRACT

In this work, alginate(AG)/chitosan(CS)/lovastatin(LS)(AG/CS/LS) composite films using polycaprolactone (PCL) as acompatibilizer were prepared by solution method with the ratio of AG/CS and LS content fixed at 4/1 and 10 wt.% (in comparison with the total weight of CS and AG), respectively. The PCL content was varied at 3, 5 and 10 wt.% (wt./wt., calculated on basis of total weight of AG, CS and LS). The role of PCL as a compatibilizer was determined by Fourier Transform Infrared Spectroscopy, Scanning Electron Microscopy and Differential Scanning Calorimetry methods. PCL was found to enhance the compatibility, interaction, and dispersion of CS, AG and LS. The structure of the composite films became more uniform and tight; LS rods were more uniformly dispersed in the AG, CS polymer mixture. The influence of PCL content on the drug release from the composite filmswas also investigated.

Keywords: compatibility, polycaprolactone, lovastatin, alginate, solution method.

1. INTRODUCTION

Polycaprolactone (PCL) is a biodegradable petroleum-based polymer. It has a semi-crystalline structure with melting pointand glass transition temperature of 55–65 °C and -60 °C, respectively. Its advantageous properties are high toughness, high elongation, and low modulus of elasticity. Thus, it can be blended with other biopolymers, such as polylactic acid (PLA), and starch, etc.to improve itstoughness as well as to produce new biodegradable materials [1-5].

Interestingly, the incorporation of small amounts (≤ 10 wt.%) of PCL into the starch or PLA/chitosan blend can enhance the compatibility and miscibility of polymers to each other. Rodrigo Ortega-Toro et al. found that melt blending 5 wt.% of PCL and corn thermoplastic starch (with 30 wt.% glycerol) gave a more stretchable and stable films without a notable phase separation [6]. In our previous study [7], PCL was used as a compatibilizer for blends of PLA and chitosan (CS). We observed that PCL increased in the degree of crystallinity, thermal stability, and the miscibility of PLA/CS blend.

Since CS is a hydrophobic polymer while alginate (AG) is a hydrophilic polymer, they are difficult to mix and interact with each other. In our previous publications, polyethylene oxide (PEO) was used as a compatibilizer for AG/CS/LS composite films [8-9]. The results showed that PEO can improve the interaction between AG and CS as well as contribute on the LS release from these composites. In literature [9], the effect of PCL on the drug release content and the drug release kinetics of AG/CS/LS composites in pH 2 and pH 7.4 buffer solutions was investigated. However, the structure, morphology, thermal behavior as well as drug release in pH 6.8 buffer solution is still limited to research. Therefore, the aim of this work was to increase the compatibility and dispersion of the components of alginate (AG)/chitosan(CS)/lovastatin (LS) composite films by addition of PCL as a compatibilizer. Fourier Transform Infrared Spectroscopy (FT-IR), Scanning Electron Microscopy (SEM) and Differential Scanning Calorimetry (DSC) were used to evaluate the effect of PCL on the compatibility, morphology as well as other characteristics of the AG/CS/LS composite films.

2. EXPERIMENT

2.1. Materials

Chitosan (CS, powder, viscosity of 1220 cPs, degree of deacetylation higher than 77 %); sodium alginate (AG, white powder, viscosity of 300–500 mpa.s); lovastatin (LS, powder, purityhigher than 98.0 %); and polycaprolac tone (PCL, melting temperature of 56-64 °C, melting flow index (MFI)of 1.8 g/10 min, number molecular weight (M_n) of 45000 g/mol) were obtained from Sigma-Aldrich, USA; 98 % ethanol 99.5 % acetic acid and dichloromethane were the commercial products of China.

2.2. Preparation of AG/CS/PCL/LS composite films

General procedure: 80 mg of AG was dissolved in 20 ml of distilled water (AG solution); 20 mg of CS was dissolved in 20 ml of 1 % acetic acid (CS solution); 10 mg of LS was dissolved in 5 ml of ethanol (LS solution); 3 mg of PCL was dissolved in 5 ml of dichloromethane (PCL solution). Next, the LS solution was poured into the PCL solution before mixing them with AG solution. Then, CS solution was added into the above mixture and they were stirred by sonication for 30 min. Finally, this solution was poured into a petri dish allowing the solvents to evaporate naturally to form the composite film. The composite films with varied PCL content were prepared similarly; the proportion and abbreviation of the composite films were presented in Table 1.

2.3. Characterization of AG/CS/PCL/LS composite films

The FTIR spectra of the composite films were recorded at room temperature in air with 4 cm^{-1} resolution, 16 scans and wave number ranging from 400 to 4000 cm^{-1} on a Nicolet/Nexus

670 spectrometer (USA) at Institute for Tropical Technology - Vietnam Academy of Science and Technology(VAST).

The morphology of the composite films was determined by Scanning Electron Microscopy (SEM) using an S-4800 FESEM instrument (Hitachi, Japan) at National Institute of Hygiene and Epidemiology.

Differential Scanning Calorimetric (DSC)diagrams of the composite films were carried out on a Shimadzu DSC-50 device under N_2 atmosphere at heating rate of 10 $^oC.min^{-1}$ from room temperature to 250 ^oC.

The LS drug release content of the composite films was determined based on the data from UV-Vis spectra with the steps as follows:50 mg of each sample was immersed in 500 ml of phosphate buffer solution (PBS, pH 6.8) at 37 ^oC and placed in an incubated shaker at 120 rpm. At predetermined time intervals, 5 ml of aliquots was withdrawn to carry out the concentration of released LS by UV Spectrophotometer (CINTRA 40, GBC, USA) and replaced with fresh PBS to maintain the total volume. The LS release percent can be determined by the following equation:

$$\text{Drug release [\%]} = C_{(t)}/C_{(0)} \times 100 \quad (1)$$

where $C_{(0)}$ and $C_{(t)}$ represent the amount of loaded and amount of drug released at a time t, respectively. All studies were done in triplicate.

Table 1. Compositionsof AG/CS/PCL/LS composite films.

Compositions	Sample No.
AG/CS = 4/1, LS 10 wt.%*, PCL 0 wt.%*	P0
AG/CS = 4/1, LS 10 wt.%*, PCL 3 wt.%*	PCL3
AG/CS = 4/1, LS 10 wt.%*, PCL 5 wt.%*	PCL5
AG/CS = 4/1, LS 10 wt.%*, PCL 10 wt.%*	PCL10

*Calculated on basis oftotal weight of AG and CS.

3. RESULTS AND DISCUSSION

3.1. FTIR spectra of AG/CS/PCL/LS composite films

The FTIR spectra of the composite films P0, PCL3, PCL5, and PCL10 are shown in Figure 1. Compared with the FTIR spectra ofAG, CS, LS and P0 [10], the peaks characterized for hydroxyl, alkyl, double bond carbon, and C-O groups show a lower intensity. The appearance of two new peaks at 3743 cm^{-1} and 2360 cm^{-1} corresponds to the presence of PCL. This can be explained by better dispersion and compatibility of AG and CS in presence of PCL, leading to stronger hydrogen bonding of hydroxyl and amine groups in CS with hydroxyl groups of AG. As a result, the shift of the stretching vibrations of hydrogen bonded amine and hydroxyl groups is occurred. The broad peak at 2155 cm^{-1} of P0 which is assigned to -NH_3C group in the polyion complex membrane (causing by the electrostatic interaction between the carboxylate groups of AG and protonated amino groups from CS) [11-13] is also shifted to 2360 cm^{-1}. This indicates an enhancement in dispersion and interaction of AG and CS due to the presence of PCL compatibilizer.

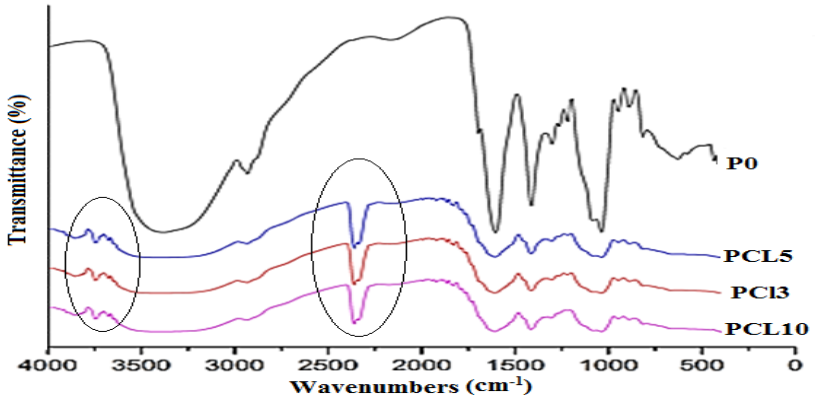

Figure 1. FTIR spectra of P0, PCL3, PCL5, and PCL10 composite films.

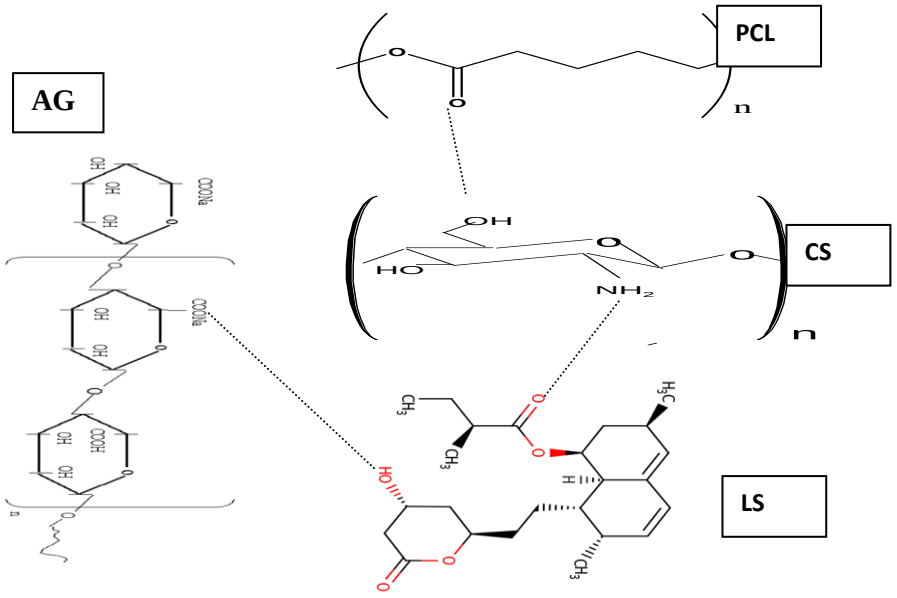

Figure 2. A hypothetical model of hydrogen bonding between AG, CS, PCL, and LS in composite films.

Table 2. Peaks assignments in AG/CS/LS and AG/CS/PCL/LS composite films.

Vibrations / Samples	Wavenumbers (cm^{-1})				
	$\nu_{-NH2, -OH}$	ν_{CH}	$\nu_{C=O, C=C}$	$\delta_{-NH2, CH}$	ν_{C-O-C}
P0	3386	2923	1604	1411	1079
PCL3	3394	2931	1606	1414	1036
PCL5	3395	2934	1606	1415	1037
PCL10	3393	2934	1607	1415	1037

Table 2 lists the position of some main peaks in spectra of the above samples. It is clear that the slight shift in wave numbers of hydroxyl, amine, and C-O groups in the FTIR spectra of PCL3, PCL5, and PCL10 proved that AG, CS, PCL, and LS can interact through hydrogen bonding between hydroxyl, amine, and C-O groups of AG, CS, PCL, and LS (a hypothetical model is shown in Figure 2).

3.2. Morphology of AG/CS/PCL/LS compositefilms

Figure 3 displays FE-SEM images of P0, PCL3, PCL5, and PCL10. It can be seen that LS rods were evenly distributed with smaller sizes in the composite films having PCL as a compatibilizer, especially in the PCL3 and PCL5 composite films. The presence of PCL enhancedinteraction of LS with AG, CS polymersas hypothesis model of hydrogen bonding in Figure 2.

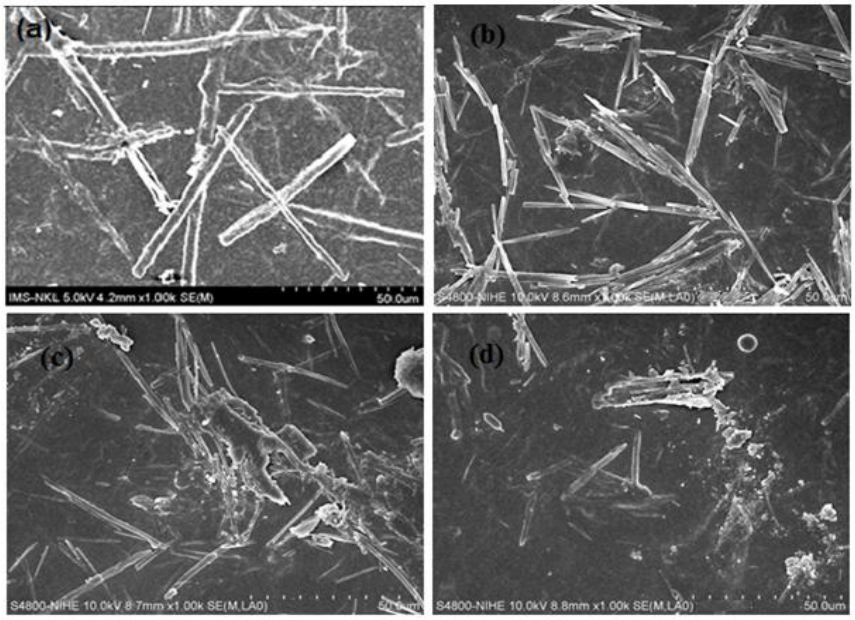

*Figure 3.*FESEM images of P0 (a), PCL3 (b), PCL5 (c), and PCL10 (d) composite films.

3.3. Thermal behavior of AG/CS/PCL/LS composite films

DSC diagrams of AG/CS/PCL/LS composite films are demonstrated in Figure 4. The DSC parameters obtained from the DSC diagrams of AG, CS, LS, P0, PCL3, PCL5, and PCL10 are listed in Table 1. The melting temperature and degradation temperature of AG were 119.6 ^{o}C and 238.8 ^{o}C [14]. There was only one endothermic peak on the DSC diagram of CS at 106.8 ^{o}C corresponding to the loss of adsorbed water due to the hygroscopicity of CS [15]. This also caused to observe difficultly the glass transition temperature of CS. It can be recognized 2 endothermic peaks at 174.6 ^{o}C and 264.7 ^{o}C in the DSC diagram of LS, corresponding to the loss of adsorbed water and the melting of LS [16-17]. From the Figure 4 and Table 1, it can be seen that there was a broad endothermic peak from 75 ^{o}C to 170 ^{o}C on the DSC diagrams of the P0, PCL3, PCL5 and PCL10 composite films attributing to overlap of the endothermic peak of CS and AG.A small endothermic peak near 185 ^{o}C was appeared in the DSC diagram of the P0

sample but it was disappeared in the DSC diagrams of the PCL3, PCL5 and PCL10 samples. In addition, the area of endothermic peak near 134 ^{o}C in the DSC diagram of P0 sample is much larger than that in the DSC diagrams of PCL3, PCL5 and PCL10 composite films. The onset melting temperature of the composite films containing PCL is higher than that of P0 composite films. These evidences mean that the structure of the AG/CS/PCL/LS composite films containing PCL is more uniform and closer than that of the P0 sample, therefore, the AG/CS/PCL/LS composites films are more difficult to be melted.

Table 1. DSC parameters obtained from DSC diagrams of AG, CS, LS, P0, PCL3, PCL5 and PCL10 composite films.

Sample	Onset melting temperature (^{o}C)	Melting temperature (^{o}C)	Melting enthalpy (J/g)
AG	76.3	119.6	358.6
CS	-	106.8	130.6
LS	-	174.6 264.7	90.3 74.1
P0	75.6	134.0	444.6
PCL3	100.9	132.1	374.5
PCL5	79.4	119.9	464.8
PCL10	94.8	125.5	488.0

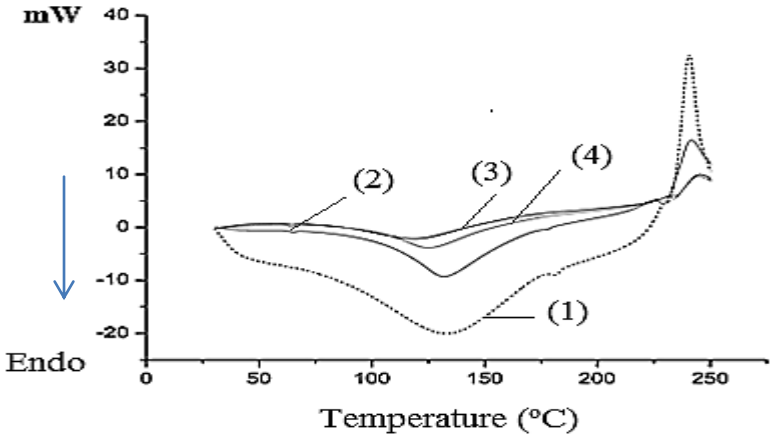

Figure 3. DSC diagrams of P0 (1), PCL3 (2), PCL5 (3) and PCL10 (4) composite films.

3.4. Drug release study

To consider the effect of PCL on the drug release from AG/CS/PCL/LS composite films, the LS release content from the AG/CS/PCL/L composite films in pH 6.8 phosphate buffer solution is calculated according to Eq. 1 and performed in Figure 4. It can be seen that the drug release content is increased as increasing the testing time and corresponded to 2 periods [18-19].

The first period is occurred for first 10 testing hours with near 90 wt.% of LS released continuously. This period is considered as the quick release process. Then, the drug release becomes slower and stable with about 5 wt.% of drug released for next 20 testing hours. The total drug release content is near 95 wt.% for all tested samples during 30 testing hours. The drug release content from the PCL3, PCL5 and PCL10 composite films is lower than that of P0 sample. This can be also explained by the improvement of the interaction between AG, CS, and LS in presence of PCL compatibilizer in the composite films.

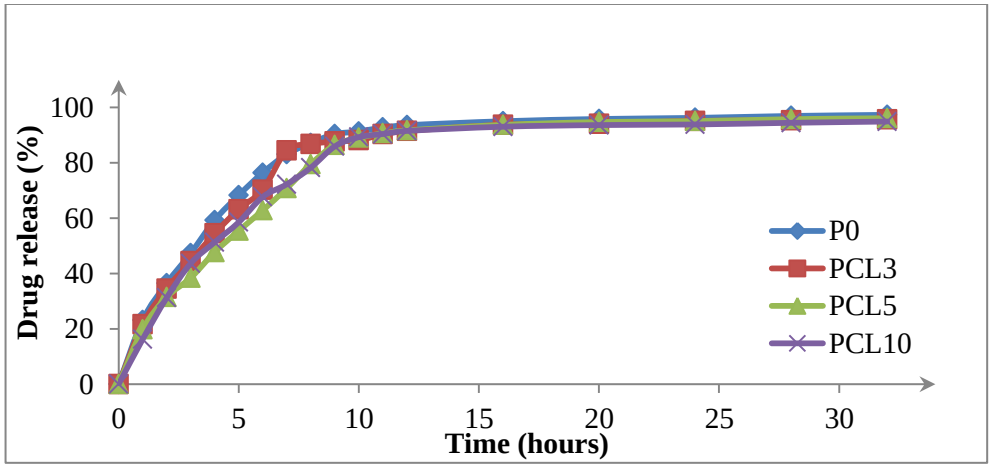

Figure 4. LS release content from P0, PCL3, PCL5 and PCL10 composite films in pH 6.8 phosphate buffer solution.

4. CONCLUSIONS

The alginate/chitosan/polycaprolactone/lovastatin (AG/CS/PCL/LS) composite films were prepared by solution method. The presence of PCL as a compatibilizer contributes to enhance the compatibility, interaction and dispersion of CS, AG and LS in the composite films, therefore, LS rods are more uniformly dispersed in the AG/CS//LS composite films, leading to the structure of the composite films is more uniform and tighter. The total LS drug release content from P0, PCL3, PCL5, and PCL10 composite films is near 95 % for 30 testing hours in pH 6.8 phosphate buffer solution.

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