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Preparation and characterization of the graft copolymer of chitosan with poly[rosin-(2-acryloyloxy)ethyl ester]

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Abstract

Graft copolymerization of rosin-(2-acryloyloxy)ethyl ester (RAEE) onto chitosan (Cts) was carried out under microwave irradiation using potassium persulfate as an initiator. The structures, morphology, and thermal properties of the Cts graft copolymer (Cts-g-PRAEE) were characterized by means of FT-IR, XRD, SEM, and TG. Also, Cts and Cts-g-PRAEE copolymer were used as carriers of fenoprofen calcium (FC), and their controlled release behavior in artificial intestinal juice were studied. The results show that the rate of release of fenoprofen calcium from the carrier of Cts-g-PRAEE copolymer becomes very slower than that of Cts in artificial intestinal juice.

Keywords: Chitosan; Rosin-(2-acryloyloxy)ethyl ester; Graft copolymer; Microwave; Drug release

1. Introduction

Chitosan is a partially deacetylated derivative of chitin, and possess the special properties such as biocompatibility, biodegradability, and biological activities, as a result it has been widely applied to biomedicals, pharmaceuticals, cosmetics, and agricultural fields (Goosen, 1997). However, chitosan is only soluble in few dilute acid solutions due to its crystalline nature (Majeti & Kumar, 2000), which limits its wide applications. Recently, the increasing importance and interest in chemical modification of chitosan by graft copolymerization to improve its solubility and widen its applications (Feng & Dong, 2006; Jayakumar, Prabaharan, Reis, & Mano, 2005; El-Tahlawy, El-Rafie, & Aly, 2006), because chitosan have both reactive hydroxy and amino groups that can be grafted. Graft copolymerization of chitosan with synthetic monomers can introduce desired properties and extend the field of potential application of them by choosing various types of side chains, and research on the graft copolymerization of vinyl monomers such as acrylic acid, methyl methacrylate, acrylonitrile, vinyl acetate onto chitosan using free radical initiation has been reported (Don, King, & Chiu, 2002; Jayakumar et al., 2005; Pourjavadi, Mahdavinia, Zohuriaan-Mehr, & Omidian, 2003; Prashanth & Tharanathan, 2003; Yazdani-Pedram, Retuert, & Quijada, 2000). On the other hand, rosin and its derivatives have degradability, excellent solubility, biocompatibility, and lower polarity compared to chitosan. Therefore, through grafting rosin and its derivatives onto chitosan, it is expected that the graft copolymer shows improved solubility and potential applications to various fields such as bioactive materials, biomedicals, and controlled drug delivery. In recent years, a number of free radical initiator systems have been developed to initiate graft copolymerization, such as ceric ammonium nitrate (CAN) (Caner, Yilmaz, & Yilmaz, 2007; Yilmaz, Adali, Yilmaz, & Bengisu, 2007; Zang & Feng, 1998), potassium persulfate (KPS) (Najjar, Yunus, Ahmad, & Rahman, 2000; Prashanth & Tharanathan, 2003; Kumbar, Soppimath, & Aminabhavi, 2003), and ammonium persulfate (APS) (Sun, Xu, Liu, Xue, & Xie, 2003). And, it is also reported that graft copolymerization is initiated by γ-irradi-

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ation (Casimiro, Botelho, Leal, & Gil, 2005; Li, Liu, Shen, & Fang, 2005) and microwave irradiation (Ge, Pang, & Luo, 2006; Liu, Li, Fang, & Chen, 2005; Singh, Tripathi, Tiwari, & Sanghi, 2006).

In this paper, graft copolymerization of rosin-(2-acryloyloxy)ethyl ester (RAEE) onto chitosan (Cts) was carried out under microwave irradiation and in the presence of potassium persulfate as an initiator. Also, Cts and Cts graft copolymer (Cts-g-PRAEE) were used as carriers of fenoprofen calcium (FC), and their controlled release behavior in artificial intestinal juice were studied.

2. Experimental

2.1. Materials and equipments

Chitosan (degree of deacetylation >92.6%) and fenoprofen calcium (degree of deacetylation >98%) were purchased from Guangxi Beihai Maogen Chitin Factory (Guangxi, China) and Jiangsu Nantong Chemical Co., Ltd., (Jiangsu, China), respectively. Rosin-(2-acryloyloxy)ethyl ester (RAEE) was synthesized as follows: firstly, *p*-toluenesulfonic acid-(2-acryloyloxy)ethyl ester (TAEE) was synthesized by *o*-acylation reaction of *p*-toluenesulfonyl chloride (TsCl) with 2-hydroxyethyl acrylate (HEA) using NaOH as catalyst at 0 °C for 2 h, then, RAEE was obtained by nucleophilic substitution reaction of TAEE with sodium rosinate at 60 °C for 3 h. Methanol (Chengdu Kelong chemical reagent Co., China, ⩾99.5%), ethyl acetate (Chengdu Kelong chemical reagent Co., China, ⩾99.5%), and tris(hydroxymethyl)aminomethane (Shanghai chemical reagent Co., China, ⩾99.5%) were used as received. A Xianghu microwave-induced synthesis/extraction apparatus (XH-100B), produced by Beijing Xianghu science and technology development Co., Ltd., China, was employed in the graft copolymerization.

2.2. Graft copolymerization

The Cts-g-PRAEE copolymer was prepared using rosin-(2-acryloyloxy)ethyl ester (RAEE) as a monomer and potassium persulfate as an initiator under microwave irradiation as shown in Fig. 1 (Prashanth & Tharanathan, 2003). The synthetic procedures are as follows: in a 100 mL one-neck flask, 0.5 g of chitosan were dissolved in 50 ml of 1%(wt) acetic acid solution. With stirring, 4.0 g of RAEE was added, and the well-proportioned emulsible solution was obtained. Under nitrogen atmosphere, the solution was pre-radiated with ^{60}Co γ-ray for certain time (the total radiation dosage 300 Gy), and then transferred to a three-neck flask and 0.2 g potassium persulfate (KPS) was added. Under nitrogen atmosphere, the three-neck flask was placed in a microwave reactor, setting microwave reaction time (2 h), temperature (60 °C), power (70 W). After reaction, with stirring, 100 ml methanol and 80 ml ethyl acetate were added gradually to the reaction mixture, respectively, and precipitate was isolated. Then, the precipitate (Cts-g-PRAEE copolymer) was filtered, washed several times with ethyl acetate and 1% acetic acid solution, and dehydrated with ethanol, and dried under vacuum at 70 °C. The grafting percentage (G%) of PRAEE on Cts was calculated by $(W_g - W_0)/W_0 \times 100$, where W_g is the weight in grams of the grafted Cts and W_0 is the weight of native Cts.

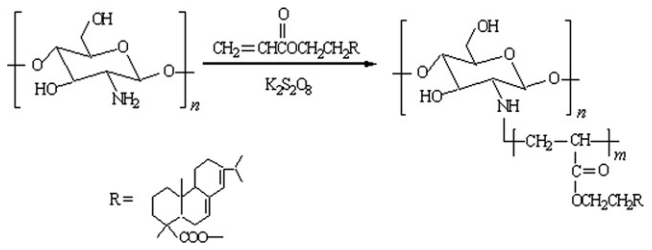

Fig. 1. Synthetic scheme of Cts-g-PRAEE copolymer.

2.3. Characterization

FT-IR spectra of chitosan and its graft copolymer were recorded in the range of wave numbers 4000–500 cm^{-1} using Nicolet Nexus 470 spectrometer (Nicolet Co., Ltd., USA). The X-ray diffraction (XRD) patterns and Scanning electron micrograph (SEM) images of chitosan and its graft copolymer were obtained by Rigaku D/max2500 V (Rigaku corporation, Japan) and JEM1200-EX/S (JEOL Ltd., Japan), respectively. The degradation process and thermal stability of chitosan and its graft copolymer were investigated using a NETZSCH STA 409PC thermogravimetric analyzer (TGA, NETZSCH Instrument Co., Ltd., Germany). The TGA measurements were carried out under an argon atmosphere at a heating rate of 10 °C/min from room temperature to 800 °C.

2.4. Drug release of Cts and Cts-g-PRAEE

The artificial intestinal juice (Tris–HCl buffer solution, pH 7.2) was prepared as follows: in a close glass vessel, 500 ml of 0.1 M tris(hydroxymethyl) aminomethane solution and 447 ml of 0.1 M hydrochloric acid solution were added, and stirred for equilibration.

Preparation of drug troche: 0.3000 g of dried Cts or Cts-g-PRAEE powder sample and 0.0200 g of fenoprofen calcium were mixed evenly, and pressed to drug troche and weighted. Then, the contents of fenoprofen calcium were calculated.

The standard curve of fenoprofen calcium was drawn as follows: 0.500 g of fenoprofen calcium was weighed accurately, and put in a beaker in which there was 500 ml of Tris–HCl buffer solution. Then, the beaker was put into a shaking bed (at 37 ± 1 °C, 180 rpm) for 24 h to make fenoprofen calcium dissolve completely. The solution was transferred to 1000 ml volumetric flask, to obtain the 0.05 g/L solution, and 100 ml of 0.000, 0.005, 0.010, 0.015, 0.020, 0.025, 0.030, 0.035, 0.040, and 0.050 M feno-

profen calcium solution was prepared, respectively. Their absorbency was determined by UV spectrophotometry at 272 nm, respectively, and the standard curve of fenoprofen calcium was drawn out by the absorbency (A) evolution with concentration (C), that is, $A = 6.319C + 0.0003$ ($R^2 = 0.9955$).

The rate of release of fenoprofen calcium for two drug troche of Cts and Cts-g-PRAEE copolymer was determined as follows: the drug troche and 10 ml of distilled water were added to dialysis tubing (molecular weight cut off 7000), and the dialysis tubing was immersed in 490 ml of Tris–HCl buffer solution. Then, the solution put into a shaking bed (at 37 ± 1 °C, 180 rpm) for 10 h, and 3 ml of the solution was sampled at every one hour. Subsequently, the amount of fenoprofen calcium released from the drug troche was evaluated by means of UV spectrophotometry at 272 nm and the standard curve of fenoprofen calcium, and the rate of release was calculated.

3. Results and discussion

3.1. Preparation and characterization of Cts-g-PRAEE copolymer

The Cts-g-PRAEE copolymer was prepared using rosin-(2-acryloyloxy)ethyl ester (RAEE) as a monomer and potassium persulfate as an initiator as shown in Fig. 1. Fig. 2 shows the IR spectra of Cts and Cts-g-PRAEE copolymer. Cts (Fig. 2a) spectrum shows —OH peak, —NH_2 and —NH— peak in the amide groups at about 3424 cm^{-1}; C=O, —NH—, and —C—N— peak in the amide groups at 1652, 1597, and 1322 cm^{-1}, respectively; —C—O— in the ether groups at 1154 and 1089 cm^{-1}. In the spectrum (Fig. 2b) of Cts-g-PRAEE copolymer, in addition to the characteristic peaks of Cts, some new peaks appeared. The peaks at 1728, 1105, and 1248 cm^{-1} attribute to C=O, —C—O—, and —O—C— peak in the ester groups from grafted PRAEE, respectively; the CH_2 peak from grafted PRAEE appears at 1456 cm^{-1}. Also, C=O and —NH— peak in the amide groups shift toward lower wavenumbers, that is, from 1652 and 1597 cm^{-1} to 1631 and 1525 cm^{-1}, respectively. From the IR spectra, it is confirmed that the Cts-g-PRAEE copolymer was successfully synthesized. According to the $G\% = (W_g - W_0)/W_0 \times 100$, the grafting percentage of PRAEE on Cts was 72.3%.

The change of Cts structure before and after graft copolymerization was investigated by means of the powder X-ray diffraction and SEM. Fig. 3 shows the X-ray diffraction patterns of Cts and Cts-g-PRAEE copolymer, and Cts sample (Fig. 3a) shows distinct crystalline peaks at around 10° and 20° compared to Cts-g-PRAEE copolymer (Fig. 3b). This is because plenty of hydroxy and amino groups exist in the Cts structure, which can form stronger intermolecular and intramolecular hydrogen bonds, and the structure of Cts molecules has certain regularity, so that Cts molecules form crystalline regions easily. However, as regards Cts-g-PRAEE copolymer, the peak at 10° disappeared and the peak at 20° weakened obviously. The reason may attribute to the destruction of the intermolecular hydrogen bonds and the crystalline regions of Cts, which indicate that the PRAEE side chains were introduced into Cts main chains.

The SEM images of Cts and Cts-g-PRAEE copolymer are shown in Fig. 4. The SEM image of Cts (Fig. 4, left) shows larger clustered structure, because there are stronger interactions between Cts molecules. After graft copolymerization of Cts, in the surface of Cts-g-PRAEE copolymer (Fig. 4, right), fluffy morphology and globular shapes with some irregularities are clearly observed. It may be attributed to the polar difference between Cts and PRAEE and the destruction of the intermolecular hydrogen bonds and the crystalline regions of Cts, which indicate intuitively that the PRAEE side chains were introduced into Cts main chains.

The degradation process and thermal stability of Cts and Cts-g-PRAEE copolymer were evaluated through thermo-gravimetric analysis (TGA) experiments, and the results are shown in Fig. 5. It can be seen in Fig. 5 that

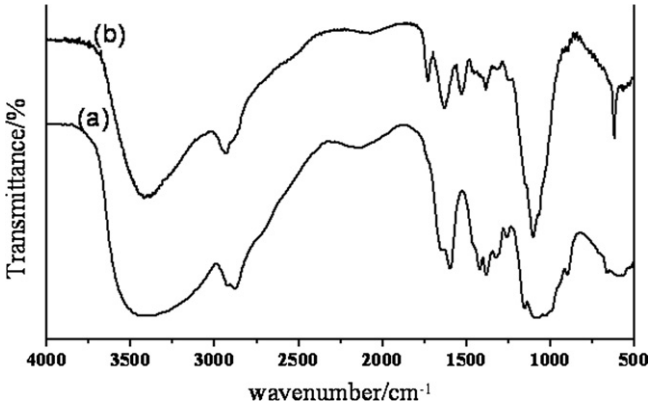

Fig. 2. FT-IR spectra of Cts (a) and Cts-g-PRAEE (b).

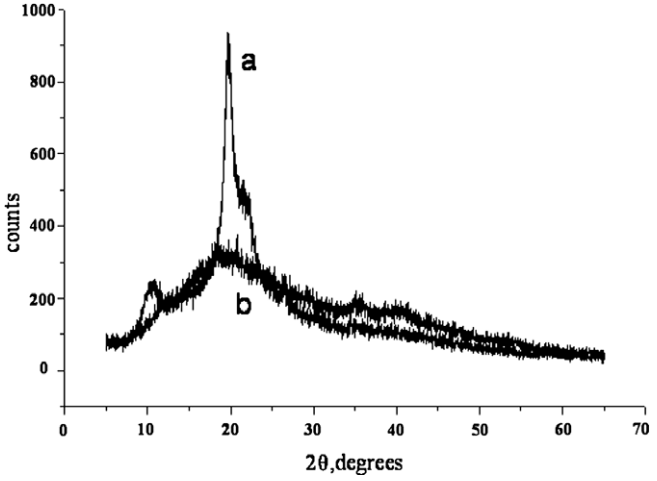

Fig. 3. X-ray diffraction patterns of Cts (a) and Cts-g-PRAEE (b).

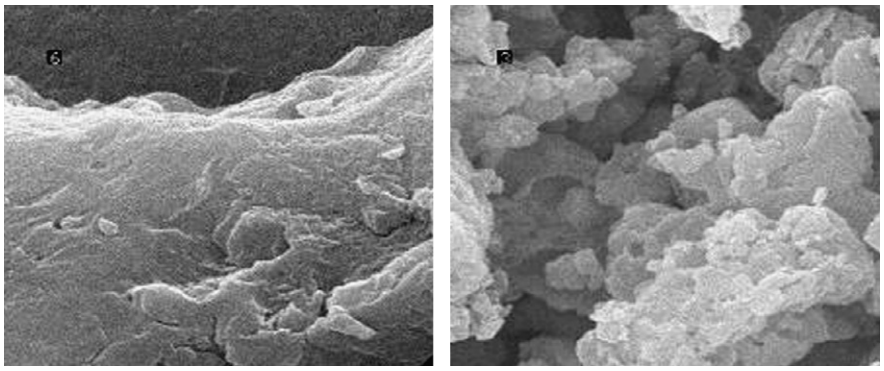

Fig. 4. SEM images of Cts (left) and Cts-g-RAEE (right).

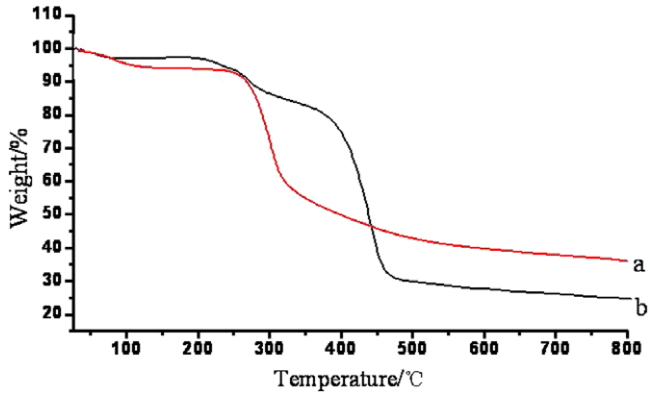

Fig. 5. TGA thermograms of Cts (a) and Cts-g-PRAEE copolymer (b).

three consecutive weight loss steps were observed in the Cts and Cts-g-PRAEE copolymer. For the TGA curve of the Cts (Fig. 5a), the first stage showed a loss of absorbed and bounded water of 6.3wt% at 55–191 °C, indicating its hygroscopic nature; the second weight loss occurred in the range 230 to 327 °C, and weight loss was about 45.7%, which corresponded to the scission of the ether linkage in the Cts backbone; the third stage showed a weight loss of 35.0wt% in range of 327–703 °C, which is responsible for the thermal decomposition of glucosamine residue. However, the Cts-g-PRAEE copolymer (Fig. 5b) has different course of the thermal degradation compared to Cts. The first stage shows that a loss of absorbed water started at 30 °C and continues up to 153 °C, and weight loss was about 3.0wt%; the second stage was from 196 to 328 °C, and weight loss was about 12.5wt%, which corresponded to the scission of the ether linkage in the Cts backbone. The onset temperature of both the dehydration and the thermal degradation was lower than the Cts, that is, the thermal stability of Cts decreased slightly after graft copolymerization. This is because more hydroxy and amino groups exist in the Cts structure and crystalline regions form easily compared to Cts-g-PRAEE copolymer. The third stage from 400 to 470 °C, showed a weight loss of 55.5wt%, which is contributed to the thermal decomposition of PRAEE side chains.

3.2. Drug release behavior

The rate of release of fenoprofen calcium for two drug troche of Cts and Cts-g-PRAEE copolymer was determined by dialysis method against the artificial intestinal juice, and the results are shown in Fig. 6. For Cts sample, the release of fenoprofen calcium increased rapidly up to 59% within an hour, which may be attributable to the solubility of fenoprofen calcium in water. Then, the rate of release increased slowly until 6 h, and the release kept in about 65%. However, the rate of release of Cts-g-PRAEE copolymer increased gradually from 10% to 55% in the determination of time, which indicates that the controlled release of fenoprofen calcium from Cts-g-PRAEE copolymer is better than that from Cts in artificial intestinal juice. The reason may be related to the fact that the PRAEE side chain surrounded fenoprofen calcium and played an important part in the controlled release. In order to interpret these phenomena, the FT-IR spectrum of the drug troche of Cts-g-PRAEE copolymer was determined and shown in Fig. 7. Compared with the FT-IR spectrum of Cts-g-PRAEE copolymer, the peak of the carbonyl groups in the drug troche of Cts-g-PRAEE copolymer slightly shifts toward lower wavenumbers, which indicates that very slight coordination between the carbonyl groups and calcium ions maybe exist, that is, calcium ions act as a

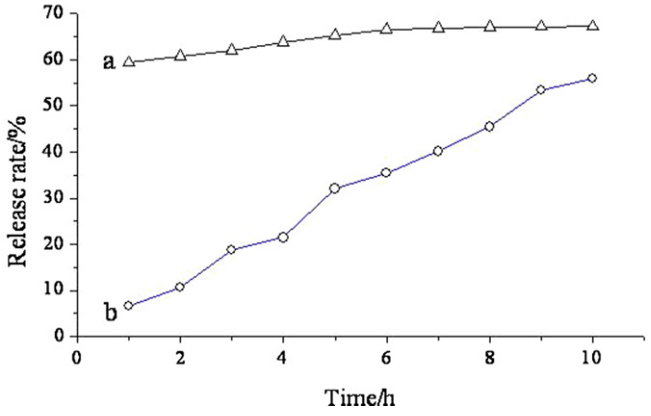

Fig. 6. The rate of release of drug troche of Cts (a) and Cts-g-PRAEE (b) in artificial intestinal juice.

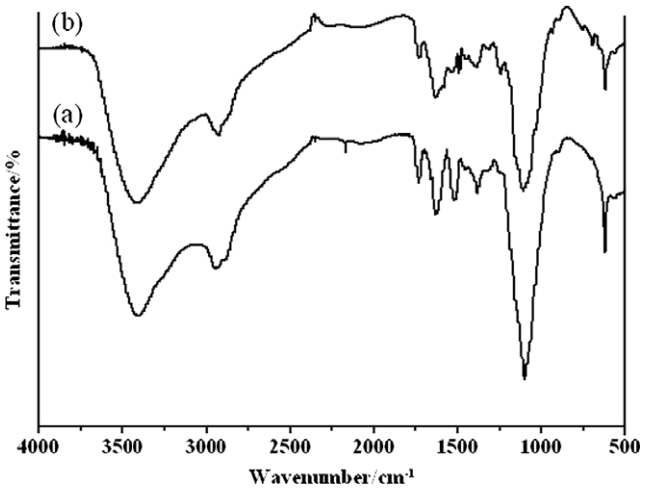

Fig. 7. FT-IR spectra of Cts-g-PRAEE (a) and the drug troche of Cts-g-PRAEE (b).

bridge between the carbonyl groups in Cts-g-PRAEE copolymer and fenoprofen calcium (Socrates, 1994). On the other hand, there are hydrophobic bonds between the hydrophobic groups in PRAEE and fenoprofen calcium. Above reasons all lead to the controlled release of fenoprofen calcium from Cts-g-PRAEE copolymer.

4. Conclusions

The Cts-g-PRAEE copolymer was prepared by a graft copolymerization of rosin-(2-acryloyloxy)ethyl ester (RAEE) onto chitosan (Cts) under microwave irradiation and using potassium persulfate as initiator. Cts and Cts-g-PRAEE copolymer were characterized by means of FT-IR, XRD, SEM, and TG, and it is confirmed that the RAEE monomer was grafted onto Cts chain and the grafting percentage of PRAEE on Cts was 72.3%. Furthermore, the rate of release of fenoprofen calcium for Cts and Cts-g-PRAEE copolymer was determined by dialysis method against the artificial intestinal juice, and the results showed that the controlled release of fenoprofen calcium from Cts-g-PRAEE copolymer is better than that from Cts.

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References

Caner, H., Yilmaz, E., & Yilmaz, O. (2007). Synthesis, characterization and antibacterial activity of poly(*N*-vinylimidazole) grafted chitosan. *Carbohydrate Polymers, 69*(2), 318–325.

Casimiro, M. H., Botelho, M. L., Leal, J. P., & Gil, M. H. (2005). Study on chemical, UV and gamma radiation-induced grafting of 2-hydroxyethyl methacrylate onto chitosan. *Radiation Physics and Chemistry, 72*(6), 731–735.

Don, T. M., King, C. F., & Chiu, W. Y. (2002). Synthesis and properties of chitosan-modified poly(vinyl acetate). *Journal of Applied Polymer Science, 86*(12), 3057–3063.

Feng, H., & Dong, C. M. (2006). Preparation, characterization, and self-assembled properties of biodegradable chitosan-poly(L-lactide) hybrid amphiphiles. *Biomacromolecules, 7*(11), 3069–3075.

Goosen, M. F. A. (Ed.). (1997). *Applications of chitin and chitosan*. Lancaster, PA: Technomic Publishing.

Ge, H. C., Pang, W., & Luo, D. K. (2006). Graft copolymerization of chitosan with acrylic acid under microwave irradiation and its water absorbency. *Carbohydrate Polymers, 66*(3), 372–378.

Jayakumar, R., Prabaharan, M., Reis, R. L., & Mano, J. F. (2005). Graft copolymerized chitosan—present status and applications. *Carbohydrate Polymers, 62*, 142–158.

El-Tahlawy, Khaled F., El-Rafie, Safaa M., & Aly, S. A. (2006). Preparation and application of chitosan/poly(methacrylic acid) graft copolymer. *Carbohydrate Polymers, 66*(2), 176–183.

Kumbar, S. G., Soppimath, K. S., & Aminabhavi, T. M. (2003). Synthesis and characterization of polyacrylamide-grafted chitosan hydrogel microspheres for the controlled release of indomethacin. *Journal of Applied Polymer Science, 87*(9), 1525–1536.

Li, Y., Liu, L., Shen, X., & Fang, Y. (2005). Preparation of chitosan(butyl acryate) hybrid materials by radiation- induced graft copolymerization based on phthaloylchitosan. *Radiation Physics and Chemistry., 74*(5), 297–301.

Liu, L., Li, Y., Fang, Y., & Chen, L. (2005). Microwave-assisted graft copolymerization of e-caprolactone onto chitosan via the phthaloyl protection method. *Carbohydrate Polymers, 60*(3), 351–356.

Majeti, N. V., & Kumar, R. (2000). A review of chitin and chitosan applications. *Reactive and Functional Polymers, 46*, 1–27.

Najjar, A. M. K., Yunus, W. M. Z. W., Ahmad, M. B., & Rahman, M. Z. A. (2000). Preparation and characterization of poly(2-acrylamido-2-methylpropane-sulfonic acid) grafted chitosan using potassium persulfate as redox initiator. *Journal of Applied Polymer Science, 77*(10), 2314–2318.

Pourjavadi, A., Mahdavinia, G. R., Zohuriaan-Mehr, M. J., & Omidian, H. (2003). Modified chitosan. I. Optimized cerium ammonium nitrate-induced synthesis of chitosan-graft-polyacrylonitrile. *Journal of Applied Polymer Science, 88*, 2048–2054.

Prashanth, K. V. H., & Tharanathan, R. N. (2003). Studies on graft copolymerization of chitosan with synthetic monomers. *Carbohydrate Polymers, 54*(3), 343–351.

Singh, V., Tripathi, D. N., Tiwari, A., & Sanghi, R. (2006). Microwave synthesized chitosan- graft-poly(methyl methacrylate): An efficient Zn_2 C ion binder. *Carbohydrate Polymers, 65*(1), 35–41.

Socrates, G. (1994). *Infrared characteristic group frequencies*. John Wiley & Sons Ltd..

Sun, T., Xu, P. X., Liu, Q., Xue, J., & Xie, W. (2003). Graft copolymerization of methacrylic acid onto carboxymethyl chitosan. *European Polymer Journal, 39*, 189–192.

Yazdani-Pedram, M., Retuert, J., & Quijada, R. (2000). Hydrogels based on modified chitosan. 1. Synthesis and swelling behavior of poly(acrylic acid) grafted chitosan. *Macromolecular Chemistry and Physics, 201*, 923–930.

Yilmaz, E., Adali, T., Yilmaz, O., & Bengisu, M. (2007). Grafting of poly(triethylene glycol dimethacrylate) onto chitosan by ceric ion initiation. *Reactive and Functional Polymers, 67*(1), 10–18.

Zang, G. D., & Feng, X. D. (1998). Mechanism of graft copolymerization of methyl methacrylate onto model compound for chitosan initiated by Ce^{4+} ion. *Acta Polymerica Sinica, 4*, 505–508.