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Synthesis of chitosan–polycaprolactone blend for control delivery of ofloxacin drug

Sarmila Sahoo [a], Abhisek Sasmal [a], Rajashree Nanda [a], A.R. Phani [b], P.L. Nayak [a,*]

[a] P.L.Nayak Research Foundation, Cuttack 753006, Orissa State, India
[b] Nano-Research for Advanced Materials & Technologies, Bangalore 560040, Karnataka State, India

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ABSTRACT

In the present research work chitosan has been blended with different amounts of polycaprolactone (PCL) (80:20, 75:25, 60:40 and 50:50) for using them for control delivery of ofloxacin. The blends were characterized by Fourier transmission infra red spectroscopy (FTIR), UV–visible spectroscopy (UV), scanning electron microscopy (SEM), X-ray diffraction (XRD) analysis. From the FTIR spectra the various groups present in chitosan and PCL blend were monitored. The homogeneity, morphology and crystallinity of the blends were ascertained from SEM and XRD data, respectively. The swelling studies have been measured at different drug loading. The kinetics of the drug delivery system has been systematically studied. Drug release kinetics was analyzed by plotting the cumulative release data vs. time by fitting to an exponential equation which indicated the non-Fickian type of kinetics. The drug release was investigated at different pH medium and it was found that the drug release depends upon the pH medium as well as the nature of matrix.

1. Introduction

During the past two decades significant advances have been made in the development of biodegradable polymeric materials for biomedical applications. Degradable polymeric biomaterials are preferred candidates for developing therapeutic devices such as temporary prostheses, three-dimensional porous structures as scaffolds for tissue engineering and as controlled/sustained release drug delivery vehicles (Peppas & Langer, 1994). Each of these applications demands materials with specific physical, chemical, biological, biomechanical and degradation properties to provide efficient therapy. Consequently, a wide range of natural or synthetic polymers capable of undergoing degradation by hydrolytic or enzymatic route are being investigated for biomedical applications (Goodwin, Braden, Downes, & Marshall, 1998; Pitt, Gratzl, Jeffcoat, Zweidinger, & Schindler, 1979; Pokharkar & Sivaram, 1996).

Carrier-mediated drug delivery has emerged as a powerful methodology for the treatment of various pathologies. The therapeutic index of traditional and novel drugs is enhanced via the increase of specificity due to targeting of drugs to a particular tissue, cell or intracellular compartment, the control over release kinetics, the protection of the active agent or a combination of the above. Polymer composites were proposed as drug carriers over 30 years ago and have received growing attention since, mainly due to their stability, enhanced loading capabilities and control over physicochemical properties. In addition to systemic administration, localized drug release may be achieved using macroscopic drug depots close to the target site. Among various systems considered for this approach, *in situ*-forming biomaterials in response to environmental stimuli have gained considerable attention, due to the non-invasive character, reduction of side effects associated with systemic administration and better control over biodistribution. In recent years biodegradable polymers have attracted attention of researchers to be used as carriers for drug delivery systems (Elbert & Hubbell, 2001; Kelner & Schacht, 2005; Lambert, Fattal, & Couvreur, 2001; Lien & Lowman, 2003; Mann, Andrea, Annabel, Rachael, & Jennifer, 2001; McAllister et al., 2002; Nanda, Rao, Kar & Nayak, 2007; Nanda, Rao, & Nayak, 2007a, 2007b; Pathak, Sawhney, & Hubbell, 1992; Swain, Rao, & Nayak, 2004, 2005).

Chitosan, a natural linear biopolyaminosaccharide is generally obtained by the alkaline deacetylation of chitin, which is the second abundant polysaccharide next to cellulose (Kas, 1997; Roberts, 1992). Chitin is the principal component of protective cuticles of crustaceans such as crabs, shrimps, prawns, lobsters and cell walls of some fungi such as Aspergillus and Mucor. Chitin is a straight homopolymer composed of β(1,4)-linked *N*-acetyl-glucosamine units while chitosan comprises of copolymers of glucosamine and *N*-acetyl-glucosamine (Fukuda, 1980; Kato, Onishi, & Machida, 2003; Singla & Chawla, 2001). Chitosan has one primary amino and two free hydroxyl groups for each C6 building unit. Due to the easy availability of free amino groups in chitosan, it carries a positive charge and thus in turn reacts with many negatively charged surfaces/polymers and also undergoes chelation with metal ions (Onsoyen & Skaugrud, 1990) like cobalt (Chandy & Sharma, 1990). Chitosan is a weak base and is insoluble in water and

* Corresponding author. Tel./fax: +91 671 2441635.
E-mail address: plnayak@rediffmail.com (P.L. Nayak).

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organic solvents, however, it is soluble in dilute aqueous acidic solution (pH <6.5), which can convert the glucosamine units into a soluble form $R–NH_3^+$ (Demarger-Andre & Domard, 1994). It gets precipitated in alkaline solution or with polyanions and forms gel at lower pH. It also acts as flocculant for the treatment of waste water (Ha et al., 1997).

PCL is one of the biodegradable polyesters which have attracted attention to be used in the controlled drug delivery due to the lack of toxicity and low cost when compared to other biodegradable polyesters. But the application of PCL for drug delivery has a drawback of slow degradation rate in vivo due to its high crystallinity and hydrophobicity (Allen, Han, Yu, Maysiger, & Eisenberg, 2000). It has been reported that the biodegradability of PCL can be enhanced by copolymerizing (Cai, Bei, & Wang, 2000; Paul & Newman, 1978) or blending with a variety of other polymers (Hubbell & Cooper, 1977; Zhu, Xiangzhon, & Shilin, 1990). Enhancement of hydrophilicity of PCL has been achieved by the chemical addition of a hydrophilic moiety, such as poly(ethylene oxide) (Cohn & Younes, 1988; Huatan, Collett, Attwood, & Booth, 1995). Manipulation of the composition can be used to modify water permeability and the degree of hydration of a copolymer matrix. However, the disadvantage is a reduction of the mechanical strength, as a result of decrease in the crystallinity of the material. Polymer blending represents an alternative means of tailoring hydrophilicity of the matrix without significantly affecting its mechanical integrity (Ratajska & Boryniec, 1998).

Blending two polymers is an approach to develop new biomaterials exhibiting combinations of properties that could not be obtained by individual polymers (Santin et al., 1996). Blends made of synthetic and natural polymers can imbibe the wide range of physicochemical properties and processing techniques of synthetic polymers as well as the biocompatibility and biological interactions of natural polymers. For example, the poor cell adhesion normally associated with poly(2 hydroxyethylmethacrylate) was mitigated by blending with gelatin (Khor & Lim, 2003). This study explored the blending of chitosan, a naturally derived polysaccharide, with a synthetic polymer PCL. The hypothesis is that blending chitosan and PCL will give a superior biomaterial where the limitations of chitosan are complemented by PCL. Chitosan has generated enormous interest due to its various advantages such as (i) low cost, (ii) easy availability (deacetylated from chitin, the second most abundant natural polymer), (iii) positive charge (allows it to interact with negatively charged glycosaminoglycans present in the extracellular matrix), (iv) biocompatibility and (v) antimicrobial activity (Susan, Maryadele, Ann, & Patricia, 1991). Hence, this blend can be a better biodegradable and biocompatible material to be used in control drug delivery systems.

Ofloxacin, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido [1,2,3-de]-1,4-benzoxazine-6-carboxalic acid (Muzzarelli, 1977) is a second generation fluorinated quinolone, a pyridone carboxylic acid derivative which exert a broad-spectrum having antimicrobial effect in a variety of systemic infections (Bassaris, Akalin, & Calangu, 1995; Drlica, 1984; Park, Chung, Lee, & Bark, 2000). It blocks bacterial DNA synthesis by inhibiting DNA gyrase and topoisomerase IV. Inhibition of DNA gyrase prevents the relaxation of positively super coiled DNA that is required for normal transcription and replication (Gellert, 1981). Ofloxacin is commonly used in clinics but its bioavailability and pharmacokinetic profile needs to be described in local population and environments.

1.1. UV spectrum

Fig. 1 shows the UV spectra of ofloxacin in aqueous acid (225, 226, 256 and 326 nm) and aqueous base (288 and 332 nm). Ofloxacin in aqueous solution has two peaks, a strong peak at 287 nm and a weak peak at 332 nm. The observed strong peak corresponds to the chromophore involving $N-1$ position to the carboxylic chromophore involving the nitrogen of the piperazinyl group to the carbonyl group while the weak absorption peak corresponds to the chromophore involving the nitrogen of the piperazinyl group to the carbonyl group.

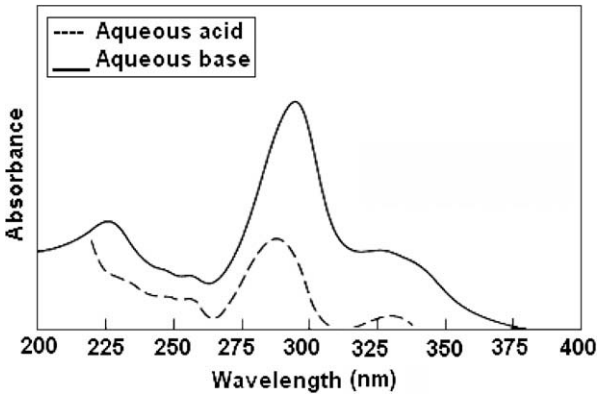

Fig. 1. UV spectrum of ofloxacin.

A survey of the literature reveals that chitosan–PCL blend, both of which are biodegradable, and biocompatible, has not been used for controlled delivery systems. In this communication we plan to report the preparation of chitosan–PCL blend by varying the proportion of PCL. The blends have been characterized using FTIR, SEM and XRD. The swelling kinetics as well as the drug delivery systems using ofloxacin has also been studied at different pH and drug loading.

2. Experimental

2.1. Materials

Chitosan (CS) (degree of deacetylation = 95% determined by ^1H NMR) was purchased from India Sea Foods, Kerala. Polycaprolactone (PCL) was purchased from Solvay Interox, USA. Ofloxacin was received as gift sample from RANBAXY, India. Acetic acid, NaH_2PO_4, NaOH and other chemicals were used as analytical grade and purchased from Sigma–Aldrich Company.

2.2. Synthesis of chitosan/PCL blends

Chitosan was dissolved in 0.5 M acetic acid and PCL in glacial acetic acid. To prepare sterile 1% (w/v) chitosan solutions, chitosan suspension in water was first autoclaved (at 121 °C in a wet cycle for 20 min) and then dissolved by adding acetic acid equivalent to 0.5 M in a sterile laminar flow hood. Three milliliters of 1% chitosan solutions were slowly added to 10 ml of 0.1%, 0.2% and 0.3% PCL solutions to obtain blends of, 70%, 60% and 50% chitosan, respectively. In order to get chitosan/PCL (80:20) ratio, 4 ml of 1% chitosan solution was added to 10 ml of 0.1% PCL solution. The mixtures were stirred at room temperature for 2 min to obtain homogeneous solutions. In all the blends, the solvent composition was kept constant. The blends were obtained after the evaporation of the solvent at room temperature.

2.3. Drug loading

Required amount of chitosan–PCL (80:20) was taken in 5 ml of acetic acid. The mixture was continuously stirred with a mechanical stirrer. Ofloxacin of different loadings, i.e., 10, 20, 30, 40 and 50 wt% were then added to the above mixture and stirred for 1 h

and then the composites were kept at room temperature for drying.

2.4. Dissolution experiments

Dissolution experiments were performed at 37 °C using the dissolution tester (Disso test, Lab India, Mumbai, India) equipped with six paddles at a paddle speed of 100 rpm. About 900 ml of phosphate buffer solution (pH 3.4 and 7.4) was used as the dissolution media to stimulate gastrointestinal tract (GIT) conditions. A 5-ml aliquot was used each time for analyzing the Ofloxacin content at a fixed time interval. The dissolution media was replenished with a fresh stock solution. The amount of ofloxacin released was analyzed using a UV spectrophotometer (Systronics, India) at the λ_{max} value of 287 nm.

3. Characterization

3.1. Fourier transmission infra red spectroscopy (FTIR)

The FTIR spectrum of the chitosan–PCL blends was obtained using a BIORAD-FTS-7PC type FTIR spectrophotometer.

3.2. X-ray diffraction (XRD)

The change in gallery height of the blend was investigated by WAXD experiments, which were carried out using a X-ray diffractometer (BEDE D-3 system) with Cu Kα radiation at a generator voltage of 40 kV and a generator current of 100 mA. Samples were scanned from $2\theta = 1–10°$ at a scanning rate of 2 °/min.

3.3. Scanning electron microscopy (SEM)

The blending of the chitosan–PCL composites containing different concentrations were characterized using SEM (440, Leica Cambridge Ltd, Cambridge, UK). The powdered specimens were placed on the Cambridge standard aluminium specimen mounts (pin type) with double-sided adhesive electrically conductive carbon tape (SPI Supplies, West Chester, PA). The specimen mounts were then coated with 60% Gold and 40% Palladium for 30 s with 45 mA current in a sputter coater (Desk II, Denton Vacuum, Moorestown, NJ). The coated specimens were then observed on the SEM using an accelerating voltage of 20 kV at a tilt angle of 30° to observe the microstructure of the chitosan–PCL composite blends.

3.4. Swelling studies

Water absorption of the polymer–drug conjugates was measured following ASTM D 570-81. The samples were preconditioned at 50 °C for 24 h and then cooled in a desiccator before being weighed. The preconditioned samples were submerged in distilled water at 25 °C for 24 h. The samples were removed and dried with a paper towel before weighing. Water absorption was calculated as a percentage of initial weight. The soluble material loss was checked by weighting the specimens after drying them in an oven at 50 °C for another 24 h. The total water absorption for 24 h was calculated including the soluble material loss.

$$\% \text{ Swelling} = \frac{W_1 - W_2}{W_2} \times 100$$

where W_1, weight of swollen composite after 24 h, W_2, weight of dry composite.

4. Results and discussion

4.1. Fourier transmission infra red spectroscopy (FTIR)

Fig. 2 shows the FTIR spectra of chitosan (CS), polycaprolactone (PCL) and chitosan–polycaprolactone (CS–PCL) blend. Chitosan is an amino glucose characterized by a small proportion of amide groups via an amide linkage with acetic acid. In the IR spectrum, powder chitosan exhibited a broad peak at 3431 cm^{-1}, which is assigned to the N–H and hydrogen bonded O–H stretch vibrational frequencies, while a sharp (shoulder) peak at 3610 cm^{-1} is that of free O–H bond stretch of glucopyranose units [42]. Further, in the C–H stretch region of FTIR spectrum, the higher intensity peak at 2923 cm^{-1} is assigned to the asymmetric and the lower intensity peak at 2857 cm^{-1} is assigned to the symmetric modes of CH_2. In addition, the characteristic band due to CH_2 scissoring, which usually occurs at 1465 cm^{-1} was also present in the sample. Since the grade of chitosan used in the present study was ⩾90% deacetylated, an amide bond peak was present in the spectra and the C═O stretch of amide bond was observed at 1661 cm^{-1}. The peaks at 1550 and 1599 cm^{-1} were assigned to strong N–H bending vibrations of secondary amide, which usually occur in the range of 1640–1550 cm^{-1} as strong band.

The IR spectra shows the characteristic peaks of both polymers, i.e., chitosan and PCL (3300–3700, 1725, 852–1480 and 720 cm^{-1}) (Nishimura, Kohgo, Kurita, & Kuzuhara, 1991). Furthermore, the IR

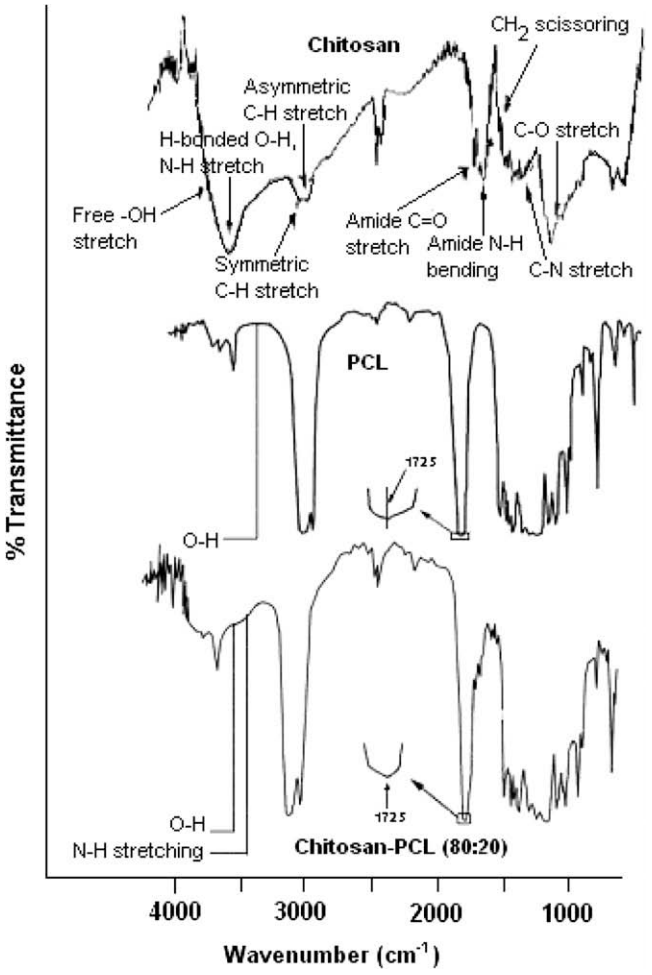

Fig. 2. FTIR spectra of chitosan (CS), polycaprolactone (PCL) and chitosan–polycaprolactone (CS–PCL) blend.

spectra of chitosan/PCL (10 wt%) produced peaks between 3200 and 3700 cm^{-1}, which were much more intense than the stretching absorbance at 3000–3600 cm^{-1} observed in the absence of chitosan. Additionally, the spectrum in Fig. 3 identifies differences in absorbance intensity at 1650 cm^{-1} (primary amide, secondary amide) and 1590 cm^{-1} (non-acylated primary amide).

4.2. X-ray diffraction analysis

The X-ray diffraction patterns of chitosan and chitosan–PCL composites are illustrated in Fig. 3. It is known that the PCL homopolymer is easy to crystallize (Detchprohm, Aoi, & Okada, 2001; Senda, He, & Inoue, 2001). Compared with the original chitosan, chitosan–PCL (80:20) showed a weaker and broader peak in the 2θ = 15–25° region, which demonstrated that the conjugation of PCL with chitosan suppressed the crystallization of both chitosan and PCL to some extent. It is suggested that chitosan and PCL chains are mixed well at a molecular level. However, when the PCL content increased up to 50% in the copolymer, a new sharp signal appeared at 2θ = 31°. It is probably due to the phase coarsening of PCL branches influenced by the stiff chitosan chain which has also been corroborated from the SEM data.

4.3. Scanning electron microscopy (SEM)

SEM has been employed for the observation of the surface morphology of the different chitosan/PCL blend composites. The microstructure obtained by SEM for the chitosan/PCL composites prepared by mixing, showed that PCL particles (with irregular forms) are relatively well dispersed in the chitosan matrix. Fig. 4 shows that chitosan/PCL is homogenous at low concentration 20% PCL, 25% PCL. As the concentration of the PCL increases from 40% to 50% the homogeneity of the surfaces decreases. In particular, 20% PCL and 25% PCL were superior to individual polymers (Yang, Zhaang, & Feng, 1999).

4.4. Swelling studies

The swelling behavior of any polymer network depends upon the nature of the polymer, polymer solvent compatibility and degree of cross-linking. However, in the case of ionic networks, swelling behavior depends upon mass transfer limitations, ion exchange and ionic interaction (Frank & Lauterbur, 1993; Korsmeyer & Peppas, 1981).

Fig. 5 represents the percentage of swelling (in terms of bar representation) for the chitosan/PCL blend with different drug loadings (pH 7.4) at 37 °C. This indicates that the percentage swelling increases with increase of drug loading in the chitosan/PCL composite.

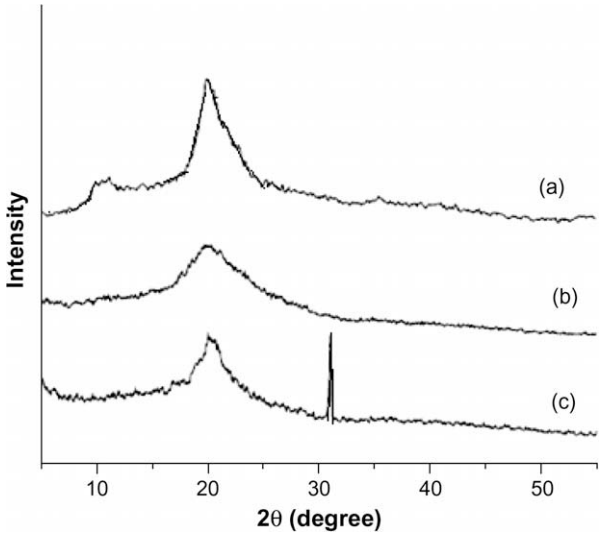

Fig. 3. X-ray diffraction patterns of (a) chitosan, (b) chitosan–PCL (80:20) and (c) chitosan–PCL (50:50).

4.5. In-vitro drug release

The drug delivery system was developed for the purpose of bringing, up taking, retaining, releasing, activating, localizing and targeting the drugs at the right time period, dose and place (Langer, 1990, 1998; Rathbone, Witchey-Lakshmanan, & Ciftci, 1999). The biodegradable polymer can contribute largely to this technology by adding its own characters to the drugs. In this connection, some biodegradable polymers such as PLA, PCL, etc., are commonly used as these polymers can be prepared in the moderate conditions, has a similar stiffness of the body and has an appropriate biodegradability and low crystallinity enough to be mixed well with many kinds of drug (Lewis, Chasin, & Langer, 1990). There are some formulations for the drug delivery systems, for example, films, gels, porous matrices, microcapsules, micro spheres, nanoparticles, polymeric micelles and polymer linked drugs (Heller, 1987; Li & Vert, 1999; Li, Vert, Scott, & Gilead, 1995).

4.5.1. Effect of pH

In order to investigate the effect of pH on the swelling of composite chitosan/PCL (80:20), we have measured the % cumulative release in both pH 3.4 and 7.4 media. Cumulative release data presented in Fig. 6 indicate that by increasing the pH from 3.4 to 7.4, a considerable increase in the cumulative release is observed for all composites. From Fig. 6(A) and (B), it is seen that the 50% drug–polymer composites have shown longer drug release rates than the other composites. Thus, drug release depends upon the nature of the polymer matrix as well as pH of the media. This suggests that the drugs in the blend can be used to be suitable for the basic environment of the large intestine, colon and rectal mucosa for which there are different emptying times.

Interestingly, ofloxacin is being released more rapidly at pH 7.4 than at pH 3.4, the release half times t_{50} (time required for releasing 50 wt% of drug) for 10%, 20%, 30%, 40%, 50% drug loading are 2.8, 1.8 and 1.7 h at pH 7.4, and 6.0, 5.0 and 4.4 h at pH 3.4, respectively are shown in Fig. 7(A) and (B). More than 80 wt% ofloxacin is released from composites at pH 7.4 within 8 h, whereas less than 44 wt% of the drug is released at pH 1.2 within 4 h. This suggests that the drugs in the composites can be used to be suitable for the basic environment. Further the electrostatic interaction of composites is more easily broken at pH 7.4 than at pH 3.4, leading to ofloxacin being released more rapidly at pH 7.4 than 3.4.

4.5.2. Effect of drug loading

Fig. 6 displays the release profiles of drug from composites at different amounts of drug loadings. Release data show that formulations containing highest amount of drug (50%) displayed fast and higher release rates than those formulations containing a small amount of drug loading. The release rate becomes quite slower at the lower amount of drug in the matrix, due to the availability of more free void spaces through which a lesser number of drug molecules could transport.

4.6. Drug release kinetics

4.6.1. Drug release mechanism from matrices

From time to time, various authors have proposed several types of drug release mechanisms from matrices. It has been proposed

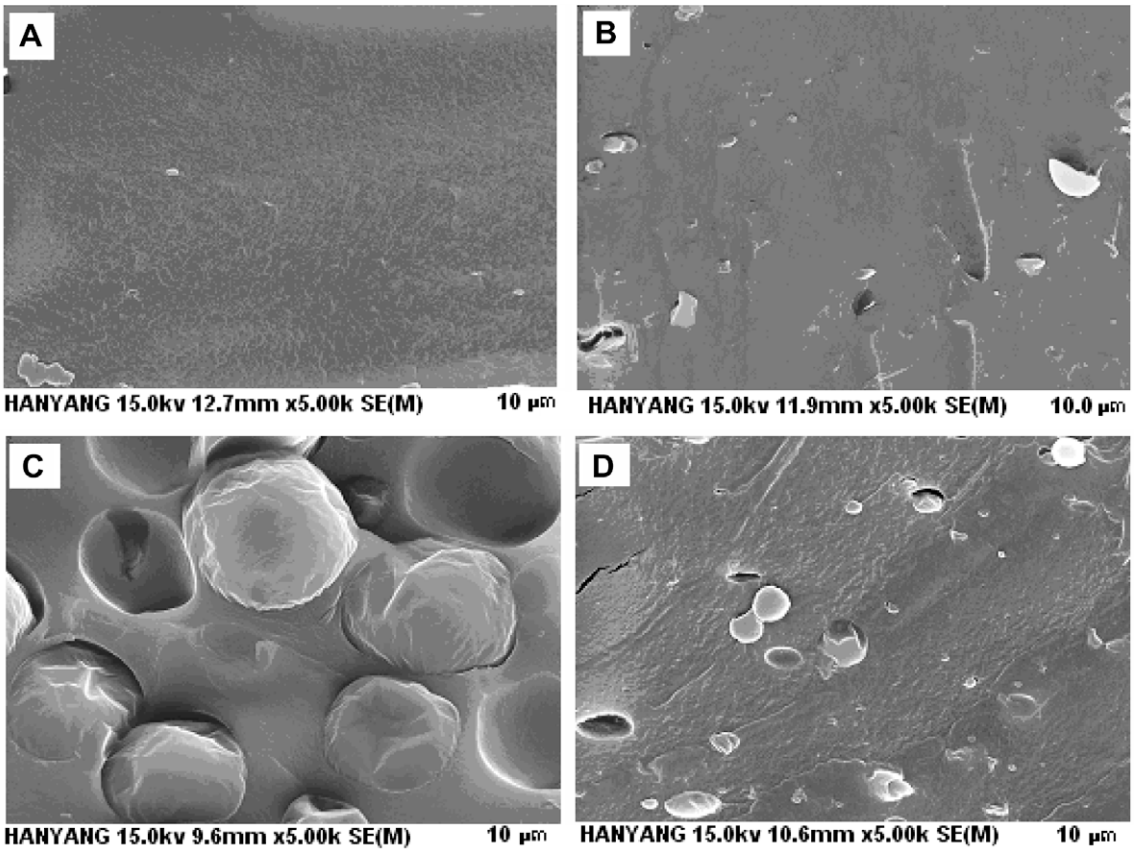

Fig. 4. Scanning electron microscope of chitosan/PCL composites. (A) 80:20, (B) 75:25, (C) 60:40 and (D) 50:50.

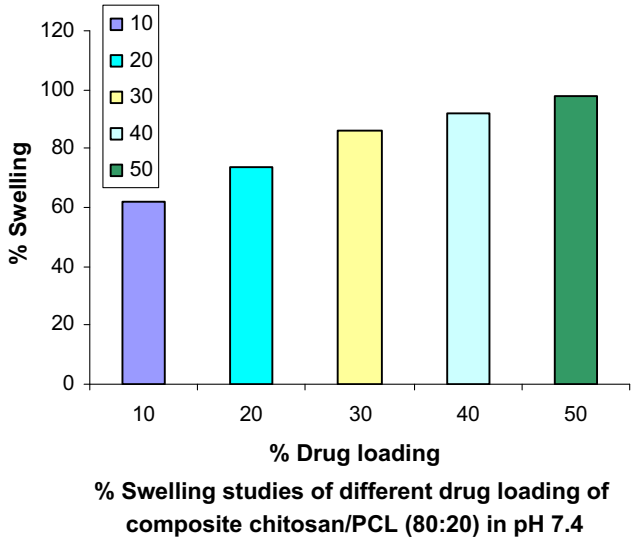

Fig. 5. Water absorption of the chitosan/PCL blend composite with different % drug loadings.

that drug release from matrices usually implies water penetration in the matrix, hydration, swelling, diffusion of the dissolved drug (polymer hydro fusion), and/or the erosion of the gelatinous layer. Several kinetics models relating to the drug release from matrices, selected from the most important mathematical models, are described over here. However, it is worth mention that the release mechanism of a drug would depend on the dosage from selected, pH, nature of the drug and, of course, the polymer used.

(i) Zero-order kinetics (Xu & Sunada, 1995).

$$W = k_1 t \tag{1}$$

(ii) First-order kinetics (Singla & Medirata, 1988; Xu & Sunada, 1995).

$$\ln(100 - W) = \ln 100 - k_2 t \tag{2}$$

(iii) Hixon–Crowel's cube-root equation (Erosin model) (Singla & Medirata, 1988).

$$(100 - W)^{1/3} = 100^{1/3} - k_3 t \tag{3}$$

(iv) Higuchi's square root of time equation (diffusion model) (Higuchi, 1963).

$$W = k_4 t \tag{4}$$

(v) Power law equation (diffusion/relaxation model) (Kulkarni, Soppimath, & Aminabhavi, 1999).

$$M_t/M_\infty = k_5 t^n \tag{5}$$

M_t/M_∞ is the fractional drug release into dissolution medium and k_5 is a constant incorporating the structural and geometric characteristics of the tablet. The term 'n' is the diffusional constant that characterizes the drug release transport mechanism. When $n = 0.5$, the drug diffuses through and is release from the polymeric matrix with a quasi-Fickian diffusion mechanism. For $n > 0.5$, an anomalous, non-Fickian drug diffusion occurs. When $n = 1$, a non-Fickian, case II or zero-order release kinetics could be observed.

Drug release kinetics was analyzed by plotting the cumulative release data vs. time by fitting to an exponential equation of the type (Kulkarni et al., 1999) as represented below.

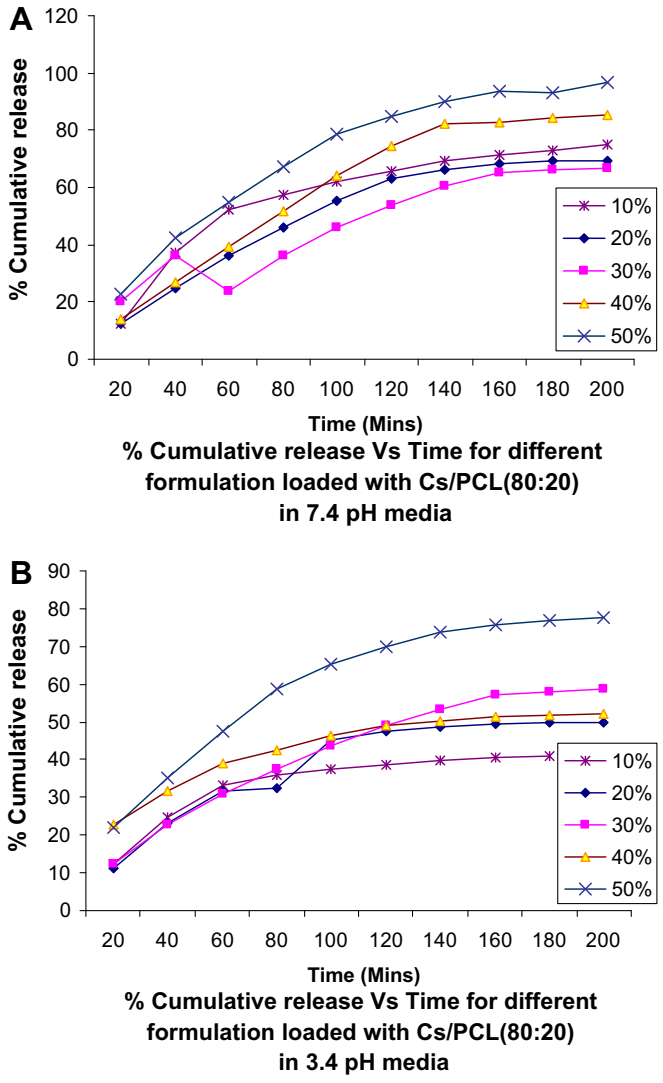

Fig. 6. % Cumulative release vs. time for different formulation loaded with CS–PCL (80:20) in (A) pH 7.4 and (B) pH 3.4 media.

$$M_t/M_\infty = kt^n$$

Here, M_t/M_∞ represents the fractional drug release at time t, k is a constant characteristic of the drug–polymer system and n is an empirical parameter characterizing the release mechanism. Using the least squares procedure, we have estimated the values of n and k for all the nine formulations and these data are given in Table 1. The values of k and n have shown a dependence on the, % drug loading and polymer content of the matrix. Values of n for composites prepared by varying the amounts of drug containing 10, 20 and 30 wt% and keeping PCL (20%) and chitosan (80%) constant, ranged from 0.57 to 0.88 suggesting shift of drug transport from Fickian to anomalous type. However, the drug-loaded composites exhibited n values ranging from 0.96 to 1.57 (Table 1), indicating a shift from erosion type release to a swelling controlled, non-Fickian type mechanism. The values of n more than 1 has also been recently reported (Kulkarni et al., 1999). This may be due to a reduction in the regions of low micro viscosity inside the matrix and closure of microcavities during the swollen state of the polymer. Similar findings have been found elsewhere, wherein the effect of different polymer ratios on dissolution kinetics was investigated (Aminabhavi & Naik, 1998; Lyu, Sparer, Hobot, & Dang, 2005; Ritger & Peppas, 1987).

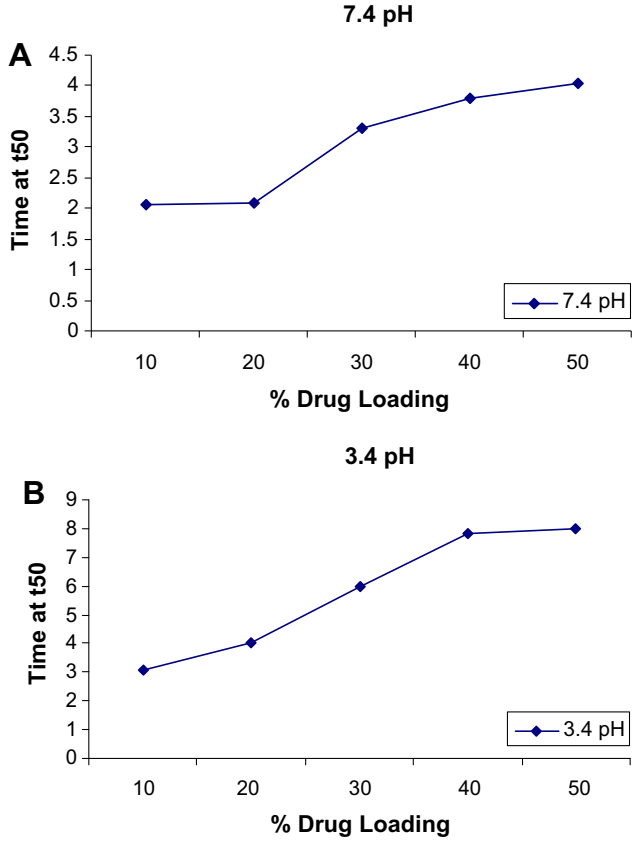

Fig. 7. Drug release at time t_{50} vs. drug loading in composite chitosan/PCL (80:20) at pH 7.4 and (B) pH 3.4.

Table 1
Release kinetics parameters of different formulations at pH 7.4 and pH 3.4.

Sample code (%)	k	n	Co-ordination coefficient, r
7.4 pH			
10	0.12	1.57	0.9749
20	0.19	1.2	0.9687
30	0.23	0.96	0.9882
40	0.25	1.55	0.9654
50	0.25	1.08	0.9723
3.4 pH			
10	0.11	1.33	0.9306
20	0.15	1.25	0.9834
30	0.21	1	0.9873
40	0.21	1.02	0.9658
50	0.24	0.70	0.9914

5. Conclusion

The last two decades of the twentieth century saw a paradigm shift from biostable biomaterials to biodegradable (hydrolytically and enzymatically degradable) biomaterials for medical and related applications The current trend predicts that in the next couple of years, many of the permanent prosthetic devices used for temporary therapeutic applications will be replaced by biodegradable devices that could help the body to repair and regenerate the damaged tissues. Chitosan is a natural biodegradable polymer where as polycaprolactone is a synthetic biopolymer. The blending of the two polymers has been carried out varying the proportion of polycaprolactone so that the composite can be a better drug carrier. From the FTIR spectra the different pendant group present in the composites have been ascertained. The morphology

as well as the compatibility of the blends have been studied using SEM and XRD methods. From these studies the homogeneity of the blends has been predicted. Swelling study is an important parameter to predict the diffusion of the drugs from the matrix. The percentage of swelling increases with increase in the percentage of drug loading. The drug release depends upon the nature of the polymer matrix as well as pH of the media. The kinetics of the drug release has been investigated. The values of k and n have been computed. Based on the values of n non-Fickian kinetics has been predicted.

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References

Allen, C., Han, J., Yu, Y., Maysiger, D., & Eisenberg, A. (2000). Polycaprolactone, poly(ethylene oxide) copolymer micelles as a delivery vehicle for dihydrotestosterone. *Journal of Control Release, 63*, 275.

Aminabhavi, T. M., & Naik, H. G. (1998). Chemical compatibility study of geomembranes-sorption/desorption, diffusion and swelling phenomena. *Journal of Hazardous Materials, 60*, 175–203.

Bassaris, H., Akalin, E., & Calangu, S. (1995). A randomised, multinational study with sequential therapy comparing ciprofloxacin twice daily and ofloxacin once daily. *Infection, 23*, 39–45.

Cai, Q., Bei, J., & Wang, S. (2000). Synthesis and degradation of a tri-component copolymer derived from glycolide, L-lactide and ε-caprolactone. *Journal of Biomaterials Science. Polymer Edition, 11*, 273.

Chandy, T., & Sharma, C. P. (1990). Chitosan—As a biomaterial biomater. *Artificial Cells Artificial Organs, 18*, 1–24.

Cohn, D., & Younes, H. (1988). Biodegradable PEO/PCL block copolymers, J. *Biomedical Materials Research, 22*, 993.

Demarger-Andre, S., & Domard, A. (1994). New properties of chitosan in lipid dispersions. In Z. S. Karnicki, A. Wojtaso Pajak, M. M. Breziski, & P. J. Bylowski (Eds.), *Chitin world* (pp. 153–158). Germany: Bremerhauser.

Detchprohm, S., Aoi, K., & Okada, M. (2001). Novel amphiphilic poly (ε-caprolactone)-*g*-poly (L-lysine) degradable copolymers. *Macromolecular Chemistry and Physics, 202*, 3560–3570.

Drlica, K. (1984). Biology of bacterial deoxyribonucleic acid topoisomerases. *Microbiological Reviews, 48*, 273–289.

Elbert, D. L., & Hubbell, J. A. (2001). Conjugate addition reactions combined with free-radical cross-linking for the design of materials for tissue engineering. *Biomacromolecules, 2*, 430–441.

Frank, S., & Lauterbur, P. C. (1993). Voltage-sensitive magnetic gels as magnetic resonance monitoring agents. *Nature, 363*, 334–336.

Fukuda, H. (1980). Polyelectrolyte complexes of chitosan carboxymethyl cellulose. *Bulletin of the Chemical Society of Japan, 53*, 837–840.

Gellert, M. (1981). DNA topoisomerases. *Annual Review of Biochemistry, 50*, 879–910.

Goodwin, C. J., Braden, M., Downes, S., & Marshall, N. J. (1998). Release of bioactive human growth hormone from a biodegradable material: Poly(ε-caprolactone). *Journal of Biomedical Materials Research, 40*, 204.

Ha, J. H., Kim, S. H., Han, S. Y., Sung, Y. K., Lee, Y. M., Kang, I. K., et al. (1997). Albumin release from bioerodible hydrogels based on semi-interpenetrating polymer networks composed of poly(ε-caprolactone) and poly(ethylene glycol) macromer. *Journal of Controlled Release, 49*, 253.

Heller, J. (1987). Fundamentals of polymer science. In J. R. Robinson & V. H. Lee (Eds.), *Controlled drug delivery fundamentals and applications* (pp. 139–212). New York: Marcel Dekker.

Higuchi, T. (1963). Mechanism of rate of sustained-action medication. *Journal of Pharmaceutical Sciences, 52*, 1145–1149.

Huatan, H., Collett, J. H., Attwood, D., & Booth, C. (1995). Preparation and characterization of poly(ε-caprolactone) polymer blends for the delivery of proteins. *Biomaterials, 16*, 1297.

Hubbell, D. S., & Cooper, S. L. (1977). The physical properties and morphology of poly-ε-caprolactone polymer blends. *Journal of Applied Polymer Science, 21*, 3035.

Kas, H. S. (1997). Chitosan: Properties, preparation and application to microparticulate systems. *Journal of Microencapsulation, 14*, 689–711.

Kato, Y., Onishi, H., & Machida, Y. (2003). Application of chitin and chitosan derivatives in the pharmaceutical field. *Current Pharmaceutical Biotechnology, 4*, 303–309.

Kelner, A., & Schacht, E. (2005). Tailor-made polymers for local drug delivery: Release of macromolecular model drugs from biodegradable hydrogels based on poly(ethylene oxide). *Journal of Controlled Release, 101*, 13–20.

Khor, E., & Lim, L. Y. (2003). Implantable applications of chitin and chitosan. *Biomaterials, 24*, 2339–2349.

Korsmeyer, R. C., & Peppas, N. A. (1981). Effect of the morphology of hydrophilic polymeric matrices on the diffusion and release of water soluble drugs. *Journal of Membrane Science, 9*, 211–227.

Kulkarni, A. R., Soppimath, K. S., & Aminabhavi, T. M. (1999). Controlled release of diclofenac sodium from sodium alginate beads crosslinked with glutaraldehyde. *Phramaceutica Acta Helvitae, 74*, 29–36.

Lambert, G., Fattal, E., & Couvreur, P. (2001). Nanoparticulate systems for the delivery of antisense oligonucleotides. *Advanced Drug Delivery Reviews, 47*, 99–112.

Langer, R. (1990). New methods of drug delivery. *Science, 249*, 1527–1533.

Lewis, D. H., Chasin, M., & Langer, R. (Eds.). (1990). *Biodegradable polymers as drug delivery systems* (Vol. 45, pp. 1–8). New York: Marcel Dekker.

Li, S., Vert, M., Scott, G., & Gilead, D. (Eds.). (1995). *Degradable polymers—Principles and applications* (pp. 43–87). London: Chapman and Hall.

Langer, R. (1998). Drug delivery and targeting. *Nature, 392*(6679), 5–10.

Li, S., & Vert, M. (1999). Biodegradable polymers: Polyesters. In E. Mathiowitz (Ed.), *Encyclopedia of controlled drug delivery* (pp. 71–93). New York: Wiley.

Lien, S., & Lowman, H. B. (2003). Therapeutic peptides. *Trends in Biotechnology, 21*, 556–562.

Lyu, S. P., Sparer, R., Hobot, C., & Dang, K. (2005). Adjusting drug diffusivity using miscible polymer blends. *Journal of Controlled Release, 102*, 679–687.

Mann, B. K., Andrea, S. G., Annabel, T. T., Rachael, H. S., & Jennifer, L. W. (2001). Smooth muscle cell growth in photopolymerized hydrogels with cell adhesive and prototypically degradable domains: Synthetic ECM analogs for tissue engineering. *Biomaterials, 22*, 3045–3051.

McAllister, K., Sazani, P., Adam, M., Cho, M. J., Rubinstein, M., Samulski, R. J., et al. (2002). Polymeric nanogels produced via inverse microemulsion polymerization as potential gene and antisense delivery agents. *Journal of the American Chemical Society, 124*(51), 15198–15207.

Muzzarelli, R. A. A. (1977). *Chitin*. New York: Pergamon Press (pp. 1–37).

Nanda, P. K., Rao, K. K., Kar, R. K., & Nayak, P. L. (2007). Biodegradable polymers: Part VI. Biodegradable plastics of soy protein isolate modified with thiourea. *Journal of Thermal Analysis and Calorimetry, 89*(3), 935–940.

Nanda, P. K., Rao, K. K., & Nayak, P. L. (2007a). Spectral, thermal, morphological, and biodegradability properties of environmentfriendly green plastics of soy protein modified with thiosemicarbazide. *Journal of Applied Polymer Science, 103*, 3134.

Nanda, P. K., Rao, K. K., & Nayak, P. L. (2007b). Thermal degradation analysis of biodegradable plastics from ureamodified soy protein isolate. *Polymer Plastics Technology and Engineering, 46*, 207.

Nishimura, S., Kohgo, O., Kurita, K., & Kuzuhara, H. (1991). Chemospecific manipulations of a rigid polysaccharide: Synthesis of novel chitosan derivatives with excellent solubility in common organic solvents by regioselective chemical modifications. *Macromolecules, 24*, 4745–4748.

Onsoyen, E., & Skaugrud, O. (1990). Metal recovery using chitosan. *Journal of Chemical Technology & Biotechnology, 49*, 395–404.

Park, H. R., Chung, H. C., Lee, J. K., & Bark, K. M. (2000). Ionization and divalent cation complexation of quinolones antibiotics in aqueous solution. *Bulletin of the Korean Chemical Society, 21*(9), 849–854.

Pathak, C. P., Sawhney, A. S., & Hubbell, J. A. (1992). Rapid photo polymerization of Immuno protective gels in contact with cells and tissue. *Journal of the American Chemical Society, 114*, 8311–8312.

Paul, D. R., & Newman, S. (1978). *Polymer blends*. New York: Academic Press.

Peppas, N. A., & Langer, R. (1994). New challenges in biomaterials. *Science, 263*, 1715.

Pitt, C. G., Gratzl, M. M., Jeffcoat, A. R., Zweidinger, R., & Schindler, A. (1979). Sustained drug delivery systems. Part II. Factors affecting release rates from poly(ε-caprolactone) and related biodegradable polyesters. *Journal of Pharmaceutical Sciences, 68*, 1534.

Pokharkar, V. B., & Sivaram, S. (1996). Permeability studies across poly(alkylene carbonate) membranes. *Journal of Controlled Release, 41*, 157.

Ratajska, M., & Boryniec, S. (1998). Physical and chemical aspects of biodegradation of natural polymers. *Reactive and Functional Polymers, 38*, 35–49.

Rathbone, M. J., Witchey-Lakshmanan, L., & Ciftci, K. (1999). Veterinary application. In E. Mathiowitz (Ed.), *Encyclopedia of controlled drug delivery* (pp. 1007–1037). New York: Wiley.

Ritger, R. L., & Peppas, N. A. (1987). A simple equation for disposition of solute release—II. *Journal of Controlled Release, 5*, 37–42.

Roberts, G. A. F. (1992). *Chitin chemistry*. Houndmills: MacMillan Press (pp. 1–50).

Santin, M., Huang, S. J., Iannace, S., Ambrosio, L., Nicolais, L., & Peluso, G. (1996). Synthesis and characterization of a new interpenetrated poly(2-hydroxyethylmethacrylate)–gelatin composite polymer. *Biomaterials, 17*, 1459–1467.

Senda, T., He, Y., & Inoue, Y. (2001). Biodegradable blends of poly (ε-caprolactone) with α-chitin and chitosan: Specific interactions, thermal properties and crystallization behavior. *Polymer International, 51*, 33–39.

Singla, A. K., & Chawla, M. (2001). Chitosan: Some pharmaceutical and biological aspects—An update. *Journal of Pharmacy and Pharmacology, 53*, 1047–1067.

Singla, A. K., & Medirata, D. K. (1988). Influence of sodium lauryl sulfate on indomethacin release patterns. *Drug Development and Industrial Pharmacy, 14*, 1883–1888.

Susan, B., Maryadele, J. O. N., Ann, S., & Patricia, E. H. (1991). *The Merck index: An encyclopedia of chemicals, drugs and biologicals*. (11th ed., p. 1071). Merckand Co.

Swain, S. N., Rao, K. K., & Nayak, P. L. (2004). Biodegradable polymers: III. Spectral, thermal, mechanical, and morphological properties of cross-linked furfural soy protein concentrate. *Journal of Applied Polymer Science, 93*, 2590.

Swain, S. N., Rao, K. K., & Nayak, P. L. (2005). Biodegradable polymers: IV. Spectral, thermal, and mechanical properties of cross-linked soy protein concentrate. *Polymer International, 54*, 739.

Xu, G. J., & Sunada, H. (1995). Influence of formation changes on drug release kinetics. *Chemical & Pharmaceutical Bulletin, 43*, 483–487.

Yang, G. L., Zhaang, H., & Feng (1999). Role of polyethylene glycol in formation and structure of regenerated cellulose microporous membrane. *Journal of Membrane Science, 161*, 31.

Zhu, K. J., Xiangzhon, L., & Shilin, Y. (1990). Preparation, characterization and properties of polylactide (PLA)–poly-(ethylene glycol) (PEG) copolymers: A potential drug carrier. *Journal of Applied Polymer Science, 39*, 1.