Characterization of soluble, salt-loaded, degradable PLGA films and their release of tetracycline

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Abstract: A local drug delivery system has been designed to release tetracycline over a period of 30 days from poly (lactide-co-glycolide) films. Incorporation of either soluble salt excipients or low molecular weight polymeric species has been found to modulate the release kinetics of the system. The following research describes the fabrication of the delivery system, monitors tetracycline release from the system, and fully characterizes the degradation of the polymer films via scanning electron microscopy, gel permeation chromatography, differential scanning calorimetry, Fourier-transform infrared spectroscopy, and X-ray diffraction techniques. Results show that the modulation via use of salts occurs without changing the inherent degradation rate of the system. We suggest that this phenomenon may be due to the increased amount of swelling and uptake of buffer by the films loaded with soluble salt. Uptake, therefore, may be creating microscopic pores that permit further diffusion of tetracycline from the polymer matrix as well as allow the free monomers to leave the system, thereby preventing autocatalysis within the system. © 1998 John Wiley & Sons, Inc. J Biomed Mater Res, 41, 18–29, 1998.

Key words: tetracycline; poly (lactide-co-glycolide); soluble salts; controlled release; excipients

INTRODUCTION

Antibiotics such as tetracycline, doxycycline, chlorhexidine, and metronidazole long have been considered for use in the treatment of chronic periodontal disease and gingivitis.[1,2] However, oral rinses of antibacterial agents cannot always reach the deeper subgingival tissues, and systemic administration possibly can result in bacterial resistance to the antibiotic as well as in toxic side effects. This is due to the high dosage required via systemic delivery to achieve a therapeutic level of antibiotic in the periodontal pocket. To address these issues, specialized controlled-release delivery systems recently have been investigated. For example, Goodson et al. released tetracycline from ethylene vinyl acetate fibers, achieving *in vitro* release of drug for periods up to 9 days.[3–6] Minabe et al. developed collagen preparations with immobilized tetracycline, which resulted in the presence of an effective dose of tetracycline in the gingival crevicular fluid of the periodontal pocket for over 10 days.[7] Many other systems formulated as films, microspheres, fibers, and gels also have been designed for insertion into the periodontal pocket and release of an appropriate antibiotic.

The goal of the present study was to achieve sustained and controlled local delivery of the antibiotic to the diseased tissue for a period of up to 30 days. More specifically, we focused on developing modulated release rates for tetracycline from poly (lactide-co-glycolide) films. There exist several approaches to the modulation of release of drugs from PLGA formulations. The use of insoluble salt to modulate the release and swelling of bioerodible polyesters has been discussed by Zhang et al.[8] They found the salts led to increased water uptake into the film and, therefore, varied the polymer degradation. This method was found to improve the release of high molecular weight proteins from PLGA films. Johnson et al. succeeded in forming a stabilizing complex by adding zinc acetate to a solution of recombinant human growth hormone (rhGH) during the fabrication process of PLGA microspheres. By stabilizing and encapsulating the protein, an injectable sustained-release form of human growth hormone was developed and, with a single injection of microspheres in monkeys, resulted in elevated serum levels of rhGH for more than one month.[9] Roskos et al. achieved complete release of tetracycline from their bioerodible poly (ortho ester) viscous paste within 24 h. However, when small amounts of $Mg(OH)_2$ excipi-

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ent were incorporated into the polymer, release could be extended to many weeks. More precisely, a loading of 0.5 wt% of $Mg(OH)_2$ resulted in sustained release for about 10 days.[10] Research by Mauduit et al. shows that the higher the amount of PLA50p oligomers added into a blend of high and low molecular weight poly (DL-lactic acid), the higher the release rate of gentamycin and the higher the degradation rate of the matrix.[11] It is clear from these examples that the incorporation of various excipients into the polymer system can be an effective method of modulating the release kinetics of the particular system.

The following research fully characterizes the use of soluble salts in the degradation of PLGA polymer films and also monitors the release of tetracycline from these films for the treatment of gingivitis and periodontal disease. These films are designed to be thin and malleable for easy insertion into the periodontal pocket. Here, scanning electron microscopy, gel permeation chromatography, differential scanning calorimetry, Fourier-transform infrared spectroscopy, and X-ray diffraction techniques are used to monitor the dissolution of the salts and degradation of the polymer films from samples loaded with different concentrations of sodium chloride and to monitor as well a system that also contains low molecular weight excipients.

MATERIALS AND METHODS

Film fabrication

For each set of control films, one gram of PLGA polymer (Boehringer Ingelheim, Resomer RG503, lot #223808, MW = 34,000) was dissolved in 10 mL of MeCl2 (Fisher Scientific) in a glass scintillation vial. A 0, 1, 5, or 25% (w/w) loading of sodium chloride predissolved in 200 μL of distilled water also was added to each vial. NaCl (25%) also was added to a polymer blend of 75% PLGA (Boehringer Ingelheim, Resomer RG503, lot #223808, MW = 34,000) and 25% PLGA (Polysciences, lot #85761, MW = 5000). For each film composition, a set of tetracycline-loaded films was made. Tetracycline (5%, w/w) predissolved in 100 μL of distilled water was used. The contents of the vials then were sonicated for 60 s each and cast into ten circular glass rings on Teflon sheets. Films were air dried for 24 h before being subjected to high vacuum for an additional 4 h to extract any residual solvent.

Drug release rate measurements

Film samples were immersed in a 1.0*M* solution of PBS buffer (FTA hemagglutination buffer) at 37°C for the duration of the study. At regular intervals the buffer was extracted from the vials and replaced with fresh buffer. The buffer samples were analyzed spectrophotometrically at 354 nm for tetracycline quantification using a Beckman DU-65 spectrophotometer. At predetermined times film samples were removed from the lot, lyophilized, and used for characterization analysis of film degradation.

Morphological studies

Surface morphology of the film was analyzed over time for evidence of film degradation. Scanning electron microscopy (SEM) was performed using a Hitachi S-2700 scanning electron microscope on film surfaces sampled at days 0, 1, 3, 7, 21, and 42 in buffer. Film samples were frozen and lyophilized, mounted on metal stubs, and sputter coated with gold–palladium (Polaron Instrument E5100) prior to viewing.

Molecular weight

Gel permeation chromatography (GPC) on a Perkin-Elmer liquid chromatography system was used to determine molecular weights and molecular weight distributions via size-exclusion chromatography. The Perkin-Elmer system consisted of an Isocratic LC pump model 250, LC-30 RI detector, LC column oven model 101, and 900 series computer interface box. Samples were lyophilized, dissolved in HPLC-grade chloroform, and filtered with a 0.2 μm syringe filter before injection to remove any insoluble particulates. The samples then were passed through a PL gel 5 μm mixed column and a 5 micron/50 angstrom column at a flow rate of 1.0 mL/min and a temperature of 40°C. All samples were compared to polystyrene standards (Polysciences) that ranged in molecular weight from 1000 to 1,860,000. Turbochrom and TC*SEC software programs from Perkin-Elmer were utilized for data analysis. Polymer films were sampled at each of the specified time points, that is, 0, 1, 3, 7, 21, and 42 days.

Thermal analysis

Differential scanning calorimetry (DSC) was performed on a Perkin-Elmer Model DSC 7 connected to a controller model TAC 7/DX (Perkin-Elmer) on lyophilized film samples at each of the above-mentioned time points, namely 0, 1, 3, 7, 21, and 42 days after immersion in PBS buffer. Samples were heated from −20° to 100°C at a rate of 10 C/min, cooled back down to −20°C at the same rate, and finally heated to 100°C, again at 10 C/min. Glass transition temperatures were calculated from the second heating ramp and examined for shifting trends, which would indicate the occurrence of film degradation. Analysis was performed using the Perkin-Elmer Thermal Analysis software.

Fourier-transform infrared spectroscopy

Film degradation was observed using Fourier-transform infrared spectroscopy (FTIR) by examining the changes in area or disappearances of certain characteristic peaks. FTIR was performed on a Perkin-Elmer FTIR Spectrometer model

1725X on solvent cast films from each composition and at the specified time points: 0, 1, 3, 7, and 21 days. The sixth time point, 42 days, had degraded to such a state that casting films substantial enough for accurate FTIR analysis were unsuccessful. Spectra then were analyzed using Infrared Data Manager (Perkin-Elmer).

X-ray diffraction

X-ray diffraction techniques, performed on a Siemens Diffraktometer D5000, were used as a final means of film degradation analysis. Samples that had been in buffer for 0, 1, 3, and 7 days were subjected to X-ray and analyzed using DiffracAt computer software for decreasing or disappearing representative crystalline or salt peaks as well as for growth changes of other peaks or amorphous areas.

Swelling experiments

PLGA films containing various concentrations of salt, including 0, 5, 10, 20, and 25%, were preweighed and left to incubate in PBS buffer at 37°C. At regular intervals, the samples were removed from the buffer and weighed. Plotting of the data revealed the extent to which the above-mentioned films swelled over time and also compared the effects of the various NaCl concentrations on the film swelling.

RESULTS AND DISCUSSION

The target of this research was to achieve release of tetracycline from bioerodible films for a period of 30 days. To achieve a modulated release system that could be manipulated to release tetracycline from 1 week to 1 month we decided to use two approaches: (1) use of soluble salts, that is, sodium chloride, and (2) use of low molecular weight polymers, poly(lactide-co-glycolide, MW 5000), which act as a plasticizer to the higher molecular weight PLGA film. The main advantage of such a system is that the excipients are nontoxic, rendering the delivery system very attractive in terms of future applications.

Drug release rate measurements

Release curves for the five systems were compared. The control films loaded with 5% tetracycline seemed to follow a more typical release pattern for PLGA, with an initial 6-day burst of drug release, probably due to diffusion, followed by a plateau phase and another sharp increase in release, possibly due to polymer degradation (see Figs. 1, 2). We wanted to be able

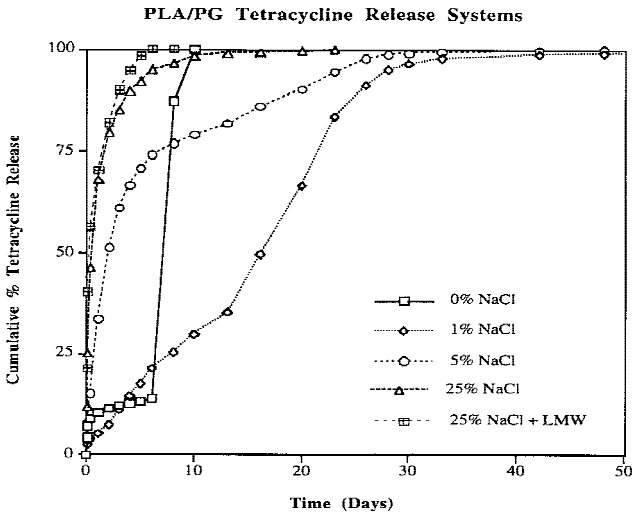

Figure 1. Release curves for the five systems over a period of 50 days.

to control this three-phase release, and incorporation of salts or low molecular weight excipients seemed to be a useful approach. However, would water soluble salts such as sodium chloride achieve this goal, or would they result in quick dissolution into the buffer solution due to high water solubility?

To our surprise, the 1% NaCl system achieved slow, sustained release of tetracycline from the drug-loaded films for periods exceeding 6 weeks. This system released 12.39% of the drug per day for the first week, decreased to a release of 4.67% of the drug over the next two weeks, and then leveled off at a release rate of 0.01% per day for the last 3 weeks.

The 5% NaCl system also released drug over a 6-week period although more of the drug was released in the initial weeks than in the 1% NaCl system or control system. Here, 23.84% of the drug per day came out of the film in the first 2 days. The rate of drug

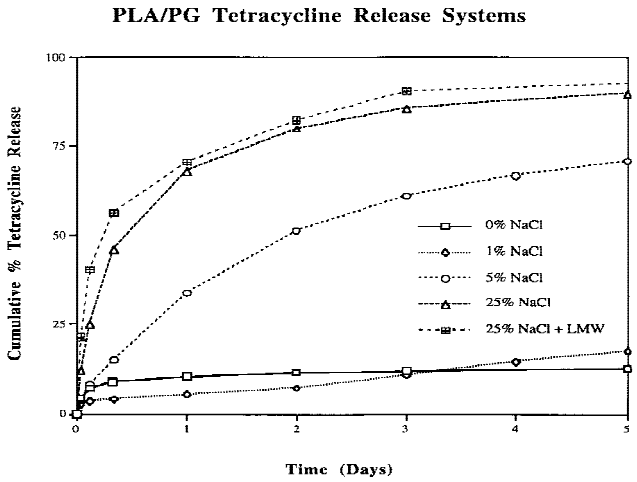

Figure 2. Release curves of the five systems over a period of 5 days.

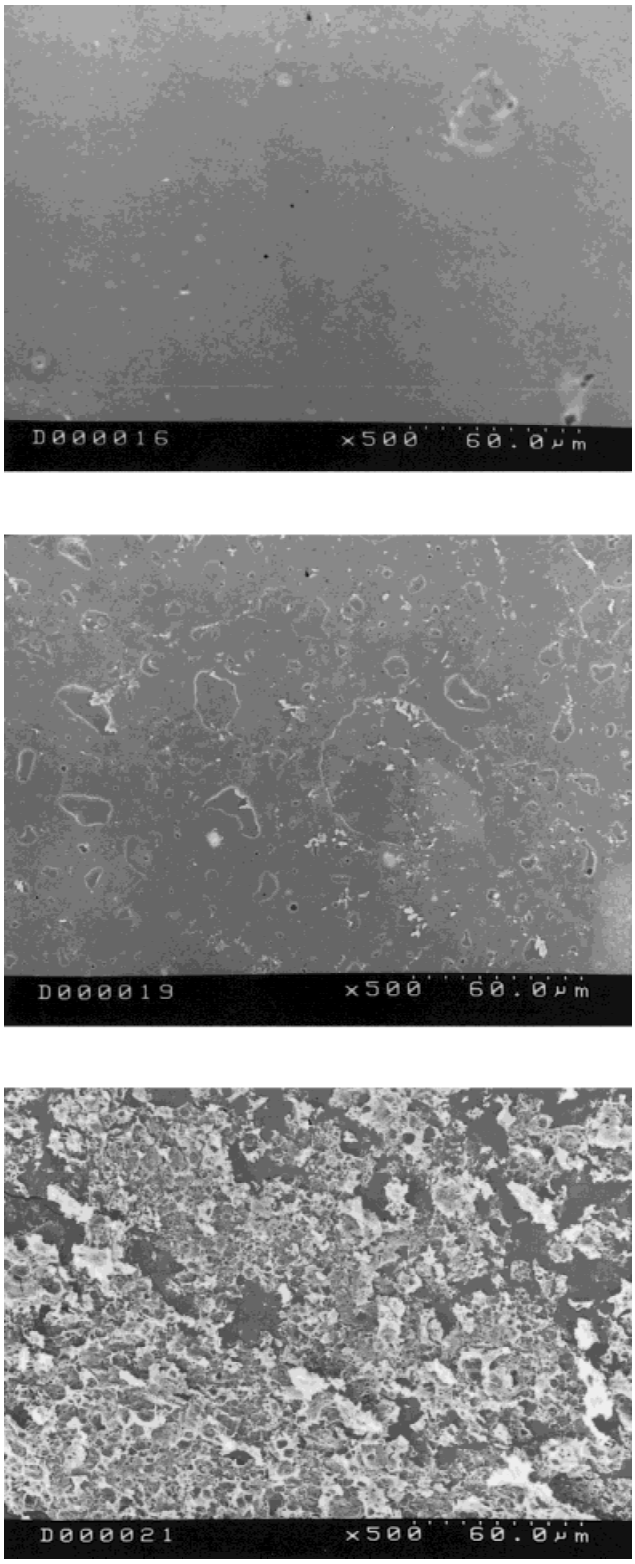

Figure 3. Scanning electron micrograph of 0% NaCl-loaded PLA/PG film at 0, 7, and 42 days (top to bottom), respectively.

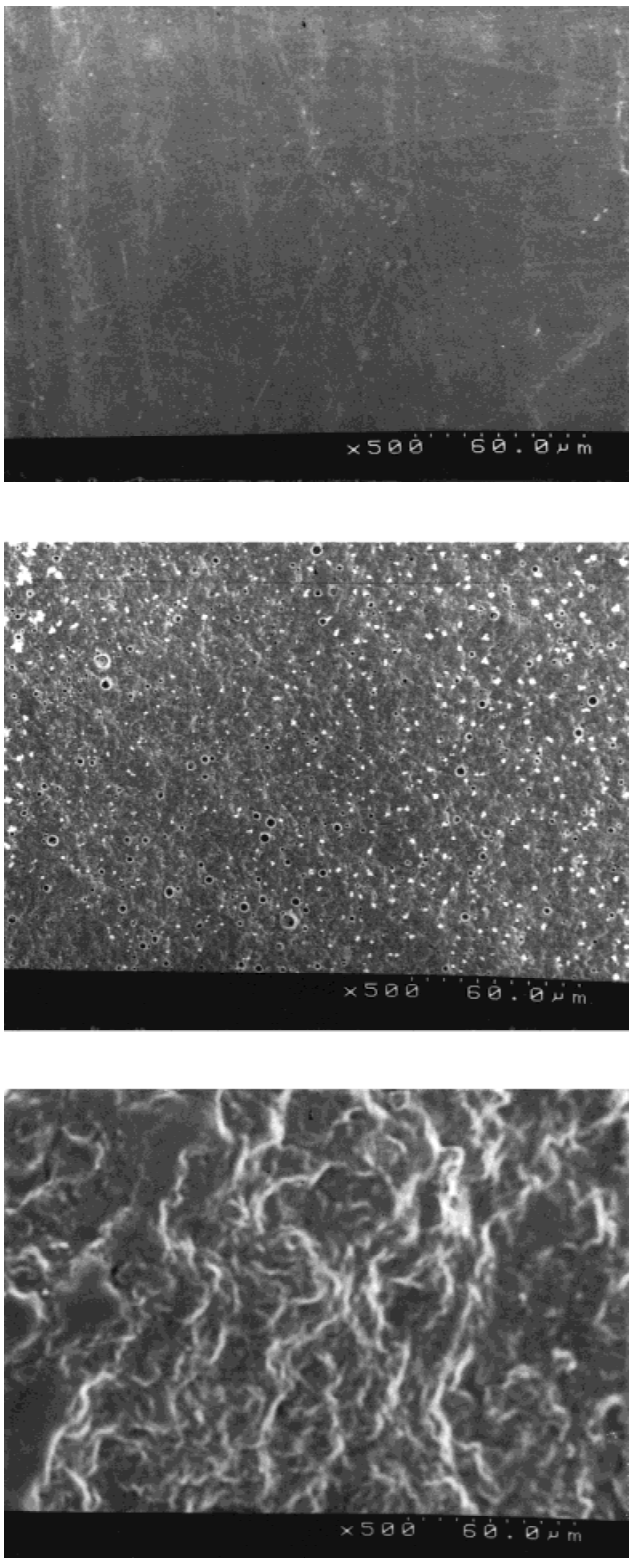

Figure 4. Scanning electron micrograph of 1% NaCl-loaded PLA/PG film at 0, 7, and 42 days (top to bottom), respectively.

release then dropped to 0.91% per day from week 1 to week 3. Then drug release plateaued at a rate of 0.005% drug release per day from week 6 to week 23 before again rising to a rate of 0.05% release per day for the final 3 weeks of the study. In both cases there was no longer any sign of the three-phase release curve that had existed prior to salt incorporation.

An increased release rate resulted from the use of

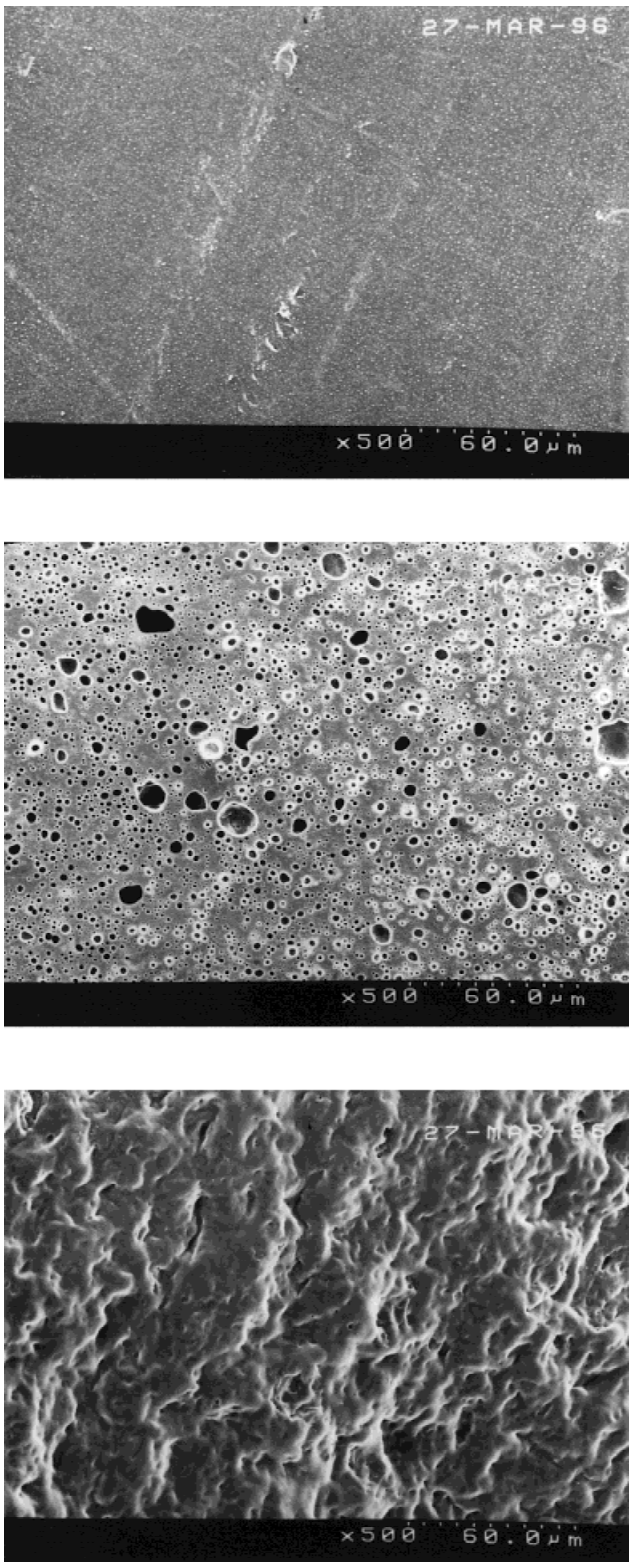

Figure 5. Scanning electron micrograph of 5% NaCl-loaded PLA/PG film at 0, 7, and 42 days (top to bottom), respectively.

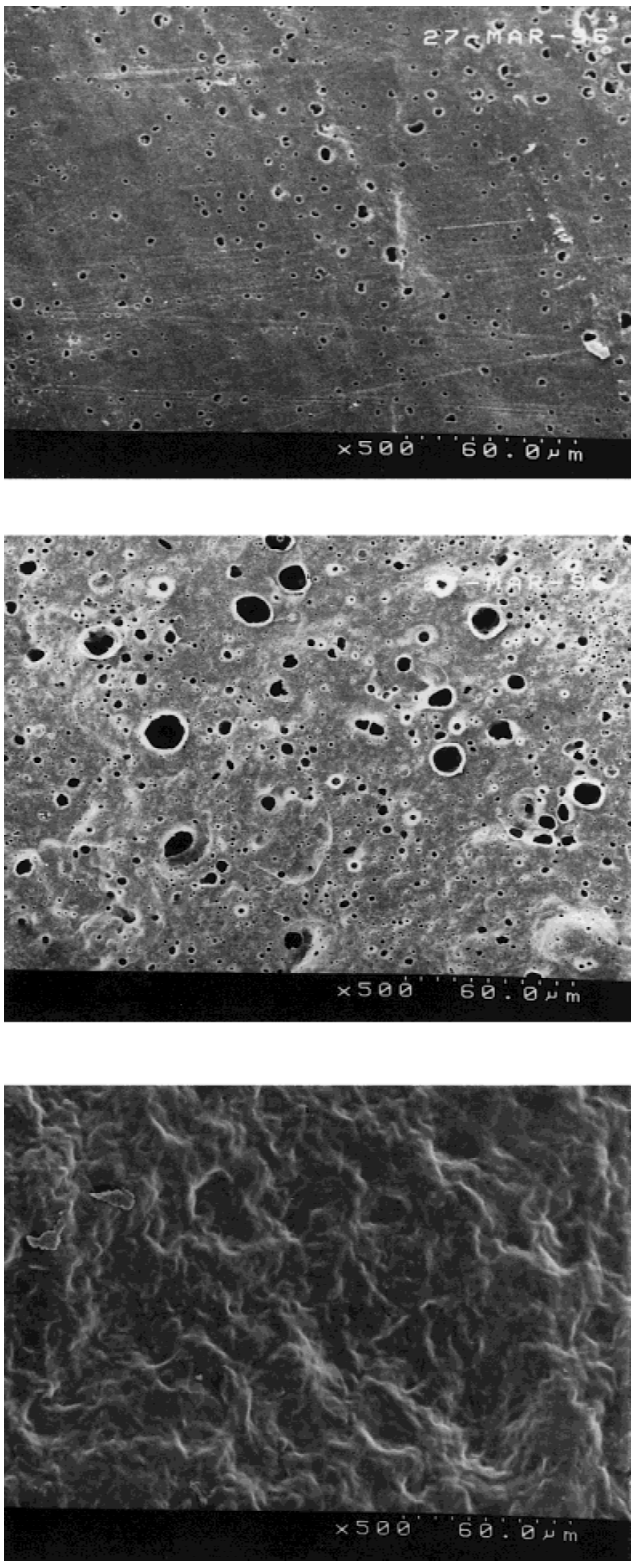

Figure 6. Scanning electron micrograph of 25% NaCl-loaded PLA/PG film at 0, 7, and 42 days (top to bottom), respectively.

25% salt, with the majority of the drug diffusing from the film within the first 3 weeks. The rate of release was measured at 58.27% per day for the first day, decreased to 0.76% per day for the next 2 weeks, and leveled off at a release rate of 0.003% drug release per day from week 6 to week 20 of the study.

The 25% salt system containing low molecular weight excipient (PLGA, MW 5K) resulted in the fast-

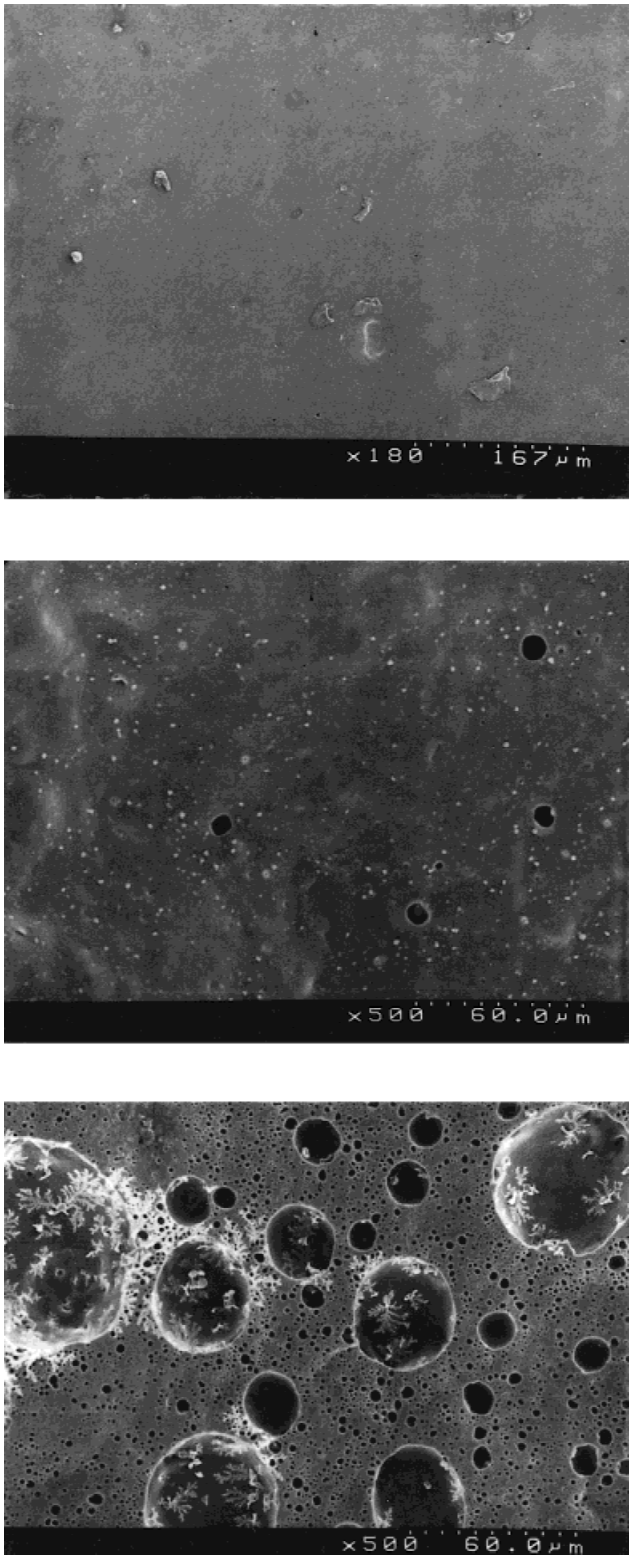

Figure 7. Scanning electron micrograph of 25% NaCl + low molecular weight PLA/PG film at 0, 3, and 7 days (top to bottom), respectively.

est release, with more drug being expelled in the first 3 days than from any of the other films. In the initial 24 h of the study 50.85% of the drug load was released, followed by a rate of 8.11% release per day for the next two days, and leveling off early at a release rate of 0.0007% per day for weeks 2–15. The increase in release rate was attributed to the increase of plasticity due to the incorporation of lower molecular weight species.

TABLE I
GPC Molecular Weights of Salt-Loaded PLA/PG Control Films

# Days in Buffer	0% NaCl	1% NaCl	5% NaCl	25% NaCl	25% NaCl + LMW
0	31,439	33,604	36,304	34,738	34,631
1	32,572	34,253	36,882	30,355	17,754
3	22,687	32,045	36,761	28,619	9,816
7	7,122	26,500	26,632	24,254	8,649
21	2,140	3,911	5,783	5,430	*
42	1,129	*	1,522	997	*

*Not enough sample remained to properly analyze.

The results so far were very exciting. Clearly, the salt significantly modulated the drug release from the PLGA films. Sodium chloride is very water soluble, so one would assume that most of the salt would come out in the first few days. However, this was not the case in the 1% and 5% salt-loaded systems, so we carried out the following characterization experiments to understand further how the salt affected the release rate of tetracycline.

Morphological studies

Films with different salt loadings and from various representative time points were examined under scanning electron microscope for changes in surface morphology. The films degraded over time, as shown by the formation of pores in the polymer matrix (see Fig. 3–7). All external surfaces appeared smooth and homogeneous at time zero. However, after being immersed in PBS buffer, pores formed on the film surfaces, indicating degradation. At 0, 1, and 3 days there was no change in the appearance of the surface of the control films. At 7 and 21 days the surface of the control film was still relatively smooth and pore free although a few minor blemishes appeared. It was not until 42 days that the control film developed actual

TABLE II
GPC Molecular Weights of Salt and Tetracycline-Loaded PLA/PG Films

# Days in Buffer	0% NaCl	1% NaCl	5% NaCl	25% NaCl	25% NaCl + LMW
0	50,534	36,161	39,661	34,303	34,017
1	44,463	34,415	38,837	29,951	17,751
3	37,159	31,465	33,370	29,791	10,947
7	26,634	25,394	25,971	23,711	3,946
21	2,963	3,329	4,917	5,791	*
42	*	*	1,393	965	*

*Not enough sample remained to properly analyze.

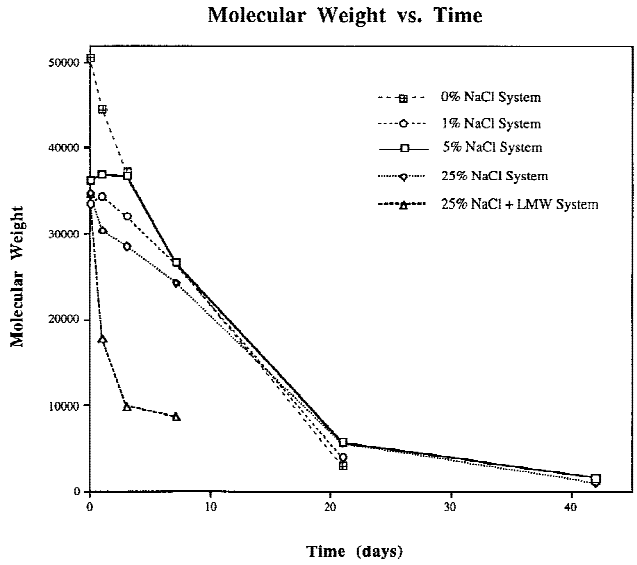

Figure 8. Graph of molecular weight decrease over time for various NaCl-loaded PLA/PG control films.

pores 5–10 μm in diameter and appeared rough and beehive-like in appearance (see Fig. 3).

In the 1% NaCl-loaded system, small irregularities in the smooth surface appeared at days 1 and 3. By 7 days the surface was covered with pinholes 1–5 μm in size. These pores increased to 5 μm in size by 21 days and resulted in a rough and rugged degraded appearance by 42 days (see Fig. 4).

Similarly, the 5% NaCl-loaded system remained pore free at 1 day but had small pinholes 1–5 μm in size in its smooth surface by 3 days. At 7 and 21 days, the film was homogeneously covered with distinct pores 5–10 μm in size. After 42 days in buffer, however, the film surface had degraded away completely, leaving a rough, irregular surface (see Fig. 5).

The 25% NaCl system formed pinhole pores 1–5 μm in diameter even prior to submersion in buffer. The pores remained this size for days 1 and 3. However, these pores enlarged significantly, resulting in pores up to 20 microns in diameter at 7 days (see Fig. 6). By 42 days the surface was rough and irregular in appearance, as if the structural integrity of the film had broken down.

TABLE III
DSC Glass Transition Temperatures of Salt-Loaded PLA/PG Control Films (C)

# Days in Buffer	0% NaCl	1% NaCl	5% NaCl	25% NaCl	25% NaCl + LMW
0	20.0	24.7	43.4	41.0	18.2
1	36.4	42.9	43.4	44.2	39.2
3	45.1	45.5	42.9	42.4	36.7
7	31.8	45.2	42.5	46.1	25.9
21	26.0	25.1	33.2	37.4	*
42	27.4	20.3	26.7	3.7	*

*Not enough sample remained to properly analyze.

TABLE IV
DSC Glass Transition Temperatures of Salt and Tetracycline-Loaded PLA/PG Films (C)

# Days in Buffer	0% NaCl	1% NaCl	5% NaCl	25% NaCl	25% NaCl + LMW
0	28.6	26.2	40.7	41.0	21.2
1	43.8	42.8	45.2	44.4	39.5
3	44.9	46.1	43.4	44.0	35.8
7	45.2	46.6	41.5	46.5	26.9
21	30.6	34.7	33.7	39.0	*
42	30.2	19.4	25.0	10.3	*

*These samples were degraded too much for accurate thermograms to be taken.

Lastly, the high and low molecular weight blend system with 25% NaCl had small pores over the entire surface at days 0, 1, and 3. By 7 days, the film was covered with large 30 micron pores (see Fig. 7). This particular system degraded too rapidly after this time for further measurements to be taken accurately.

Molecular weights

Tables I and II indicate degradation of the films as monitored by GPC. The molecular weights decreased as time in buffer increased. Despite the variation in salt loading, the basic trend in molecular weight decrease was similar in all salt systems except for the polymer blend system. The blend system utilized a low molecular weight excipient to hasten degradation, speed up release, and cause the film to degrade the fastest as the molecular weight no longer was measurable after 1 week in buffer. Figure 8 graphs the change in molecular weight over time for the five different systems. From the graph, it appears that soluble salts

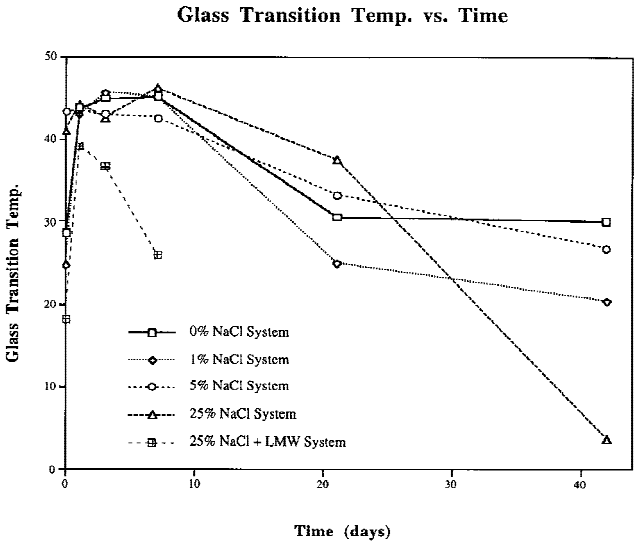

Figure 9. Graph of glass-transition temperature decrease over time for various NaCl-loaded PLA/PG control films.

added to the system have very little effect on molecular weight. It is evident from Table II that the tetracycline-loaded films follow the same pattern of molecular weight decrease as do the control films.

Thermal analysis

The glass transition temperature of the control films increased over the first few days, then showed dramatic decrease over the next few weeks. At day 7 the Tg was below the glass transition of PLGA. This correlated well with the time at which the molecular weight decreased significantly. However, pores were not visible on the control films under SEM at the 21 day point, which could be explained by the fact that the system collapsed due to the low Tg.

Samples of 1, 5, and 25% salt-loaded PLGA films, as well as the 25% salt-loaded high and low molecular weight blend, also were lyophilized and subjected to differential scanning calorimetry (DSC). Thermograms were analyzed for changes in glass-transition temperature, which would indicate film degradation. In Tables III and IV, one can see that very little change occurred in glass-transition temperature in the 1, 5, and 25% salt systems until the day 21, when the Tg fell below the glass transition of PLA/PG. This also is the time at which the molecular weight of these films as seen by GPC dropped dramatically and pores 10–50 microns in diameter were visible under SEM.

The 25% NaCl system with low molecular weight excipient dropped in Tg noticeably by 1 week, then hastily degraded to a point such that no further thermograms could be measured. This corresponded well with the low molecular weight of less than 4000 seen at 1 week for this system. Figure 9 depicts the change in glass transition over time for the various systems. As seen from Tables III and IV, the salt does not seem to impact the degradation of the various systems as the DSC results follow a similar trend.

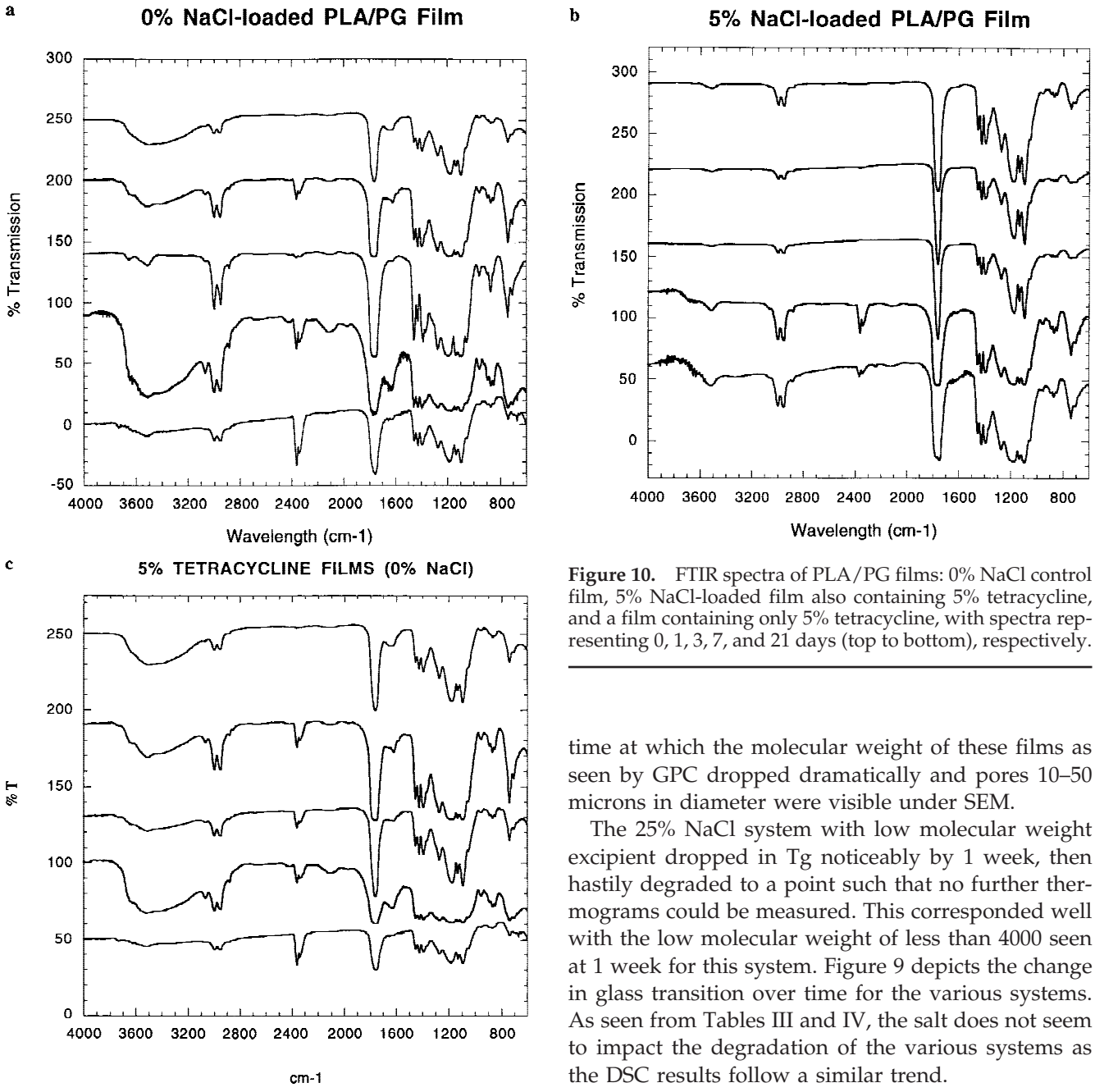

Figure 10. FTIR spectra of PLA/PG films: 0% NaCl control film, 5% NaCl-loaded film also containing 5% tetracycline, and a film containing only 5% tetracycline, with spectra representing 0, 1, 3, 7, and 21 days (top to bottom), respectively.

Fourier-transform infrared spectroscopy

FTIR spectra for the PLGA systems at 0, 1, 3, 7, and 21 days are shown in Figure 10 (a–c). The triplet of peaks appearing in the 1400–1500 cm^{-1} range are the characteristic peaks for lactic acid, glycolic acid, and PLGA, respectively. Despite the incorporation of either tetracycline or salt, no significant change was apparent in relative the sizes of the peaks in this area of the spectrum during the first day, indicating homogeneous degradation of the PLGA film [see Fig. 10 (a–c)]. The polymer composition has remained constant to this point. However, at 3 days, the relative peak size begins to change, with first the GA and then both the GA and PLGA peaks becoming shorter with respect to the LA peak than they were previously. This shows that the glycolic acid components of the polymer degraded faster than the lactic acid components.

A significant difference exists between the FTIR spectra of the films that do and do not contain salt. The group of peaks at 1000–1300 cm^{-1} is broad and rather undefined in the control films with 0% NaCl. However, in the films containing salt, the peaks in this range are sharp and distinct, evidence of a more crystalline system. Another difference between salt and non-salt-containing systems is the shoulder appearing at 1600 cm^{-1} in the control films. This shoulder does not appear in the systems containing salt, possibly due to the dissociation of the sodium chloride with the true carboxylic groups and formation of carboxylate.

X-ray diffraction

From the X-ray diffraction spectra of Figure 11(a), one can see that the characteristic peak for NaCl appears in the 32 range on the two-theta axis. The height of this peak increased in size as the loading of salt increased from 5% to 25%, indicating an increase in crystallinity. Likewise, pure PLA/PG polymer has its most pronounced peak appearing at 30, with smaller peaks at 25, 29, 36, 40, 43, 48, and 49 [see Fig. 11(b)]. Evidence of salt leaching and decrease in crystallinity was seen as the salt peak for both the 5% and the 25% systems decreased over time as the salt dissolved and washed out of the system (see Fig. 12, 13). This dramatic decrease in the peak appearing around 32 occurred at day 1, which indicates that salt dissolution began immediately upon introduction into the buffer solution. These occurrences are all most pronounced in the 25% salt system. However, in both systems the salt peak was still evident after 1 week in buffer, showing that not all of the salt leached out of the system immediately. The salt may have stabilized the system in some manner, leading to the modulated release that is visible in Figures 1 and 2.

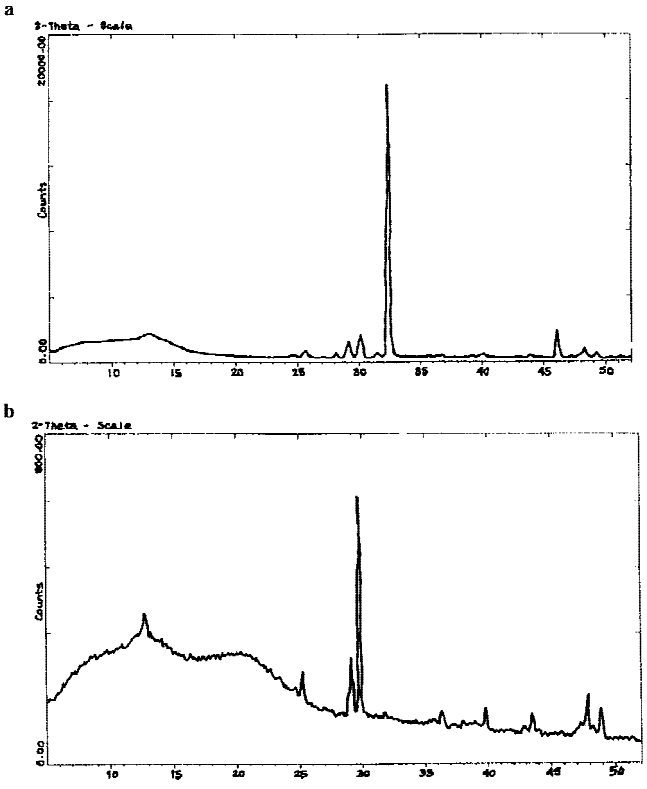

Figure 11. (a) X-ray diffraction spectrum for powderized NaCl; (b) X-ray diffraction spectrum for pure PLA/PG 50:50 (RG503, lot #223808, MW = 34,000).

Swelling experiments

To further elucidate the mechanism of action, we conducted swelling experiments on the PLGA films. Figures 14(a) and (b) graph the percentage of the original film weight as a function of incubation time in PBS buffer at physiologic temperature over the long term and short term, respectively. The 0% NaCl control films remained very close to their original weight throughout the 50 h. However, all salt-containing systems jumped up to at least 200% of their original weight within 1 h upon introduction into buffer. This is equivalent to a 100% gain in weight. All systems maintained this ''swollen'' state for the duration of the study (almost 500 h). The salt appeared to have a significant impact on water uptake into the system, especially during the initial hours when the majority of the salt still was trapped in the system. This phenomenon also may have been responsible for the modulated release of tetracycline as the water that was pulled into the system by the salt may have forced out the hydrophobic tetracycline as it entered.

SUMMARY

The above data suggest that although the addition of soluble salts to PLGA film formulations does not

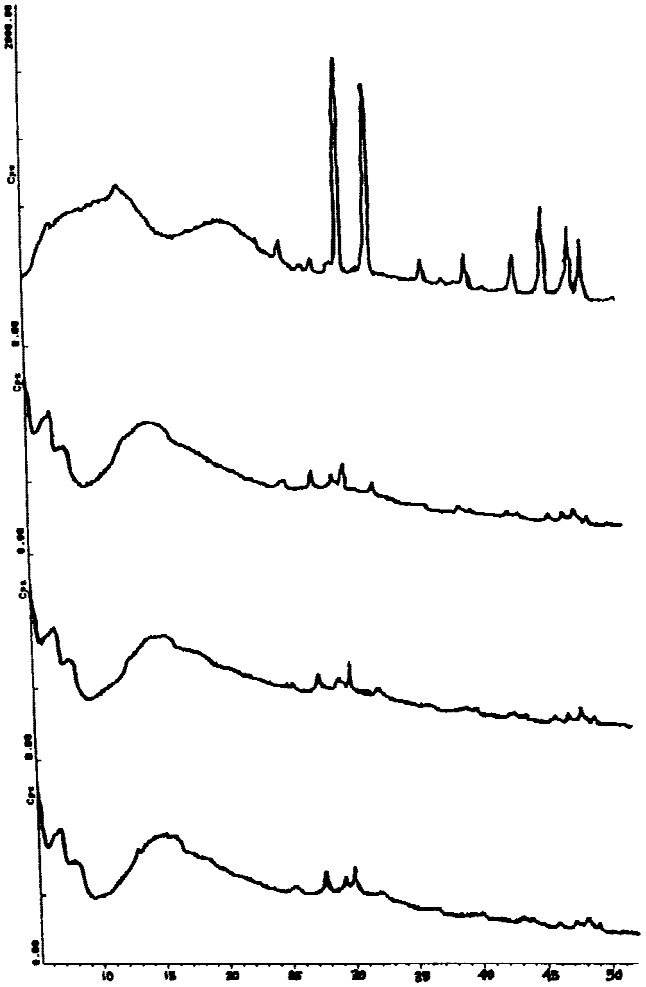

Figure 12. X-ray diffraction spectra of 5% NaCl system at 0, 1, 3, and 7 days (top to bottom) after being submerged in PBS buffer.

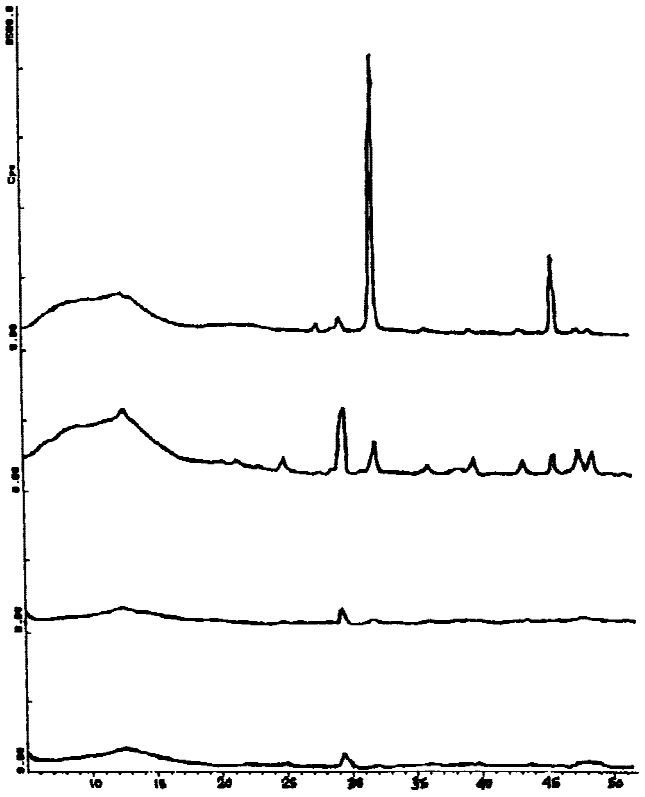

Figure 13. X-ray diffraction spectra of 25% NaCl system at 0, 1, 3, and 7 days (top to bottom), respectively, after being submerged in PBS buffer.

affect overall trends of degradation, as seen in molecular weight and glass transition decrease, it does accomplish significant modulation of tetracycline release. Here, drug-release modulation was achieved via the addition of various concentrations of soluble salts to the system, increased salt loading resulting in increased initial drug release, as seen in Figures 1 and 2. The three-phase release profile typical of PLGA systems disappeared, which makes the technology more desirable for controlled drug delivery systems. Overall, the morphological changes, molecular weights, and glass transition temperatures over time were very similar in the various systems despite differences in salt concentration. This indicates that the salt content may have a negligible effect on the degradation and maintenance of structural integrity of the films in the documented 6-week period after immersion in PBS buffer although FTIR spectra did show the salt systems to be more crystalline than the systems without salt. X-ray diffraction techniques proved vital in showing the presence of salt in the system for at least 1 week. This was a crucial piece of data in showing that although some of the salt does come out within the first 24 h, there is evidence that salt remained trapped in the system beyond 7 days.

Incorporation of the salt dramatically increased the amount of swelling and uptake of buffer by the films. Uptake, therefore, may be creating more pores that are not necessarily visible yet permit further diffusion of tetracycline from the polymer matrix. The fact that the salts did not affect film degradation can be explained by the formation of these pores by the salts, preventing the accumulation of acids within the film by providing these acids with an outlet. Accumulation of acids has been known to participate in the phenomenon of autocatalysis when the carboxylic acid endgroups catalyze the cleavage of main-chain ester bonds. In our system, the leaching out of salts led to increased pore formation, which allowed the free monomers to leave the system.

The addition of low molecular weight PLGA excipient into degradable PLGA polymer films sped up film degradation, as observed via DSC and GPC, as well as the formation of pores, visually observed on SEM. Molecular weights and glass transition temperatures visibly decreased over time faster than the 0% NaCl controls as the films incubated in PBS buffer. Addition of the low molecular weight excipient, as evidenced in

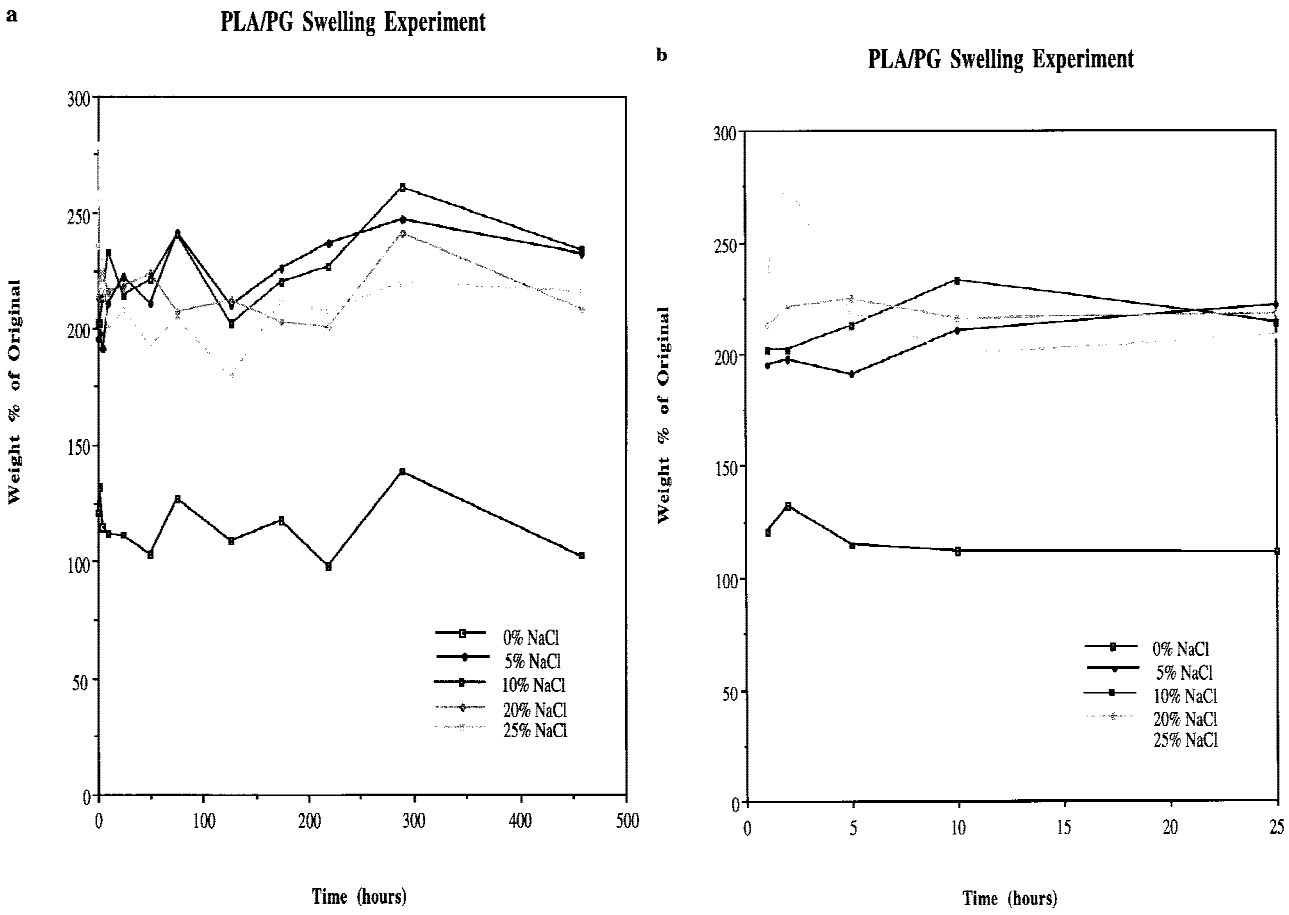

Figure 14. (a) Swelling data of PLA/PG films over a period of 500 h; (b) swelling data of PLA/PG films over a period of 25 h.

the high and low molecular weight blend system, appeared to hasten pore formation and overall structural degradation as well as increase the release rate of the antibiotic. The increased release rate is attributed to the increased plasticity due to the presence of the lower molecular weight species.

This technology is an ideal way to manipulate the polymer degradation and release of therapeutics from films that are nontoxic, biocompatible, and malleable for easy insertion into the periodontal pocket. Degradation and drug release rates can be modulated and controlled by adding soluble salt excipients as well as low molecular weight excipients to the polymer system. Another benefit to adding salt to the system is its frequent use in postdental work hygiene as it is helpful in killing harmful oral bacteria and maintaining low plaque levels. This technology most likely will be useful in many other future applications of drug delivery, but it is especially beneficial for 1-month delivery systems where the goal is to deliver a therapeutic for 30 days and then have the delivery system degrade.

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