Formation of Antibiotic, Biodegradable/Bioabsorbable Polymers by Processing with Neomycin Sulfate and Its Inclusion Compound with β-Cyclodextrin

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ABSTRACT: Samples of pure neomycin sulfate and its inclusion compound (IC) with β-cyclodextrin were implanted into films of poly(L-lactic acid) (PLLA) and poly(ε-caprolactone) (PCL). Both polymers have been widely used commercially to make sutures. The antibacterial activity of these films against *Escherichia coli* was tested. Films made by either solution casting or melt pressing were divided into the following three groups: (1) plain polymer films, (2) those embedded with pure neomycin sulfate, and (3) those embedded with neomycin sulfate-β-cyclodextrin IC. Filter paper treated with 1.5 μL of 10 mg/μL Kanamycin and neomycin were used as controls and resulted in 11- and 8-mm zones of inhibition/or antibacterial activity, respectively. Small discs (ca. 2% of total area) cut from solution-cast films of PLLA and PCL containing 50 wt % neomycin sulfate IC had 17- and 16-mm zones of inhibition, and PLLA and PCL containing 50 wt % pure neomycin sulfate deterred bacterial growth, resulting in 19-mm zones of inhibition. Melt-pressed films containing 10 wt % pure neomycin sulfate or its IC, showed 17- and 11-mm zones of inhibition for PLLA films, respectively, while PCL films showed 13- and 9-mm zones of inhibition, respectively. For melt-pressed films that contain 0.01 wt % pure neomycin sulfate or its IC, PLLA films showed 11- and 9.5-mm zones of inhibition, respectively, while PCL films showed 11- and 10-mm zones of inhibition, respectively. Since an antibiotic, bioabsorbable suture does not require surgical removal, implanting an inclusion compound in the suture might allow the slow release of antibiotic, thereby guarding against postsurgical infection and also protecting the antibiotic from degradation during the melt-spinning process used to make the suture. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 74: 937–947, 1999

INTRODUCTION

In recent years, aliphatic polyesters have been widely studied for biomedical applications, such as synthetic absorbable sutures. Surgical sutures are sterile filaments used to close wounds and provide support during the healing process. The ideal suture normally would have many demanding characteristics. For example, the suture would initially have high tensile strength to provide support to the tissues, it would be biocompatible to minimize tissue reaction, it would be sterilizable by conventional methods to eliminate all microorganisms, it would be absorbable to avoid a second intrusion, it would be nonabrasive to minimize tissue tear, it would be easily stored

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to reduce preoperative handling complexities, and, also, it would be easy to manufacture and have a low cost.[1]

The earliest sutures were obtained from natural and often exotic materials, like beetle heads and the jaws of giant ants. The most common materials used for the earliest sutures were metal wire and natural fibers, such as cotton, linen, and silk. They are not used extensively today since they are natural fibers, making control of diameter and strength uniformity difficult, and requiring special processing before use. Also, they either show significant tissue reaction during *in vivo* degradation since they are nonabsorbable or they cause severe mechanical irritation to the tissue due to their stiff, sharp edges.

Synthetic nonabsorbable fibers, such as polyamides, polyesters, and polyolefins, were introduced during the 1950s and 1960s. They did not degrade over a long period of time, so they had virtually constant tensile properties *in vivo* and were more compatible with human tissues compared to natural fibers. Polyamides were the first completely synthetic fibers employed as sutures, but they still have lots of disadvantages. For example, polyamide sutures produce a mild tissue reaction after several months *in vivo* and may eventually require surgical removal because of their nonbioabsorbable properties.

Synthetic absorbable sutures emerged after Kulkarni et al.[2,3] reported in 1966 that poly(lactic acid) (PLLA) was found to be an absorbable, nontoxic, and nonirritating synthetic material suitable for sutures and other surgical implants. As expected from a controlled synthetic material, PLLA shows more predictable behavior than natural sutures. Also, PLLA was shown to undergo hydrolytic scission to lactic acid, a natural metabolite in the glycolytic cycle of carbohydrate metabolism. These discoveries led to the investigation of polyester fibers derived from lower α-hydroxy acids that have suitable mechanical and biological properties.

Current research has been focused toward modifying existing absorbable polymers and developing new polymers from proven nontoxic absorbable monomers. There are limited types of absorbable suture materials. Only certain chemical linkages have the potential for being absorbable and nontoxic. In order to be nontoxic, the degradation products should also be nontoxic, low-molecular-weight residues, which can be eliminated from the body or metabolized in the body to natural products. Polymers containing acetals and esters linkages along the backbone

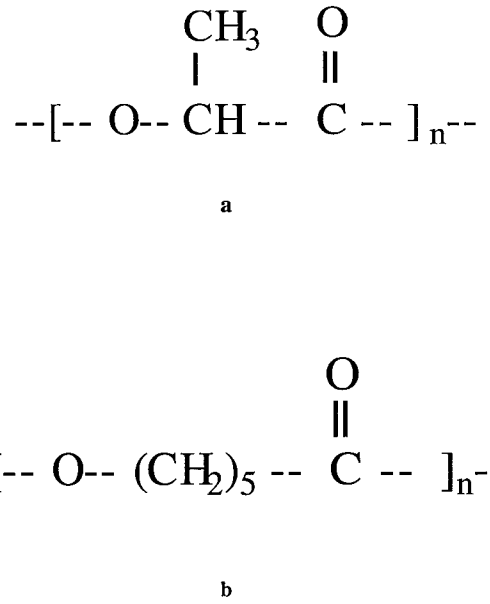

Figure 1 The chemical structures for poly(L-lactic) acid (PLLA) and poly(ε-caprolactone) (PCL).

are currently the materials widely used for absorbable sutures.

In 1966, Kulkarni et al.[2,3] first reported the potential of PLLA for bioabsorbable surgical devices. Since the degradation product of poly(L-lactic acid) (PLLA) is L-lactic acid, a normal intermediate of carbohydrate metabolism, it was reasoned that PLLA would be suitable for suture materials. Since PLLA is highly crystalline and has a high glass transition temperature of 67°C, it is stiff at body temperature.

Poly(ε-caprolactone) (PCL) is an aliphatic polyester, which has been proven to degrade by a hydrolytic mechanism under physiological conditions.[4] Compared to PLLA, PCL is a semicrystalline polymer, and it is unique in that it has a low T_g of −60°C. Hence, it is in a leathery state at body temperature. It degrades significantly slower than PLLA, which has made if suitable for long-term, implantable drug-delivery systems.

PCL and PLLA were selected as model polymers of aliphatic polyesters in our current study. Their chemical structures are shown in Figure 1. Both have gained popularity because of their biocompatible and bioabsorbable properties.

A six-month prospective surveillance conducted by the department of General Surgery at the Rio de Janeiro University Hospital reported a significant rate (16.9%) of surgical site infections detected by surveillance in a series of surgical interventions where 45% were classified as clean.[5] The majority (52.7%) of these bacterial

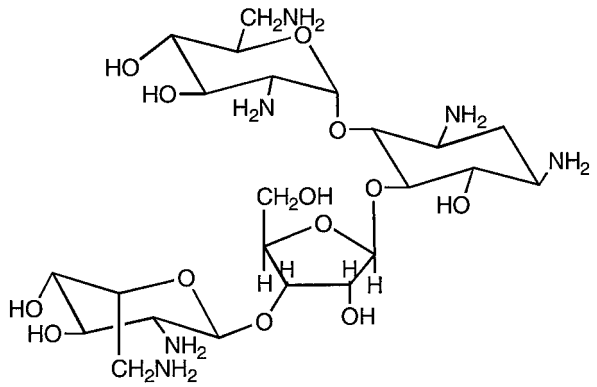

Figure 2 The chemical structure for neomycin sulfate.

infections were only apparent after patients were discharged from the hospital. Bacterial cultures were obtained from 42 out of 55 infected wounds. *Staphylococcus aureus* was the most frequently found pathogen (33.9%), followed by *Escherichia coli* (*E coli*) (20.3%).

A study performed by Medetbekov[6] on animal bite victims showed *E coli* and *Staphylococci* to be the most common causes of bacterial infections. *E coli,* the bacterium used during this experiment, is associated with intestinal and urinary infections. It is a multipotent pathogen that could cause disease in several body systems.[7]

The methods currently available for the administration of antibiotics after operations are oral, intravenous injections with a long-term in-dwelling catheter, and local implants of antibiotic poly(methylmethacrylate) beads.[8] These methods have disadvantages. The intravenous injection requires an operation for catheter placement, and, along with oral administration, requires multiple daily antibiotic doses. Complications with the intravenous catheter are infection and catheter failure. Poly(methylmethacrylate) beads alone usually provide local, effective antibacterial levels of antibiotics for only 2–4 weeks and require a second operation for their removal.[7]

Neomycin sulfate ($C_{23}H_{46}N_6O_{13} \cdot 3H_2SO_4$) is an antibiotic discovered by Waksman and Lechevalier in 1949 from a strain of Streptomyces fradiae.[7] It is a water-soluble, amorphous aminoglycoside effective against gram-negative and gram-positive bacteria, mycobacteria, and actinomycetes. It inhibits protein synthesis by binding to the small subunit of prokaryotic ribosomes. Also, it is comparatively nontoxic, the 50% lethal dose (LD50) in mice being 220 mg/kg when given subcutaneously. Neomycin sulfate is one of the active ingredients in market antibiotics, such as Neosporin™. The chemical structure of neomycin sulfate is shown in Figure 2, and some properties are listed in Table I.

Lebedev's 4-year study using bioabsorbable surgical sutures containing neomycin sulfate showed that the antibacterial properties are retained for 2 months in the body tissue.[9] When bioabsorbable, cordlike sutures are used to sew up wounds, they may be dissolved into the patient's blood stream after wounds have closed and begin to heal, leaving no need for further surgical removal. Because sutures dissolve, the wounds slowly fill with tissue, so there is no need for reconstructive surgery.

Certain molecular hosts, such as urea, thiourea, perhydrotriphenylene, and cyclodextrins (CDs), can form crystalline inclusion compounds (ICs) during their cocrystallization with appropriate guest molecules.[10–13] The IC host molecules crystallize into a three-dimensional lattice that surrounds and isolates the included guest molecules into well-defined cavities. These IC crystals may be thought of as host molecule crystalline containers, whose contents are the included guest molecules. Both small-molecule and polymer guests may be included in ICs. The included guest molecules are kept isolated from the environment except when the IC crystals are disrupted by melting or dissolution, or when ICs are embedded in a biodegradable carrier polymer phase, and the included guest molecules can be slowly released, suggesting great potential applications in the controlled release area.

Cyclodextrin ICs formed with low-molecular-weight guests can either have channel or cage structures. Figure 3 presents the chemical structures for β-cyclodextrin, and Figure 4 presents the schematic descriptions of channel type, cage herringbone-type and cage-brick-type cyclodextrin IC crystal structures.[14] The average diameter of cyclodextrins' doughnut-shape cavity is 7.0 Å for β-cyclodextrin. In channel structure ICs, the

Table I Properties of Neomycin Sulfate

Properties	Neomycin Sulfate
Form	Off-white solid
Molecular weight	908.9
Melting point	Indefinite (turns to charcoal on heating)
LD_{50} in mice	220 mg/kg given subcutaneously
Solubility in water	20 mg/mL

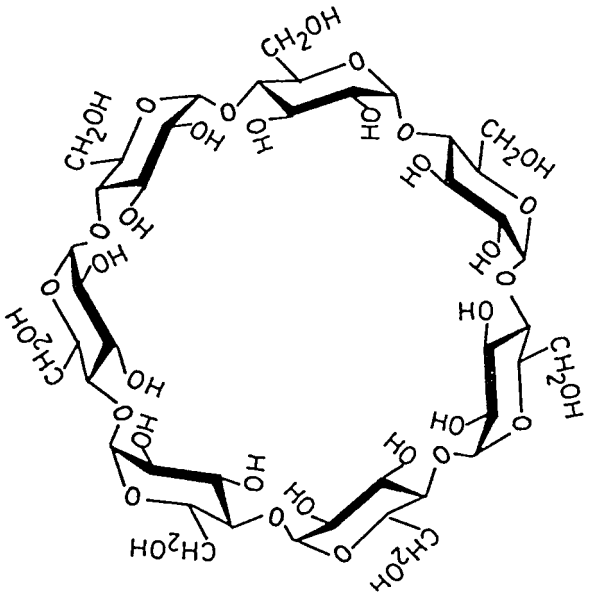

Figure 3 The chemical structure for β-cyclodextrin.

cyclodextrin rings are stacked on top of each other to produce cylindrical central cavities; in cage structures, the cavity of one cyclodextrin molecule is closed on both sides by adjacent molecules. Mole ratios of host cyclodextrin and guest molecule will depend on the size of the molecule and on the extent to which the CD channels are filled.

Sutures made with a neomycin sulfate IC may provide extended bactericidal concentration of the antibiotic for the prolonged time needed to completely prevent the particular infection. In the present report, we describe our research results concerning biodegradable antibiotic sutures made with PLLA, PCL, and neomycin sulfate–β-CD–IC, having the potential to provide improved treatment methods for the long-term administration of antibiotics for infections.

EXPERIMENTAL

Materials

PLLA and PCL pellet samples with molecular weights of approximately 285 and 40 kg/mol were obtained from Research Triangle Institute and Aldrich Chemical Company, respectively.

A neomycin sulfate powder sample was purchased from Calbiochem Company, and β-cyclodextrin was obtained from CERESTAR Company.

Preparation of Neomycin Sulfate IC Sample by Solution Heating Technique

3.0 g of β-cyclodextrin (β-CD) were added into a beaker containing 50 mL of distilled water and put onto a hot plate at 70°C until dissolved. 1.2 g of neomycin sulfate were added to a beaker containing 10 mL of distilled water and placed on a hot plate at 70°C until dissolved. Then, the neomycin sulfate solution was dripped into the β-CD and heated at 70°C for 3 h to form an IC. The beaker was taken off the hot plate and set overnight. The IC crystal product formed by the neomycin sulfate, and β-CD was filtered and dried in a vacuum oven. The dried product was crushed into a fine powder.

X-Ray Diffraction Characterization

Wide-angle X-ray diffraction (WAXD) patterns of powder samples were obtained at ambient conditions on a Siemens type-F X-ray diffractometer with a nickel-filtered CuKa radiation source (wavelength = 1.54 Å). The supplied voltage and current were set to 30 kV and 20 mA respectively. Samples were mounted on a sample holder with Scotch tape, and the diffracting intensities were recorded every 0.05° from 2θ scans in the range of 5–40°.

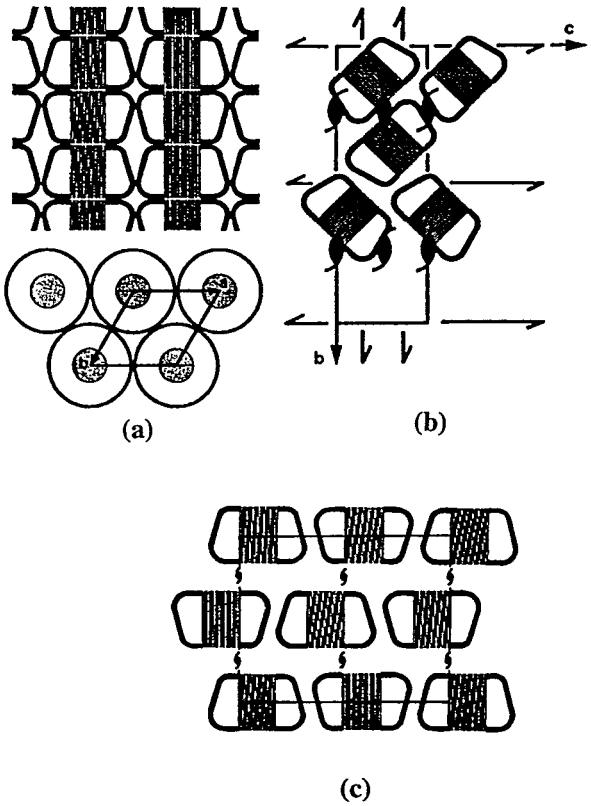

Figure 4 Schematic description of (a) channel-type, (b) cage-herringbone-type, and (c) cage-brick-type crystal structures formed by crystalline cyclodextrin inclusion complexes.

Table II Parameters Used to Study IC-Embedded Polymer Films by Video Microscopy

Parameter	Measurement
Amplifier	2.0X
Supplementary objective lens	2.0X
Magnification	46.3–324X
Field diameter	5–0.72 mm
Working distance	36 mm
Field depth	0.28–0.01 mm

Film Preparation

Solution Casting Technique

0.15 g of each of the polymer pellets (PCL or PLLA) were dissolved in 10 mL of dichloromethane on a hot plate at 60°C while stirring. Then, 0.15 g (50 wt %) of pure neomycin sulfate or neomycin sulfate–β-CD–IC samples were added individually to petri dishes. The polymer solution was pipeted into the bottom half of the glass petri dishes. Finally, air evaporation of the solvent in a hood was used to form the very thin and uniform neomycin sulfate or neomycin sulfate–β-CD–IC embedded polymer films. Two plain polymer films were made the same way without embedding neomycin sulfate or neomycin sulfate–β-CD–IC.

Melt Pressing Technique

A Carver Laboratory Press (Model B) was used along with a 3.5-in-diameter thin die, which was supported by two smooth stainless steel plates covered with aluminum foil, to melt and press PLLA and PCL pellets with 0.15 g (10 wt %) or 0.15 mg (0.01 wt %) pure neomycin sulfate or neomycin sulfate–β-CD–IC powder samples at 180 and 80°C, under 5000 lb/in^2 pressure for 30 s. Thin and uniform PLLA and PCL films with pure neomycin sulfate or neomycin sulfate–β-CD–IC were obtained. Two plain polymer films were made the same way without embedding neomycin sulfate or neomycin sulfate-β-CD–IC.

Film Thickness Test

Film thickness was determined using a THWING-ALBERT Electric Thickness Tester Model II. A 0.63 in^2 pressure foot weighing 468.18 g rests on the film for a predetermined time span and records a thickness to within 0.01 mils. For each individual film, the thickness was tested six times along the length of the film, and an average thickness was reported.

Morphology Study by Optical Microscope

A Bausch & Lomb Video Optical Microscope was used to study the morphology of neomycin sulfate–IC embedded polymer films at low magnification. Table II lists the parameters that were used.

Bacterial Testing

A bacterial agar culture was marked off with an eight-division template. The culture was swabbed with *E coli*. A disc sample of each film, which was approximately 1/50th of the original film sample size, was punched out with a sterilized office hole puncher and placed onto each region. Blank sterilized filter paper disks impregnated with 0, 0.75, 1.5, and 3.0 μL of 10 mg/μL aqueous solutions of Kanamycin (Sigma Chemical) or Neomycin Sulfate were used as controls. The culture was maintained at 37°C for 18–24 h; and each film sample was measured for its zone of inhibition, which is the area around the disc that did not have bacterial growth. A digital camera was used to photograph the resulting agar cultures and their zones of inhibition.

RESULTS AND DISCUSSION

Figure 5 presents the comparison of WAXD patterns observed for β-CD, neomycin sulfate, a β-CD and neomycin sulfate physical mixture, and neomycin sulfate–β-CD–IC at room temperature from $2\theta = 5$ to 40°. From the WAXD pattern of neomycin sulfate [Fig. 4(b)], we observed two broad peaks centered around 10.5 and 19.5° (2θ), which indicate that pure neomycin sulfate is an

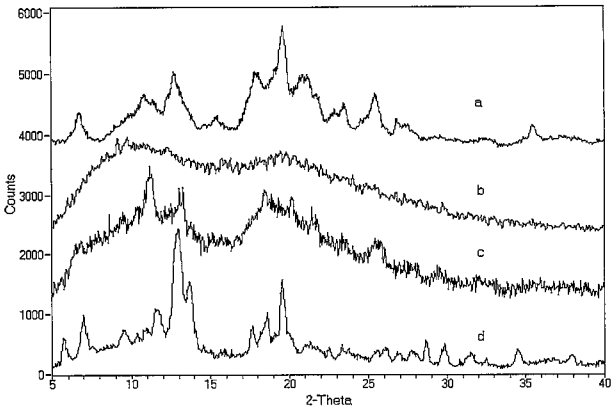

Figure 5 Wide-angle X-ray diffraction of (a) β-CD, (b) neomycin sulfate, (c) the physical mixtures of β-CD and neomycin sulfate, (d) neomycin sulfate–β-CD–IC.

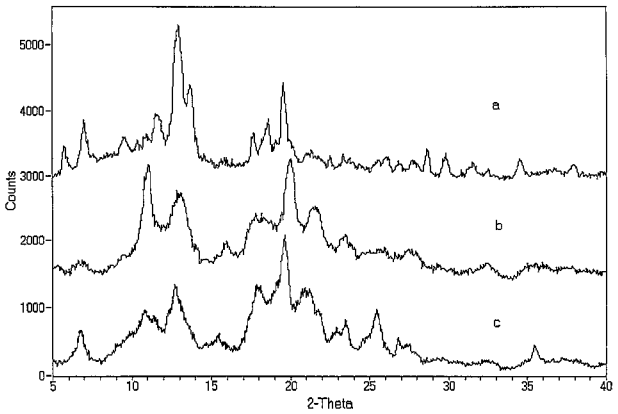

Figure 6 Wide-angle X-ray diffraction of (a) neomycin sulfate–β-CD–IC, (b) 1-propanol–β-CD–IC, and (c) β-CD · $12H_2O$.

amorphous sample. The neomycin sulfate–β-CD–IC showed a diffraction pattern quite different from the diffractogram of β-cyclodextrin, and this constitutes primary evidence that a different crystal type was formed.

Because of the relatively bulky structure for neomycin sulfate, we expect the cage-type of IC structure for its CD–IC sample.[15] Figure 6 shows the X-ray patterns of β-CD · $12H_2O$ (c) and the complexes of β-CD with neomycin sulfate (a) and with 1-propanol (b). Although it is seen that all the samples are crystalline and are all different from each other, the pattern of the neomycin sulfate–β-CD–IC is more similar with β-CD · $12H_2O$, which was reported to be a cage crystal structure, but is less similar to that of the complex with 1-propanol, which has been proven to have a channel structure by the X-ray study of their single crystal complexes. We may need to further study β-CD–IC because of its complicated diffraction pattern. Our results[15] indicate, however, that the neomycin sulfate–β-CD–IC sample exhibits a packing somewhat different from that of free β-CD.

The thickness study results of all polymer films embedded with/without pure neomycin sulfate or neomycin sulfate–β-CD–ICs are included in Tables III–V. It has been found that ultrathin (0.02–0.03 mm thickness) and uniform plain PLLA and PCL films were made by the solution-casting technique, compared to 0.18–0.29 mm plain PLLA and PCL films made by the melt pressing technique. On the other hand, PLLA and PCL films embedded with neomycin sulfate or neomycin sulfate–β-CD–IC by melt-pressing were in the range of 0.20–0.45 mm thick, compared to those produced by solution casting, which were around 0.29–0.79 mm thick.

Micrographs of the film samples embedded with/without pure neomycin sulfate or neomycin sulfate–β-CD–ICs are presented in Figures 7 and 8. The neomycin sulfate domains are approximately 200 μm in size, and the neomycin sulfate–β-CD–IC domains are approximately 50–200 μm in size.

Kanamycin ($C_{18}H_{36}N_4O_{11}$), which has a structure similar to neomycin, is also a common anti-

Table III Comparison of Thickness and Zone of Inhibition of Solution-Cast PLLA and PCL Films Embedded with/without 50 wt % Neomycin Sulfate or Neomycin Sulfate IC

Disc Samples Punched from Filter Paper and PLLA, PCL Films	Average Thickness (mm)	Zone of Inhibition Diameter (mm)
Filter paper disc with 0 mg of kanamycin	0.18	0
Filter paper disc with 7.5 mg of kanamycin	0.18	11
Filter paper disc with 15 mg of kanamycin	0.18	13
Filter paper disc with 30 mg of kanamycin	0.18	14
Filter paper disc with 0 mg of neomycin sulfate	0.18	0
Filter paper disc with 7.5 mg of neomycin sulfate	0.18	8
Filter paper disc with 15 mg of neomycin sulfate	0.18	9
Filter paper disc with 30 mg neomycin sulfate	0.18	12
Pure PLLA disc	0.02	0
Pure PCL disc	0.03	0
PLLA disc with 50 wt % of pure neomycin sulfate	0.79	19
PCL disc with 50 wt % of pure neomycin sulfate	0.49	19
PLLA disc with 50 wt % of pure neomycin sulfate IC	0.39	17
PCL disc with 50 wt % of pure neomycin sulfate IC	0.29	16

Table IV Comparison of Thickness and Zone of Inhibition of Melt-Pressed PLLA and PCL Films Embedded with/without 10 wt % Neomycin Sulfate or Neomycin Sulfate IC

Disc Samples Punched from Filter Paper and PLLA, PCL Films	Average Thickness (mm)	Zone of Inhibition Diameter (mm)
Filter paper disc with 0 mg of kanamycin	0.18	0
Filter paper disc with 7.5 mg of kanamycin	0.18	11
Filter paper disc with 15 mg of kanamycin	0.18	13
Filter paper disc with 30 mg of kanamycin	0.18	14
Filter paper disc with 0 mg of neomycin sulfate	0.18	0
Filter paper disc with 7.5 mg of neomycin sulfate	0.18	9
Filter paper disc with 15 mg of neomycin sulfate	0.18	10
Filter paper disc with 30 mg neomycin sulfate	0.18	11
Pure PLLA disc	0.20	0
Pure PCL disc	0.18	0
PLLA disc with 10 wt % of pure neomycin sulfate	0.25	17
PCL disc with 10 wt % of pure neomycin sulfate	0.20	13
PLLA disc with 10 wt % of pure neomycin sulfate IC	0.45	11
PCL disc with 10 wt % of pure neomycin sulfate IC	0.21	9

bacterial agent used against *E coli*. It is a water-soluble broad-spectrum aminoglycoside antibiotic produced during fermentation by *Streptomyces kanamyceticus*. It has a narrow therapeutic range and is potentially oto- and nephrotoxic, like other aminoglycosides. Its chemical structure is shown in Figure 9.

In the bacterial tests, filter paper treated with 1.5 μL of 10 mg/μL aqueous solutions of kanamycin and neomycin were used as controls and resulted in 11- and 8-mm zones of bacteria growth inhibition, respectively. The pure PLLA and PCL discs both made by solution-casting and melt-pressing techniques did not deter bacterial growth.

Both PLLA and PCL discs cut from films impregnated with 50.0 wt % pure Neomycin Sulfate were antibacterial resulting in 19-mm zones of inhibition. The PLLA and PCL discs cut from films impregnated with 50 wt % neomycin sulfate IC, which are estimated by molar ratio in neomycin sulfate–β-CD–IC to have approximately only half as much effective component; neomycin sulfate inside, also deterred *E coli* growth, the PLLA film with a 17-mm zone of inhibition and the PCL film a 16-mm zone of inhibition (see Fig. 10 and Table III).

The PLLA and PCL films made by the melt-pressing technique also show similar results. (see Fig. 11 and Table IV). The PLLA and PCL

Table V Comparison of Thickness and Zone of Inhibition of Melt-Pressed PLLA and PCL Films Embedded with/without 0.01 wt % Neomycin Sulfate or Neomycin Sulfate IC

Disc Samples Punched from Filter Paper and PLLA, PCL Films	Average Thickness (mm)	Zone of Inhibition Diameter (mm)
Filter paper disc with 7.5 mg of kanamycin	0.18	11
Filter paper disc with 7.5 mg of neomycin sulfate	0.18	9
Pure PLLA disc	0.20	0
Pure PCL disc	0.18	0
PLLA disc with 0.01 wt % of pure neomycin sulfate	0.25	11
PCL disc with 0.01 wt % of pure neomycin sulfate	0.21	11
PLLA disc with 0.01 wt % of pure neomycin sulfate IC	0.23	9.5
PCL disc with 0.01 wt % of pure neomycin sulfate IC	0.20	10

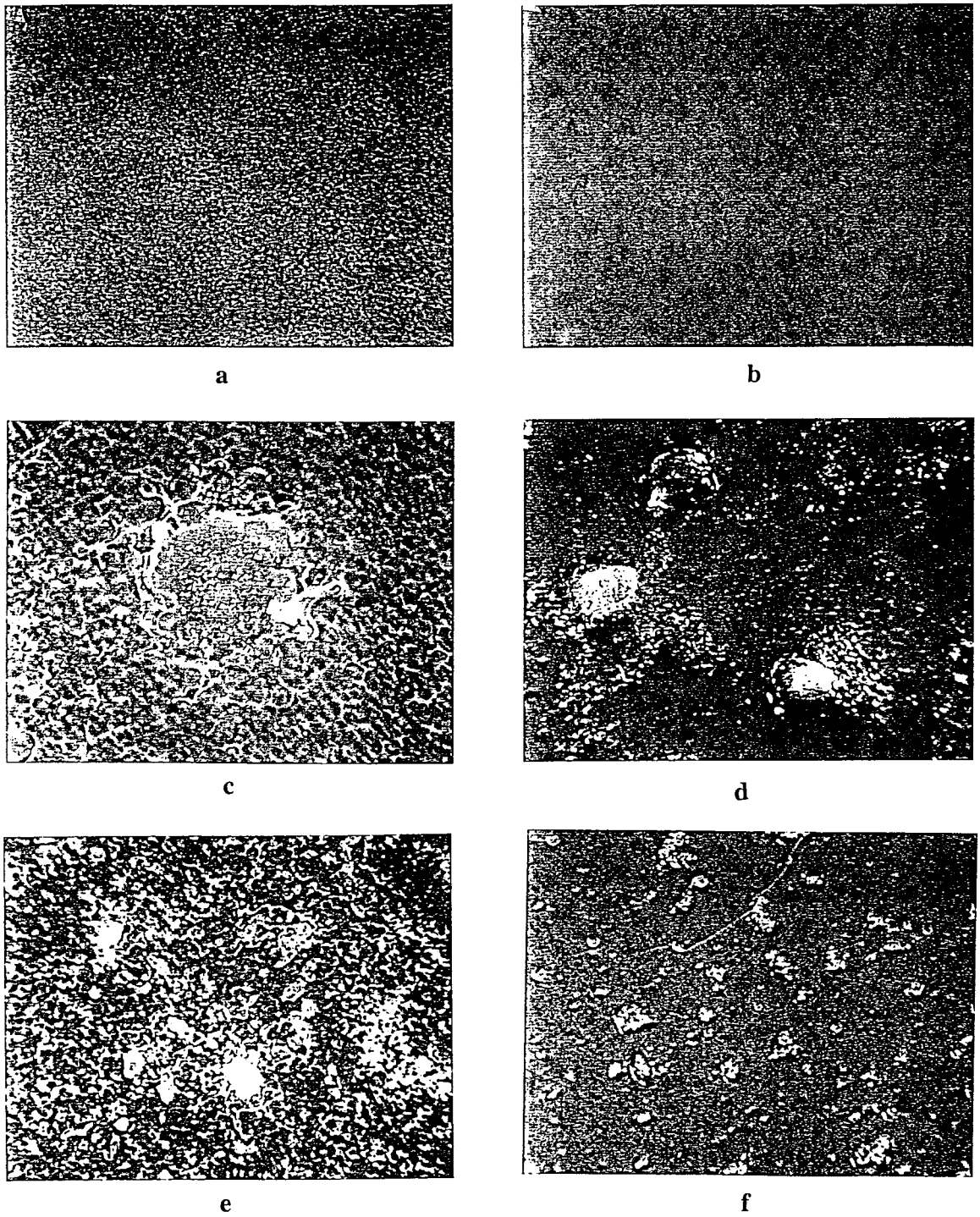

Figure 7 Low magnification (70X) micrographs of solution-cast films: (a) pure PCL, (b) PLLA, (c) embedded with neomycin sulfate PCL, and (d) PLLA and embedded with (e) neomycin sulfate–β-CD–IC PCL and (f) PLLA.

discs cut from films impregnated with 10 wt % pure neomycin sulfate deterred *E coli* growth, the PLLA film with a 17-mm zone of inhibition and the PCL film with a 13-mm zone. The PLLA and PCL discs cut from films impregnated with 10.0 wt % neomycin sulfate IC, which have only half as much neomycin sulfate inside as the effective component, were also antibacterial, resulting in 11- and 9-mm zones of inhibition, respectively.

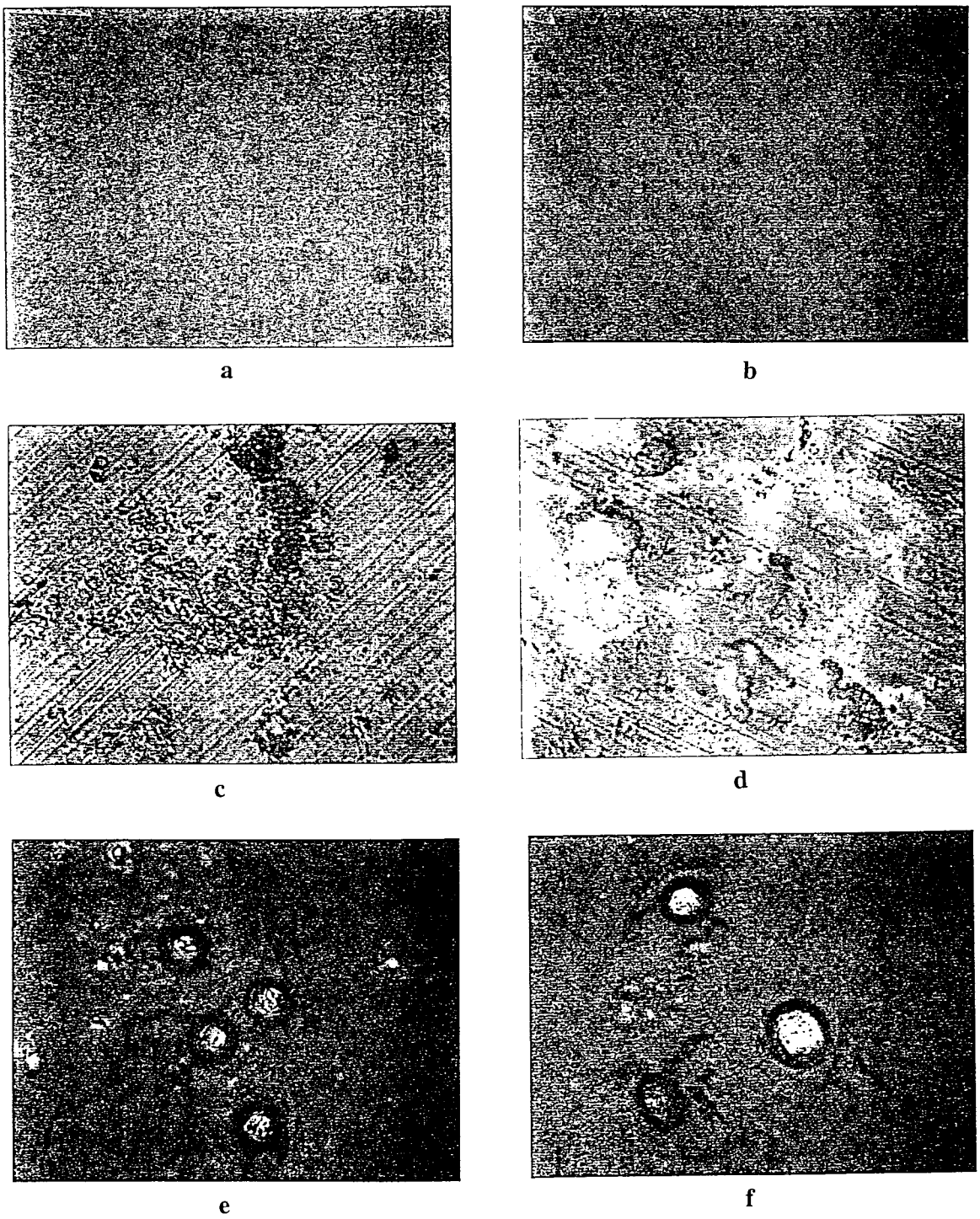

Figure 8 Low magnification (70X) micrographs of melt-pressed films: (a) pure PCL, (b) PLLA, (c) embedded with neomycin sulfate PCL, and (d) PLLA and embedded with (e) neomycin sulfate–β-CD–IC PCL and (f) PLLA.

In order to study the potential of reducing the manufacturing cost of using IC technology in industrial applications and to ensure that the same high strength and desirable physical properties were maintained after embedding, films embedded with a much lower concentration (0.01 wt %) of pure neomycin sulfate and neomycin sulfate IC were made by melt pressing, and their bacterial

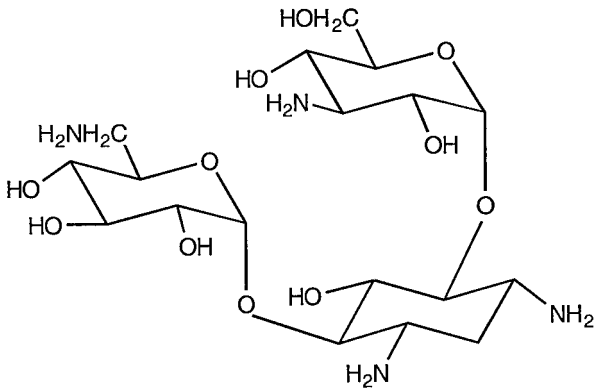

Figure 9 The chemical structure for kanamycin.

test results are shown in Table V. We can see that they still show very good antibiotic properties, based on their zones of inhibition. Both PLLA and PCL discs cut from films impregnated with 0.01 wt % pure neomycin sulfate were antibacterial, resulting in 11-mm zones of inhibition. The PLLA and PCL discs cut from films impregnated with 0.01 wt % of neomycin sulfate IC, but containing only half as much neomycin sulfate, also deterred *E coli* growth, the PLLA film with a 9.5-mm zone of inhibition and the PCL film with a 10-mm zone of inhibition.

Other than the use of fibrinogen and plaster of paris, there are few studies on the use of antibiotics administered by biodegradable implants.[15] The hypothesis that a neomycin sulfate IC will deter the growth of *E coli* is supported by the results shown in Tables III–V. Although the films with pure neomycin sulfate were also effective against deterring *E coli,* the neomycin sulfate IC films that deterred bacteria allow the possibility of the slow release of antibiotics by having the antibiotic in a cyclodextrin IC. Formation of the

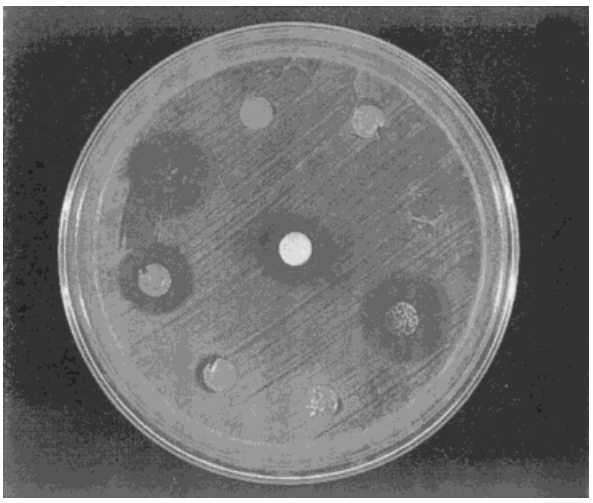

Figure 10 Zones of inhibition of *E coli* bacterial growth in cultures containing discs cut from PLLA and PCL solution-cast films embedded with/without 50 wt % neomycin sulfate or neomycin sulfate–β-CD–IC.

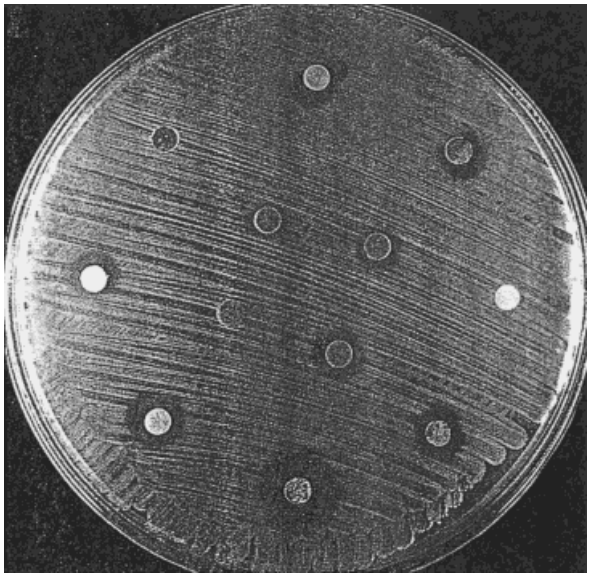

Figure 11 Zones of inhibition of *E coli* bacterial growth in cultures containing discs cut from PLLA and PCL melt-pressed films embedded with/without 10 wt % neomycin sulfate or neomycin sulfate–β-CD–IC.

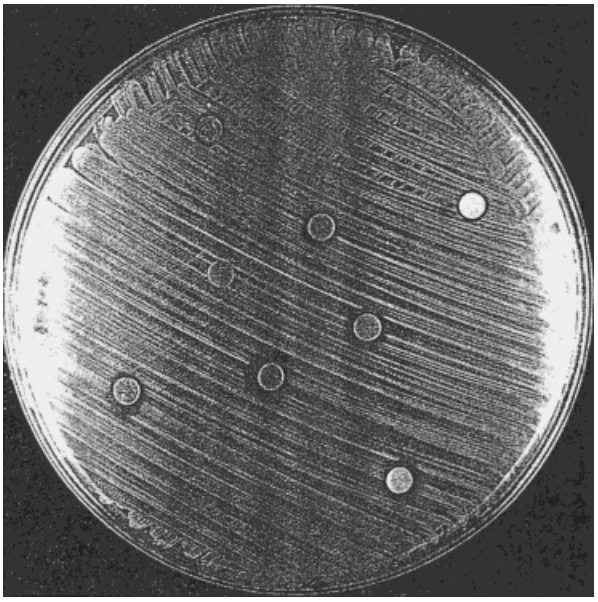

Figure 12 Zones of inhibition of E coli bacteria growth in cultures containing discs cut from PLLA and PCL melt-pressed films embedded with/without 0.01 wt % neomycin sulfate or neomycin sulfate–β-CD–IC.

drug IC can also serve to protect the drug during processing; and other drugs, in addition to antibiotics, could also be administered in the form of their ICs.

CONCLUSION

In summary, we report that, for the first time, neomycin sulfate–β-cyclodextrin–IC was successfully made by a heating technique and has a different crystal structure than pure β-cyclodextrin. Neomycin sulfate has been included inside the IC cavities provided by β-cyclodextrin molecules, resulting in the protection of neomycin sulfate from high-temperature manufacturing film-pressing and fiber-spinning processes, and also provides a controlled-release of the antibiotic. Biodegradable antibiotic sutures obtained by making and embedding antibiotic ICs may be an excellent alternative to the antibiotic methods currently used to treat surgical infections. Additional research is being conducted in our laboratory, including melt-spinning biodegradable PLLA and PCL fibers containing the antibiotic CD–IC and study of the controlled-release properties of the embedded polymer materials. The effectiveness of these antibiotic biodegradable polymers on other types of bacteria is also worth examination, as we approach a new way to produce antibiotic biodegradable/bioabsorbable medical/textile products by using the CD–IC technology described here.

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