Formation of Antibiotic, Biodegradable Polymers by Processing with Irgasan DP300R (Triclosan) and Its Inclusion Compound with β-Cyclodextrin

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ABSTRACT: The inclusion compound (IC) between the FDA-approved antibacterial Irgasan DP300 (Trichlosan), and β-cyclodextrin (CD) has been formed. When the Irgasan–β-CD–IC is embedded in biodegradeable/bioabsorbable films of poly(ϵ-caprolactone) (PCL) at low levels (a few wt %), they are rendered resistant to the growth of *E. coli* bacteria. When these same PCL films embedded with Irgasan–β-CD–IC are used as the adhesive for laminating cotton fabrics, we observe the resulting cotton laminates to also be resistant to the growth of *E. coli* bacteria. These results hold promise for the fabrication of bacteria-resistant polymer films and fibers, as well as antibacterial fabrics, by means of simple melt processing with Irgasan–β-CD–IC. © 2001 John Wiley & Sons, Inc. J Appl Polym Sci 82: 300–309, 2001

Key words: biodegradable polymers; Irgasan DP300R; Triclosan; β-cyclodextrin

INTRODUCTION

Inclusion compounds (ICs) are crystalline structures that are composed of a host and a guest molecule. The host molecule surrounds and isolates the guest molecule during the cocrystallization process. The stability of these ICs depends on the physical proportions of the guest and host molecules, i.e., their stoichiometry. Cyclodextrins (CDs) are cyclic oligosaccharides that are able to form complexes with hydrophobic compounds by incorporating the compound, or more frequently some hydrophobic moiety of the compound, into the CD cavity[1] (see Fig. 1). No covalent bonds are formed or broken during the complex formation, and in solution unbound molecules may be in equilibrium with molecules bound in the complex.[2,3] Cyclodextrins have a hydrophobic interior, but the ends of the cavity have hydrophilic hydroxyl groups, making the molecule water soluble (see Fig. 2). Due to its hydrophobic interior, hydrophobic guest molecules can reside inside the channel if they have dimensions that meet the size restrictions of the cavity. There are three types of CDs: α, β, and γ. The Greek prefixes indicate the number of glucose residues; α-CD contains 6, β-CD contains 7, and γ-CD contains 8. Cyclodextrins with less than six glucose residues are not commonly known to exist. The average diameter of the doughnut-shaped cavity of β-CD is 7.0 Å, and the physical properties of β-CD are listed in Table I.

Huang and Tonelli[4] noted that ICs are not held together by classical chemical bonds, but rather

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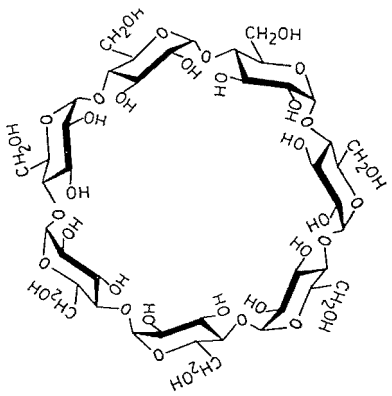
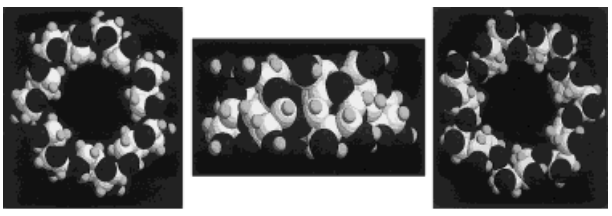


Figure 1 The chemical structure for β-cyclodextrin.

by weak forces that are related primarily to the shapes and dimensions, and not the chemical natures of the guest molecules. The two types of crystalline structure arrangements that are formed with CD-ICs are channel and cage structures[4] (see Fig. 3). Channel structures restrict only the lateral dimensions of the molecule, and place no restriction on the long dimension. Cage structures are different: both openings of the cavity are closed off by another CD, leaving the guest molecule caged in, hence the name. This is also known as molecular encapsulation. More than one CD molecule may be required to fully encapsulate the entire guest molecule.

The guest molecule that is of concern in the present study is an antibiotic. In a previous work by Huang et al.,[5] the antibiotic neomycin sulfate (see Fig. 4) was combined with β-CD to form an inclusion compound. Waksman and Lechevalier discovered neomycin sulfate in 1949 from a strain of Streptomyces fradiae.[6] Its molecular formula is $C_{23}H_{46}O_{13} \cdot 3H_2SO_4$, and is an amorphous amino glycoside that is soluble in water. It is effective against Gram-negative and Gram-positive bacteria, as well as mycobacterium and actinomycetes. Neomycin sulfate inhibits protein synthesis by binding to the small subunit of prokaryotic ribosomes. It is also one of the active ingredients in Neosporin™.[7]



White = Carbon
Shaded = Hydrogen
Dark = Oxygen

Figure 2 Chemical model for β-cyclodextrin.

Table I Physical Properties of β-Cyclodextrin

Properties	β-Cyclodextrin
Molecular weight	1135
Glucose residues	7
Internal cavity diameter (Å)	6–7
Water solubility (g/100 mL, 25°C)	18.5
Melting range (°C)	255–265

The neomycin sulfate–β-CD–IC formed by Huang et al.,5 was embedded into to poly(ϵ-caprolactone) (PCL) (see Fig. 5) films, and was then tested for its effectiveness against *Escherichia coli* (*E. coli*) bacteria. PCL is a biodegradable polymer that melts at 63°C, and exhibits a glass transition at −60 to −70°C. Hence, it is in a leathery state at body temperature.[8] Upon storage at ambient temperature, PCL polymers display a gradual decrease in molecular weight with time, which proceeds autocatalytically and is related to a random hydrolytic reaction.[9] Due to its biocompatible and bioabsorbable properties and slow degradation rate, it is suitable for long-term, implantable drug-delivery systems.

Inclusion compounds are being used widely in the food, pharmaceutical, medical, chemical, and textile industries. In the medical field, the use of antibiotic ICs in biodegradable/bioabsorbable films has already been proposed. Antibiotic inclusion compounds have been incorporated into bandages, dressings, and sutures. Sutures are sterile filaments used to close a wound after surgery, and

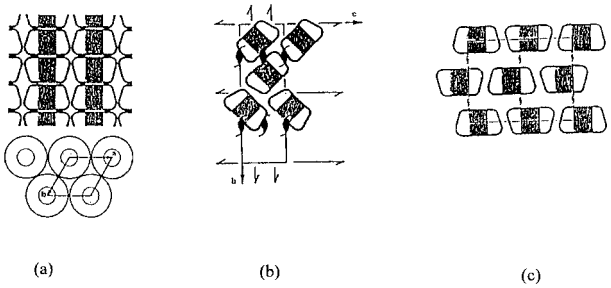


Figure 3 Schematic description of (a) channel-type, (b) cage herringbone-type, and (c) cage brick-type crystal structures formed by crystalline cyclodextrin inclusion complexes.

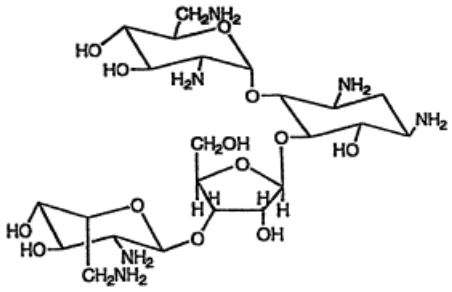


Figure 4 Chemical structure for neomycin sulfate.

provide support during the healing process. Sutures were made by implanting an antibiotic IC made with neomycin sulfate and β-cyclodextrin, into PCL and poly(L-lactic acid) fibers. Because an antibiotic, bioabsorbable suture does not require surgical removal, implanting the IC in the suture might allow for the slow release of antibiotic to completely prevent postsurgical infection and also protect the antibiotic from degradation during the melt-spinning process used to make the suture.

The antibiotic Triclosan used in this study is called Irgasan DP300R (see Fig. 5), and is manufactured in the U.S. by Ciba-Geigy. Irgasan DP300R is its trade name, and its chemical name is 2,4,4′-Trichloro 2′-Hydroxydiphenyl Ether, with a molecular formula $C_{12}H_7Cl_3O_2$. It is a nonionic, off-white, odorless, and tasteless crystalline powder, and is a FDA-approved formulation of Triclosan. Triclosan was originally developed by Ciba-Geigy Company in Basel, Switzerland, in the early 1960s. Ciba Specialty Chemicals Corporation produced Irgasan DP300 for skin applications and Irgacare MP for oral care products. Irgasan DP300 is used as a disinfecting active ingredient in toothpaste, deodorant, soaps, deodorant soaps, antiperspirants, body washes, detergents, dish washing liquid, cosmetics, shaving cream, antimicrobial creams, lotions, and hand soaps. Irgasan DP300R helps prevent the establishment of bacteria on consumable plastic products such as kitchen and bathroom utensils, flooring materials, and toys.[10] It inhibits growth of bacteria, yeast, and molds by blocking the synthesis of lipids, and it has recently been suggested that Irgasan does this by specifically inhibiting the enzyme enoyl-acyl carrier protein reductase (ENR).[11] By carrying out a structural analysis and inhibition experiments on a complex of ENR, from the bacterium *E. coli*, using triclosan and NAD^+, Levy et al. found out that Irgasan acts as a site-directed, very potent inhibitor of the enzyme by mimicking its natural substrate.[12] Its properties are listed in Table II.

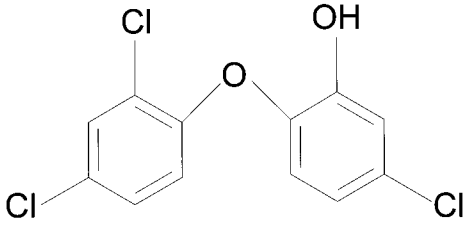


Figure 5 The chemical structure for Irgasan DP300R.

Table II Physical and Chemical Properties of Irgasan DP300R

Properties	Irgasan DP300R
Chemical name	2,4,4′-Trichloro-2′-hydroxy-diphenyl ether
Molecular formula	$C_{12}H_7C_{13}O_2$
Formula weight	289.5
Form	Crystalline powder
Color	White to off-white
Odor	Faintly aromatic
Solubility in water (0.01 g/L) at 20°C	Sparingly soluble
Melting point	55–60°C

In crystalline CD–ICs, the included guest molecules are isolated from the outside environment until the IC crystals are disrupted by melting or dissolution. If the IC is embedded into a biodegradable carrier polymer phase, the included guest molecules can be slowly released, suggesting potential applications in the controlled release area. For example, in high-risk areas, such as intensive care units, many facilities currently use chlorhexidine gluconate (CHG) surgical scrub solutions, which have excellent antimicrobial activity and long-lasting residual effects. Although this can control the resident microflora under the gloves of surgical personnel, the control of the spread of transient microorganisms requires frequent hand washing with an antimicrobial agent that is fast acting and possesses persistent activity.[13] Irgasan offers bactericidal activity, and through incorporation inside crystalline CD–IC channels, it may provide excellent persistent activity on the skin when embedded into a carrier polymer. Because CD–ICs have exceptional thermal stability (with a melting point above 275°C),

they can be embedded into any biodegradable film with a T_m lower than ca. 275°C. Pure Irgasan alone, which melts at about 58°C, may not be homogeneously melt pressed into a film unless it is thermodynamically compatible with the carrier polymer.

The purpose of this study is to form and analyze a new antibiotic inclusion compound, and to discover its advantages and disadvantages with regard to antibacterial activity. A wide variety of *in vitro* test methodologies exist to analyze the antimicrobial spectrum and speed of bactericidal and bacteriostatic activity. The principle methods used include zone of inhibition, MIC, minimum bactericidal concentration, D-value, and time kill. *E. coli* is a bacterium associated with intestinal and urinary infection, and is a multipotent pathogen that could cause disease in several body systems.[5] In this study, the zone of inhibition method is implemented to test the effectiveness of Irgasan and its cyclodextrin inclusion compound against the bacteria *E. coli*. PCL films embedded with small amounts (~5%) of Irgasan or its β-CD–IC, as well as fabrics laminated by bonding with PCL/Irgasan or PCL/Irgasan–β-CD–IC, were tested for their antibacterial properties.

Materials and Method for Inclusion Compound Formation

A PCL pellet sample with molecular weight of 42,500 g/mol was obtained from Aldrich Chemical Co. Irgasan DP300R was obtained from Ciba Specialty Chemicals, and β-CD was obtained from the Cerestar Company. The Irgasan–b-CD–IC was formed by adding a 50-mL solution of 0.5 g of Irgasan in a solvent composed of 40 mL Hexane and 10 mL tetrahydrofuran to a 50-mL aqueous solution containing 3 g of β-CD. The Irgasan solution was gradually added to the CD solution while continuously warming at 60°C and stirring for 3 h, then cooling to room temperature; finally, stirring was discontinued. A white precipitate was obtained overnight, and was then filtered and dried in a vacuum oven.

CHARACTERIZATION

Thermal Property Analysis

Thermal characteristics of samples were determined with a Perkin-Elmer Model 7 differential scanning calorimeter (DSC). Samples from 4–6 mg were used in the test. A heating rate of 10°C/min was employed, and the temperature range was from 0 to 250°C. Nitrogen was used as the purge gas.

FTIR Spectroscopy

Absorbance Fourier transform infrared spectra were collected using a Nicolet 510p FTIR spectrometer with OMNIC E.S.P. software. Frequencies were set from 400 to 4000 cm^{-1}. The resolution was set at 2 cm^{-1}, the number of scans was 32, and the gain was automatic. The samples were mixed with potassium bromide and pressed into small, transparent disks.

Wide-Angle X-ray Diffraction

X-ray diffraction was recorded on powdered samples in a wide-angle set-up using a Siemens type-F X-ray diffractometer. The radiation source used was Ni-filtered, CuKα radiation with a wave length of 1.54 Å. The voltage was set to 30 kV, and the current was set to 20 mA. Samples were mounted on a circular sample holder with scotch tape, and the proportional counter detector collected data at a rate of $(2\theta = 5°)$ min^{-1} over the range $2\theta = 5–40°$.

Film Preparation

A Carver Laboratory Press (Model B) was employed along with a 3.5 inch diameter thin die, which was supported by two smooth stainless steel plates covered with aluminum foil. PCL powder containing different concentrations of pure Irgasan (0, 0.07, 0.143, 0.28, 0.732, 1.22, 2.44, 3.66, and 4.88 wt %) and Irgasan–β-CD–IC (0, 0.5, 1, 2, 3, 5, 10, 15, and 20 wt %) were melt pressed at 4000 lb/in^2 for 10 s at about 70°C. The pressure was released, and then increased to 7500 lb/in^2 for 30 s. The films were then immediately submersed in ice water for 30 s.

Film Thickness Test

Film thickness was determined using a THWING-ALBERT Electric Thickness Tester Model II. A 0.63 in^2 pressure foot with a mass of 468.18 g rests on the film for a predetermined time span and records a thickness to within 0.01 mils. For each film, the thickness was tested 10 times around the film, and an average thickness was calculated.

Fabric Lamination

A Carver Laboratory Press (Model B) was employed along with a 3.5 inch diameter thin die,

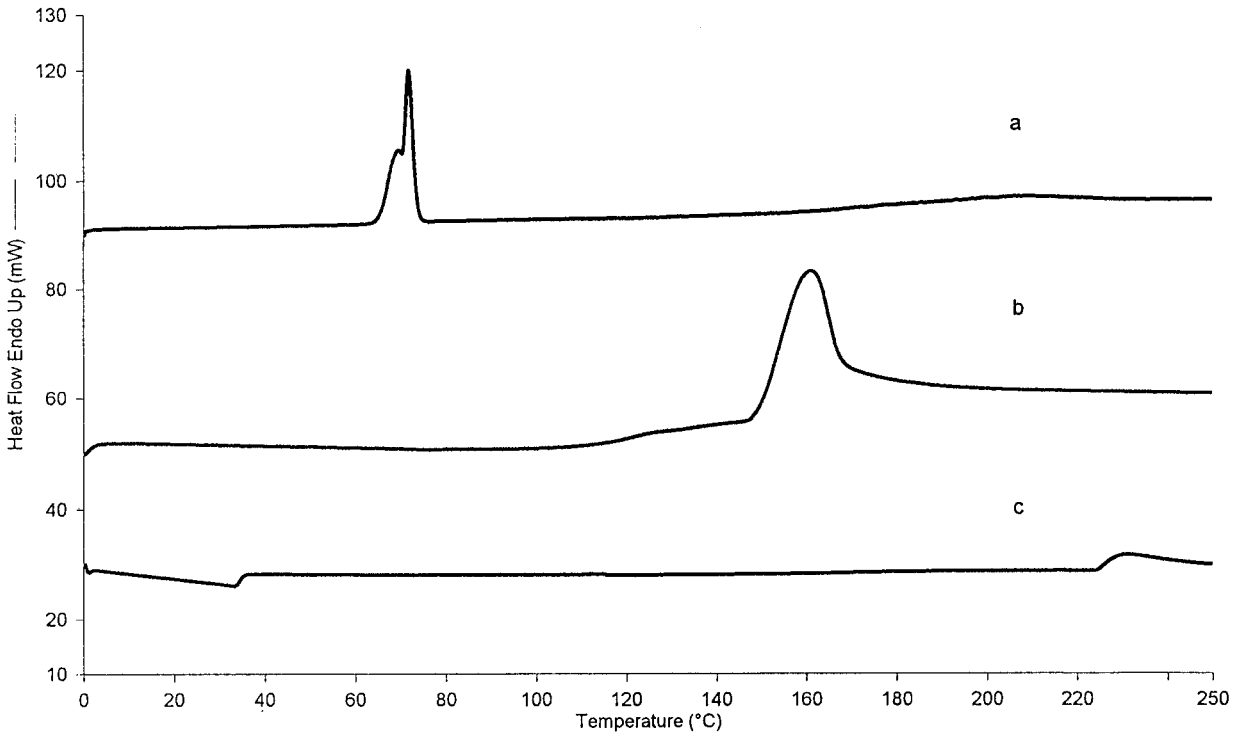


Figure 6 DSC scan of (a) pure Irgasan DP300R (b) β-cyclodextrin, and (c) Irgasan DP300R–β-cyclodextrin–IC at a heating rate of 10°C/min.

which was supported by two smooth stainless steel plates covered with aluminum foil. Three polymer films were pressed and three cotton fabric samples were laminated. The three separate films that were pressed contained (a) 1 g PCL, (b) 1g PCL and 0.1 g Irgasan, and (c) 1 g PCL and 0.1 g Irgasan–β-CD–IC, respectively. Three cotton fabric samples were pressed and also contained (a) 1 g PCL, (b) 1 g PCL and 0.1 g Irgasan, and (c) 1 g PCL and 0.1 g Irgasan–β-CD–IC, respectively. The films and the fabric samples were melt pressed at 4000 1b/in^2 for 10 s at about 70°C. The pressure was released, and then increased to 7500 lb/in^2 for 30 s. The films and the fabric samples were then immediately submersed in ice water for 30 s.

Bacterial Testing

Tubes of L broth were inoculated with *E coli* strain AF42 and then incubated overnight at 37°C with shaking. The next day part of the culture was swabbed onto an L agar plate in several different directions to promote the formation of a uniform layer of growth. A disk sample of each film was punched out with a sterilized office hole puncher and placed on the agar plate. A set of neomycin sulfate "controls" was prepared by pipetting 0, 0.75, 1.5, and 3.0 μL of 10 mg/mL aqueous solutions of neomycin sulfate onto paper disks that had been placed on the agar plate. The plate was maintained at 37°C overnight, and the zone of each sample's inhibition for bacterial growth was measured.

RESULTS

The inclusion complex formed between Irgasan and β-CD has been characterized by DSC, FTIR spectroscopy, and X-ray diffraction. From DSC and FTIR, the formation of the complex can be confirmed, and based on X-ray diffraction, the crystalline structure can be determined. Because cyclodextrins and their ICs will decompose upon melting, they were only tested below their melting temperature in the DSC. Figure 6 presents the DSC thermograms of pure β-CD, Irgasan, and Irgasan–β-CD–IC. Note that the melting peak of Irgasan cannot be seen in the scan of Irgasan–β-CD–IC. This indicates that there was no free crystalline Irgasan in the sample. Figure 7 presents the FTIR spectral scans of β-CD, pure Irgasan,

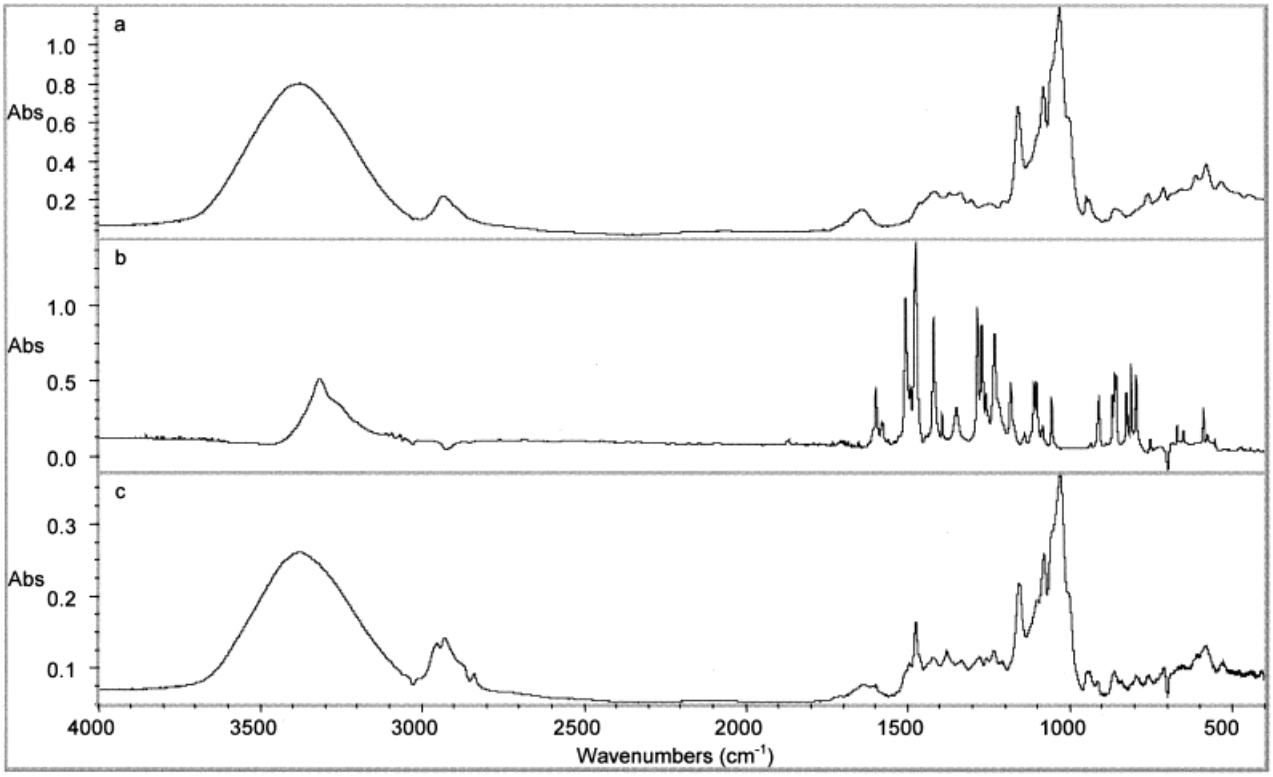


Figure 7 Fourier transform infrared spectra in the region of 4000 to 400 cm^{-1} : (a) β-cyclodextrin, (b) Irgasan DP300R, and (c) Irgasan DP300R–β-cyclodextrin–IC.

and the Irgasan–β-CD–IC. Note the presence of a vibrational band unique to Irgasan (1474 cm^{-1}) in the Irgasan–β-CD–IC spectrum, which together with the absence of free Irgasan in the sample (DSC) clearly implies that the antibacterial is included inside the Irgasan–β-CD–IC crystals. Figure 8 presents the wide-angle X-ray patterns observed for pure β-CD $\cdot$ $12H_2O$ (a), Irgasan–β-CD–IC (b), and pure Irgasan (c). The Irgasan–β-CD–IC showed a diffraction pattern quite different from the diffractogram of irgasan, and this provides primary evidence that a different crystal type was formed. By comparing the diffraction pattern of Irgasan–β-CD–IC with that of the β-CD $\cdot$ $12H_2O$ crystals, which has been proven to adopt a cage crystal structure[14] by X-ray analyses of single crystals, we observe similar diffractogram patterns. This may indicate that Irgasan–β-CD–IC also adopts a cage type structure.

By melt pressing, we embedded different concentrations of the Irgasan and Irgasan–β-CD–IC into biodegradable PCL films to test their effectiveness against the bacteria *E. Coli*. Table III shows the thickness and zone of inhibition of different films. Because the same amounts of samples were used and melt pressed under the same condition, all the samples had comparable thicknesses in the range from 0.37 to 0.46 mm.

In the bacterial tests, filter paper treated with 0, 0.75, 1.5, and 3.0 μL of 10 mg/mL aqueous solutions of neomycin sulfate were used as controls and resulted in 0, 10, 11, and 14 mm zones of bacteria growth inhibition, respectively (Fig. 9).

Table III compares the thicknesses and zones of inhibition of melt-pressed PCL films embeded with different concentrations of pure Irgasan and Irgasan–β-CD–IC. The pure PCL disc made by the melt-pressing technique did not deter bacterial growth. A series of PCL films embedded with 0.07, 0.143, 0.28, 0.732, 1.22, 2.44, 3.66, and 4.88 wt % of Irgasan show different amounts of antibiotic effectiveness. PCL films embedded with Irgasan did not deter bacterial growth until the Irgasan concentration increased to 0.732 wt %, with a 9-mm zone of inhibition. However, with further increase of Irgasan concentration, the effectiveness of PCL films did not improve much.

To evaluate the effectiveness of Irgasan included inside the β-CD channel, antibacterial tests were performed on PCL films impregnated

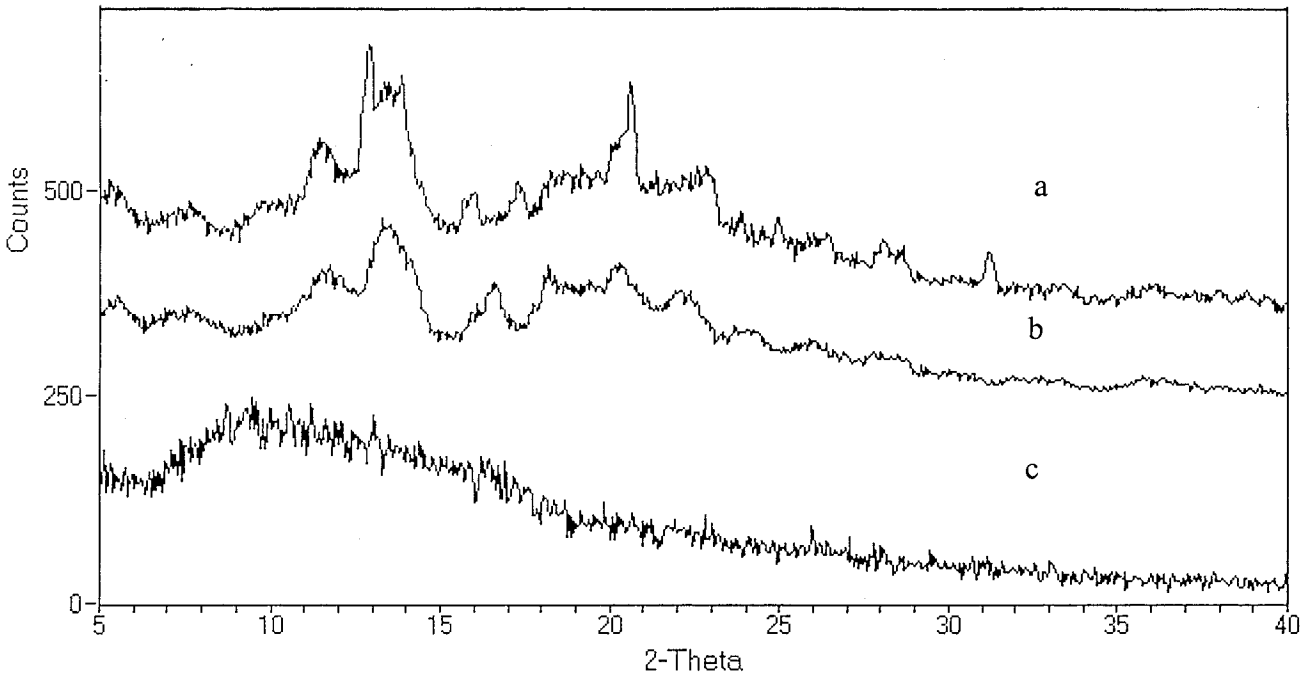


Figure 8 Wide-angle X-ray diffraction of (a) β-CD · $12H_2O$, (b) Irgasan DP300R–β-CD–IC, and (c) pure Irgasan DP300R.

with 0.5, 1.0, 2.0, 3.0, 5.0, 10, 15, and 20 wt % of Irgasan–β-CD–IC, which only contained 0.07, 0.143, 0.28, 0.732, 1.22, 2.44, 3.66, and 4.88 wt % of the effective Irgasan, respectively. The results showed that PCL films impregnated with low concentration (lower than 3 wt %) Irgasan–β-CD–IC could not inhibit bacterial growth. However, when the complex concentration increased to 5 wt % (1.22 wt % of Irgasan), the PCL film was effective against the *E. coli* growth with a 12–13-mm zone of inhibition, which was larger than the zone of inhibition of PCL film impregnated with the same amount of pure Irgasan. This indicates that Irgasan incorporated inside the β-CD channels not only shows very good antibiotic properties, but also improved effectiveness against *E. coli*. Similar to the results of PCL films embedded with different concentrations of Irgasan, further increases of Irgasan–β-CD–IC concentration do not improve their antibiotic properties much.

The results of our testing for the antibacterial properties of cotton fabric laminates bonded with PCL embedded with Irgasan or Irgasan–β-CD–IC are presented in Table IV and in Figure 10. Note that the cotton fabric laminates bonded by PCL embedded with small amounts (a few %) of Irgasan–β-CD–IC effectively deter the growth of *E. coli* bacteria.

DISCUSSION

Inclusion compounds are being used widely in the food, pharmaceutical, medical, cosmetic, textile, biotechnological, and materials industries. Because central cavities in CDs are lipophilic and the outer surfaces are hydrophilic, they can incorporate most lipophilic compounds based on their polarity, molecular mass, and structure. The complex cannot only improve the water solubility of lipophilic compounds, thus enhancing their biological absorption, but also prevents them from oxidation and thermodecomposition.[15] Therefore, we are forming the inclusion complexes between cyclodextrin and the antibiotic Irgasan to control the release of Irgasan and protect it during processing. Antibiotic inclusion compounds can be incorporated into bandages, dressings, and sutures to treat surgical infection.[7] A study on animal bite victims by Medetbekov[16] showed *E. coli* and *Staphylococci* to be the most common causes of bacterial infection, which is also supported by a study of the department of General Surgery at the Rio de Janeiro University Hospital. In our study, we embedded Irgasan and its inclusion complex into the biodegradable polymer PCL to test their effectiveness against *E. coli* bacteria.

Table III Comparison of Thickness and Zone of Inhibition of Melt-Pressed PCL Films Embedded with Triclosan and Triclosan-βCD-IC

Disc Samples Punched from PCL Fims	Average Thickness (mm)	Zone of Inhibition Diameter (mm)	Disc Samples Punched from PCL Films	Average Thickness (mm)	Zone of Inhibition Diameter (mm)
Pure PCL disc	0.41	0			
PCL disc with 0.07 wt % of pure triclosan	0.45	0	PCL disc with 0.5 wt % of tricolsan IC (containing 0.07 wt % of triclosan)	0.37	0
PCL disc with 0.14 wt % of pure triclosan	0.45	0	PCL disc with 1 wt % of tricolsan IC (containing 0.14 wt % of triclosan)	0.40	0
PCL disc with 0.28 wt % of pure triclosan	0.41	0	PCL disc with 2 wt % of tricolsan IC (containing 0.28 wt % of triclosan)	0.38	0
PCL disc with 0.732 wt % of pure triclosan	0.48	0	PCL disc with 3 wt % of tricolsan IC (containing 0.73 wt % of triclosan)	0.41	0
PCL disc with 1.22 wt % of pure triclosan	0.43	9	PCL disc with 5 wt % of tricolsan IC (containing 1.22 wt % of triclosan)	0.42	12–13
PCL disc with 2.44 wt % of pure triclosan	0.44	12	PCL disc with 10 wt % of tricolsan IC (containing 2.44 wt % of triclosan)	0.41	12–15
PCL disc with 3.66 wt % of pure triclosan	0.45	12	PCL disc with 15 wt % of tricolsan IC (containing 3.66 wt % of triclosan)	0.46	11–13
PCL disc with 4.88 wt % of pure triclosan	0.40	12	PCL disc with 20 wt % of tricolsan IC (containing 4.88 wt % of triclosan)	0.46	12–13

To ensure the same desirable physical properties of the suture after embedding the antibiotic, we also attempted to determine the minimum concentration of the antibiotic necessary for effectiveness against *E. coli*.

In a preliminary study, we tried to employ a 1 : 15 molar ratio of Irgasan : β-CD to form the complex, so that all the Irgasan can be incorporated inside the CD cavities. The absence of the Irgasan melting peak in the DSC scan of Irgasan–β-CD-IC shows that there is no free Irgasan in the sample. However, a large amount of free CD was also precipitated out, and mixed with the complex. When we embedded 5 wt % of the sample into PCL film, it did not inhibit bacterial growth. This maybe due to the low effective Irgasan concentration (0.16 wt %); however, when we embedded 50 wt % of that sample into PCL film (about 1.6 wt % of Irgasan), it did inhibit bacterial growth with a 15-mm zone of inhibition.To maintain the desirable physical properties of films after embedding, we are trying to form effective antibiotic PCL films using the least possible amount of Irgasan–β-CD–IC. Therefore, it is necessary to form the stoichoimetric complex. By using different molar ratios of Irgasan and β-CD (1 : 0.5, 1 : 1, 1 : 1.5, 1 : 2) and testing with DSC, we found there were free Irgasan molecules in the first two samples, while no free Irgasan molecules are present in the latter two samples. This may indicate that the stoichoimetric ratio of the complex is between 1 : 1 to 1 : 1.5. Thus, we embedded the PCL film samples with the Irgasan–β-CD–IC sample made with a 1 : 1.5 molar ratio. The concentration of Irgasan in the complex is about 14 wt %.

The formation of the complex can be confirmed by combination of DSC, FTIR, and wide-angle X-ray techniques. The disappearance of the melting peak of Irgasan in the scan of the complex shows that there is no free Irgasan in the complex; however, we can observe Irgasan peaks in the FTIR spectrum of the complex. Furthermore, X-ray data is consistent with the formation of a cage-type inclusion complex.

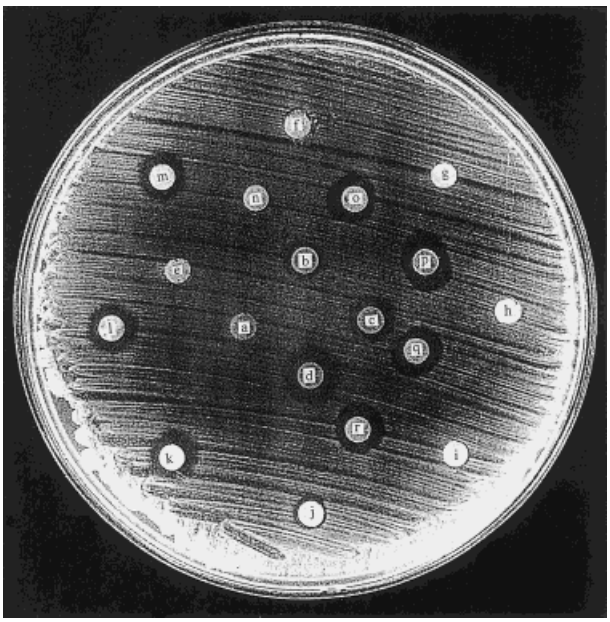


Figure 9 Bacterial culture plus filter paper discs containing 0 (a), 7.5 (b), 15 (c), and 30 μg (d) of neomycin sulfate, pure PCL film (e), PCL film discs with 0.07 wt % (f), 0.14 wt % (g), 0.28 wt % (h), 0.73 wt % (i), 1.22 wt % (j), 2.44 wt % (k), 3.66 wt % (l), 4.88 wt % (m) of Irgasan, and PCL film discs with 3.0 wt % (n), 5.0 wt % (o), 10.0 wt % (p), 15.0 wt % (q), and 20.0 wt % (r) of Irgasan–β-CD–IC.

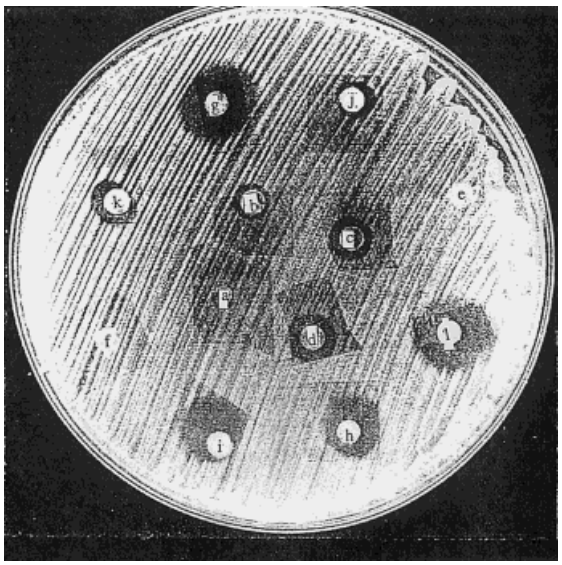


Figure 10 Bacterial culture plus fiilter paper discs containing 0 (a), 7.5 (b), 15 (c), and 30 μg (d) of neomycin sulfate, PCL film discs with 2.5 wt % (e) and (f) and 5.0 wt % (g) and (h) of Irgasan–β-CD–IC, and discs of cotton fabric laminated with PCL containing 2.5 wt % (i) and (j), and 5.0 wt % (k) and (l) of Irgasan–β-CD–IC.

By embedding 0.5, 1, 2, 3, 5, 10, 15, and 20 wt % Irgasan–β-CD–IC into PCL films, we found that the PCL films cannot inhibit the *E. coli* growth at low concentrations (0.5, 1, 2, and 3 wt %), but become effective with the 12–13-mm zone of inhibition when the Irgasan–β-CD–IC concentration is 5 wt % and does not improve much with increased concentration. To compare with the effectiveness of pure Irgasan embedded into the

Table IV *E. coli* Test Results for Cotton Fabric Laminated with PCL Films Embedded with Irgasan or Irgasan-β-CD-IC

Sample	Zone of Inhibition (Diameter in mm)
Trial 1:	
PCL (between pieces of fabric) (1 g of PCL)	0
PCL (1 g of PCL)	0
PCL + triclosan (between pieces of fabric) (1 g of PCL and 0.1 g of triclosan)	15
PCL + triclosan (1 g of PCL and 0.1 g of triclosan)	15
PCL + triclosan-β-CD-IC (between pieces of fabric) (1 g of PCL and 0.1 g of triclosan-β-CD-IC)	12–15
PCL + triclosan-β-CD-IC (1 g of PCL and 0.1 g of triclosan-β-CD-IC)	14–17
Trial 2:	
PCL (between pieces of fabric) (1 g of PCL)	0
PCL (1 g of PCL)	0
PCL + triclosan (between pieces of fabric) (1 g of PCL and 0.1 g of triclosan)	16
PCL + triclosan (1 g of PCL and 0.1 g of triclosan)	15–16
PCL + triclosan-β-CD-IC (between pieces of fabric) (1 g of PCL and 0.1 g of triclosan-β-CD-IC)	12
PCL + triclosan-β-CD-IC (1 g of PCL and 0.1 g of triclosan-β-CD-IC)	10–11

PCL films, we embedded the corresponding concentrations of Irgasan into the PCL films. The bacterial tests show similar resuls. This demonstrates that when the antibiotic Irgasan is fabricated with biodegradable PCL films, they show antibiotic property with a minimum concentration of 0.732 wt %. Incorporating Irgasan inside the β-CD cavities does not affect the antibiotic properties of Irgasan, and at low concentrations (2.5–5.0 wt %), the PCL film shows reasonable inhibition of bacterial growth. This indicates that Irgasan and Irgasan–β-CD–IC have much potential in making sutures and dressings. By coating Irgasan with β-CD, it can be protected from high-temperature processing and provides a controlled-release of the antibiotic. Embedded in the fabrics and latexes used in surgical gowns, drapes, and gloves, Irgasan–β-CD–IC might provide excellent persistent activity on skin and other surfaces due to the slow release of the Irgasan antibacterial from the IC crystals.

When cotton fabric was laminated with PCL films containing small amounts (2.5 wt %) of embedded Irgasan–β-CD–IC they were rendered antibacterial also. We note in Figure 10 that while the PCL film containing 2.5 wt % Irgasan–β-CD–IC was not antibacterial, the cotton fabric laminated with this same PCL film did, in fact, deter the growth of *E. coli* bacteria. However, when the Irgasan–β-CD–IC concentration was increased to 5 wt % in the PCL film it also inhibited bacterial growth.

CONCLUSIONS

In summary, we report the formation of Irgasan–β-CD–IC by a heating technique. DSC and FTIR techniques confirm that Irgasan has been included inside the IC cavities provided by β-CD, and X-ray diffractograms indicate that the crystalline structure of Irgasan–β-CD–IC seems to adop a cage-type structure due to its similarity to the pattern of β-CD · $12H_2O$. The advantage of cyclodextrin inclusion compound formation is the protection of Irgasan from high temperature during manufacture by melt-pressing or fiber-spinning processes, and provision of a controlled release of the antibiotic.

The bacterial tests show that by embedding low concentration of Irgasan–β-CD–IC antibiotic, biodegradable PCL polymer films can be formed, which may be an excellent alternative to the antibiotic methods currently used to treat surgical infections. Therefore, by melt spinning biodegradable PCL fibers or nylon fibers with Irgasan–β-CD–IC, we can make sutures and form fabric with very good antibiotic properties. An alternate means of conferring antibacterial properties to fabric may be achieved by lamination with adhesives containing small amounts of the antibacterial CD–IC. We therefore believe we have demonstrated that CD–IC technology has a lot of potential as a promising method to produce antibiotic medical and textile products.

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