

## Aqueous-based polymeric dispersion: preparation and characterization of cellulose acetate pseudolatex

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### Abstract

The objective of the present study was to prepare and characterize the cellulose acetate (CA) pseudolatex as a semipermeable membrane provider for atenolol gastrointestinal therapeutic system (GITS). For the polymer film coating, it is important to relate the macroscopic properties such as tensile strength and toughness to the atomic-scale property, free-volume. Using ethyl acetate as the solvent, CA pseudolatex was prepared by a phase inversion emulsification technique. The particle size of the pseudolatex was reduced to nanometer size range by passing through a microfluidizer. Diacetin was used as the plasticizer. Mechanical properties showed a considerable decrease in their values except % elongation as the plasticizer concentration increased from 90 to 150%. Glass transition temperatures of the CA pseudolatex membranes were 160°C (unplasticized pseudolatex), 63°C (90% plasticizer), 17.6°C (110% plasticizer), –60°C (160% plasticizer), and 20.1°C (actual film from tablet surface). Approximate  $F_v$  (free-volume fraction), as a function of diacetin concentration, was estimated by positron annihilation spectroscopy (PAS). There was an increase in  $F_v$  from 5.800 to 6.082 as the diacetin concentration increased from 90 to 170%. Tritium tracer diffusion experiments revealed that the permeability of the pseudolatex films increased as the diacetin concentration increased. The CA pseudolatex provided a mechanically strong film on bilayered osmotically controlled tablet dosage forms. © 1998 Elsevier Science B.V. All rights reserved.

**Keywords:** Cellulose acetate pseudolatex; Positron annihilation spectroscopy; Gastrointestinal therapeutic system

### 1. Introduction

Polymeric coating is very common on the solid dosage forms for many good reasons including modified drug release for enteric, sustained or osmotically controlled drug delivery. The USP

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has defined a modified release dosage form as 'one for which the drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms' (USP, 1985). Amongst the sustained/controlled release dosage forms, the coated delivery systems are proven to release the drug in a tailored fashion to achieve the required pharmacological effect (Sastry et al., 1997a,b). One of the methods to achieve coating involves spraying the polymer organic solutions onto the dosage forms in a coating chamber followed by the solvent evaporation. Several problems such as explosion and health hazards are associated with organic solvents, and therefore, the solvents such as acetone, methylene chloride and methanol must not be expelled into environment (Cole, 1995). After the legislation of Clean Air Act of 1970, regulatory agencies such as EPA started monitoring air and water pollution. The solvent recovery costs escalated steeply, leading to the substantial economic impact on the dosage form manufacturing. Therefore, scientists have shifted the focus from organic based to aqueous-based coating. As a result, several aqueous coating systems such as Aquacoat® from FMC Corp., and Surelease® from Colorcon, Inc. are now commercially available. However, the availability of information for preparation and characterization of cellulose acetate dispersion is very limited.

Artificial Latices are prepared by emulsion polymerization method where the monomers are initiated to form polymer in the presence of an initiator (Singh et al., 1995, 1996). The toxic effect of residual monomer concentration is a serious disadvantage of this system. Pseudolatices, on the other hand, are prepared by organic polymer solution emulsification in water followed by removal of organic solvent in vacuum (Bankar and Peck, 1981). Latices/pseudolatices are characterized by low viscosity, even with high solids content (Lehmann, 1989). In the present study a novel cellulose acetate pseudolatex has been prepared and characterized to provide a semipermeable membrane for the atenolol gastrointestinal therapeutic system (GITS).

Pseudolatices should possess suitable characteristics to act as a film former on a solid substrate.

The particle size and its distribution are the most important specifications of a pseudolatex or latex. The particle size typically should fall between 10 and 1000 nm. Selection of a compatible plasticizer and its concentration in the dispersion, mechanical properties, permeability characteristics, glass transition temperatures ( $T_g$ ), minimum film forming temperature (MFT), and free volume fraction of the membranes of the pseudolatex are a few of the critical parameters that define the end use of the product (Lehmann, 1989). The permeability characteristics of the films are very vital for the product performance, especially in oral controlled drug delivery (Binschaedler et al., 1986). This in turn is governed by the free-volume spaces available in the membranes. The estimation of free-volume values by positron annihilation spectroscopy (PAS) can provide a direct evaluation of the membrane mechanical and viscoelastic characteristics.

Positron annihilation spectroscopy (PAS) provides a unique means of estimating microscopic free-volume spaces in the polymers. The theoretical importance of free-volume of polymers is in understanding viscoelastic and mechanical properties of the substances (Nakanishi et al., 1989). The William-Landel-Ferry (WLF) equation shows that the fractional free-volume,  $F_v$ , varies with temperature and pressure (Jean, 1990). Molecular mobility and relaxation rate of the local motion of chains increase when temperature is increased while decreasing the pressure. Therefore, the dependency of viscoelastic behavior of a polymer on temperature and pressure can be monitored by PAS. Viscoelasticity of a polymer undergoes dramatic changes around the glass transition temperature ( $T_g$ ) of the polymer and the positron life times (Stevens, 1980). Positron life times can be directly related to the free-volume of the polymer (Jean, 1990). Thus the PAS technique can be used to study the effect of temperature and pressure on free-volume of the polymer. In the present study, PAS technique was employed to understand the free-volume behavior as a function of plasticizer concentration. Plasticizer, also a solvent for the polymer, can change the viscoelastic behavior of polymers significantly. Essentially, a plasticizer transforms hard, brittle polymer into a soft, rub-

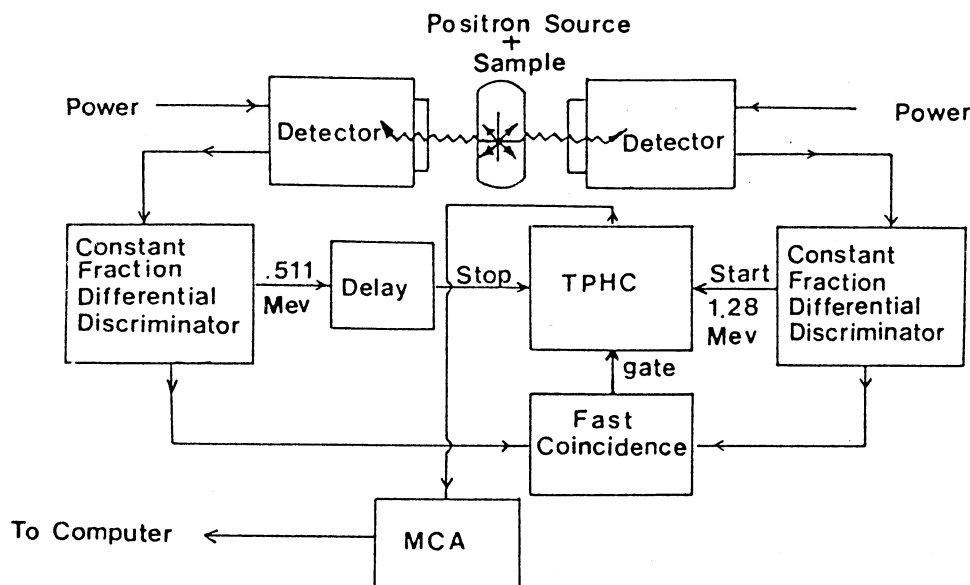


Fig. 1. A schematic diagram of the positron lifetime spectrometer.(Source: Jean, 1990).

bery material. It provides greater resistance to the polymers when mechanical stresses are applied. The substantial modifications in the mechanical properties also affect the polymer permeabilities (Guo, 1993). It is likely that the increase in plasticizer concentration may result in an increased free-volume of the polymer. The increased free-volume may provide an increased permeability characteristics of the films prepared by the polymeric dispersions (Guo et al., 1991).

## 2. Materials and methods

### 2.1. Materials

The following materials were received as gifts: glyceryl diacetate or diacetin from CP Hall Company, Chicago, IL and cellulose acetate (39.8% acetylation) from FMC Corporation, Philadelphia, PA. Sodium lauryl sulphate and ethyl acetate were purchased from Spectrum Chemical Mfg. Corporation, Gardena, CA. All materials were used as received.

### 2.2. Methods

#### 2.2.1. Preparation of experimental CA pseudolatex

A CA solution (100 g in 700 ml of ethyl acetate) and 0.5% solution of sodium lauryl sulfate (1000 ml) were prepared. The temperature of the aqueous phase was maintained at  $37 \pm 1^\circ\text{C}$ . Phase inversion emulsification technique was applied where organic phase was emulsified by adding sufficient aqueous phase while subjecting the mixture to high commuting force (Silverson homogenizer, model L4R) to obtain w/o type emulsion. Upon addition of the remaining amount of the aqueous phase, phase inversion yielded o/w emulsion. This crude emulsion was then passed through a microfluidizer (M-110T, Microfluidics Corp., Newton, MA). The operating pressure was 15000 psi and the emulsion was passed through the microfluidizer five times. This process reduces the coarse emulsion particle size to nano particle size range. The organic solvent from the resulting colloidal dispersion was removed by stripping under reduced pressure in a rotary evaporator (Büchi Rotavapor R). The pH of the system was adjusted to 8 by adding  $\text{NH}_4\text{OH}$  solution. The

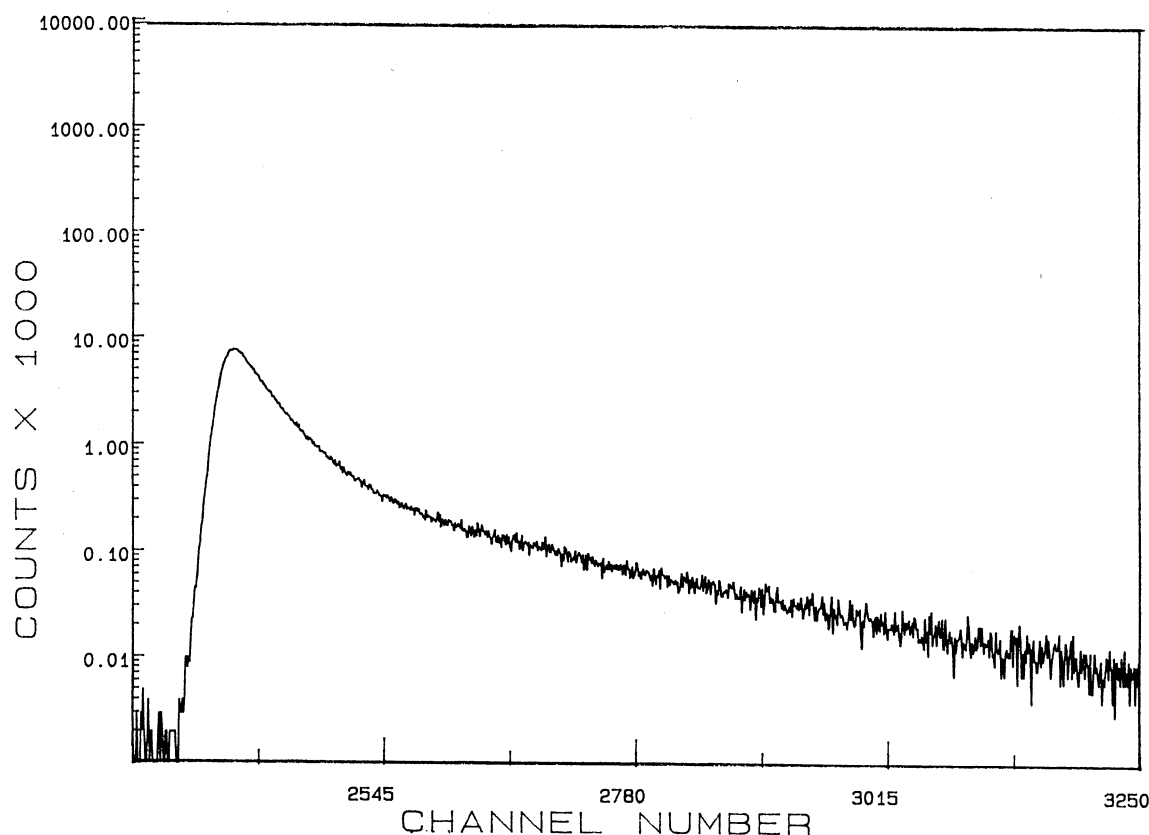


Fig. 2. Representative PAL spectra for CA pseudolatex film with 130% diacetin.

final solids content was estimated by drying 5 ml samples of CA pseudolatex in an oven at 45°C to a constant weight. The solids content was 10% w/v. The CA pseudolatex was then stored at 5°C until used for coating.

Table 1  
Processing conditions for latex coating

Tablet bed size	500 g
Inlet temperature	80 ± 2°C
Outlet temperature	60 ± 20°C
Inlet air pressure	9.9 psig
Atomizing pressure	0.67 kp/cm <sup>2</sup>
Coating spray rate	7–10 g/min
Proportionating pump speed	2
Air flap opening	30°

#### 2.2.2. Glass transition temperature ( $T_g$ ) and minimum film forming temperature (MFT)

The  $T_g$  for the CA pseudolatex films was obtained by thermal mechanical analysis (TMA) using a Perkin-Elmer TMA7 instrument with UNIX software. Plasticized pseudolatex cast films and the films peeled from the coated tablet surfaces were used in the test. Penetration of a quartz probe into sample film was measured at 5°C/min heating rate and with applied force of 1 mN in a nitrogen atmosphere. The membranes were scanned from –30 to 200°C. The casted films contained diacetin at 90 and 110%, based on solids content of the pseudolatex. The  $T_g$  and MFT for the casted film with 160% plasticization were measured by dynamic mechanical analysis (DMA) (Rheometrics, RDA-2) and MFT Bar (Paul N. Gardner Company Inc., FL), respectively. The sample size for DMA was 4 × 0.5 cm

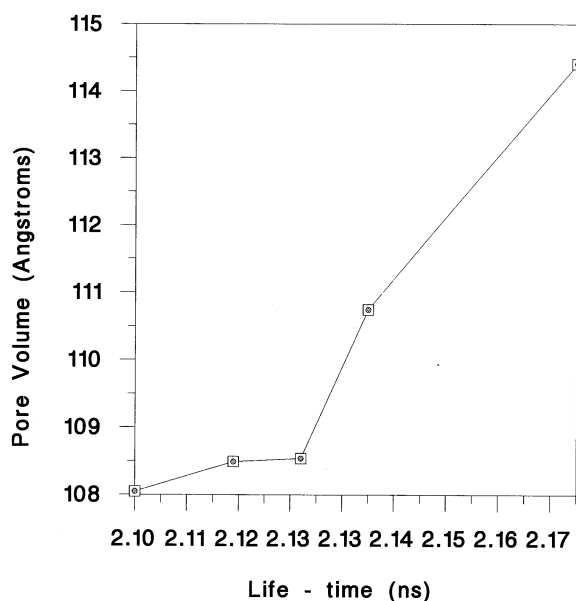


Fig. 3. Correlation curve for pore volume and life-time values of CA pseudolatex films obtained from PAS experiments.

and 1.5 mm thickness, and the analysis was performed according to the ASTM-D5279 method. The MFT was obtained by applying the pseudolatex sample from the warm end to the cold end of the nickel plated copper platen of the instrument in a nitrogen blanket. The temperature was monitored with the help of roving probe temperature sensors mounted on the platen. The standard ASTM-D2354 method was applied in measuring the MFT.

### 2.2.3. Mechanical properties

Stress and strain tests were performed on CA pseudolatex films with varying concentrations of plasticizer. The concentrations of plasticizer tested were 90, 110, 130 and 150% diacetin based on the solids content of pseudolatex. Plasticized pseudolatexes were casted on the glass plates and dried for 72 h at 60°C. The dried films were retrieved from the plates and stored in a desiccator until the test. Instron model 1011 test instrument was employed to obtain the mechanical properties of the films. The average thickness of each film sample was measured across the gauge length before mounting the film on crossheads.

### 2.2.4. Positron annihilation spectroscopy and free-volume estimation

The films were prepared according to the method described in previous sections, by adding 90, 110, 130, 150 and 170% diacetin based on the solids content of the latex. A 10  $\mu\text{Ci}$   $^{22}\text{NaCl}$  positron source was sandwiched between the two sample disks (5 mm diameter  $\times$  1 mm thickness) and this assembly was then placed between the detectors of the PAS (EG and G ORTEC) (Fig. 1). The time resolution for this equipment was 225 ps. The positron life time measurements were performed by fast-fast coincident method (Jean, 1990). The life time spectra were resolved into three exponential components using the Positronfit Extended computer program (Nakanishi et al., 1989). The positron annihilation lifetime (PAL) spectra were fitted into three lifetimes. Representative PAL spectra are shown in Fig. 2. The long-lived component, life-time  $\tau_3 = 0.5\text{--}3.0$  ns and intensity  $I_3 = 10\text{--}30\%$ , is *o*-Ps annihilation in free-volume spaces (Jean, 1990).

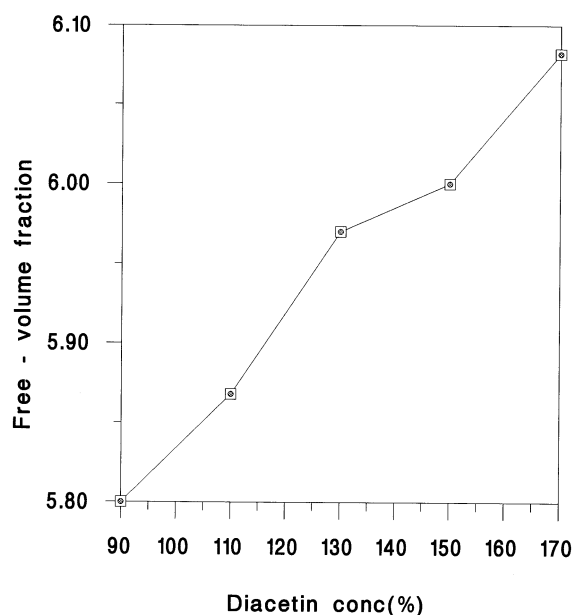


Fig. 4. Plot showing the near linear relation between free-volume fraction ( $F_v$ ) and diacetin concentration.

Table 2  
Positron annihilation spectroscopy experimental values for CA films

Diacetin concentration (%)	Life time ( $\tau_3$ ) (ns)		Intensity ( $I_3$ )		Volume ( $V_p$ )	Free-volume fraction ( $F_v$ )
	Average	S.D.	Average	S.D.	Average	Range
90	2.095	0.02	21.45	0.23	108.05	5.605–5.986
110	2.114	0.04	21.62	0.47	108.49	5.613–6.121
130	2.127	0.03	22.00	0.44	108.54	5.745–6.200
150	2.140	0.07	21.66	0.49	110.74	5.523–6.476
170	2.180	0.04	21.26	0.32	114.41	5.798–6.366

### 2.2.5. Tritium-tracer diffusion experiments

Diffusion experiments on the free films were performed with tritiated water using Perm Gear Membrane Transport Systems (Amie H3 60809, three side by side cell assembly) connected to a thermostated (Haake, DIN 12879) water-bath system. The volume of each cell was 3 ml. The films were prepared according to the method described in previous sections, by adding 90, 110, 130, 150 and 160% diacetin based on the solids content of the latex. Before mounting the membranes on diffusion cells, the thickness of each membrane was measured and they were soaked in distilled water for 10 min. A stock solution of tritiated water was made by adding 1  $\mu$ l of 25  $\mu$ Ci tritium per 3 ml of distilled water. The soaked membranes in triplicates were mounted on the cells and clamped tightly to seal. A 3-ml volume of tritiated water was then added to the donor compartment and 3 ml of distilled water was added to the receiver compartment. At time intervals of 0.083, 0.17, 0.25, 0.5, 0.75, 1, 1.5, 2, 3 and 5 h a

10  $\mu$ l sample was collected from the receiver compartment into scintillation vials. The sample volume was replaced with 10  $\mu$ l distilled water. The collected samples were suitably diluted with scintillation liquid and analyzed in a  $\gamma$ -scintillation counter (Beckman LS3801). The counts so obtained were converted to total amount of tritium permeated (g/3 ml). The tritium activity in the receiver compartment was divided by the tritium activity per unit volume in the donor compartment. The exchange flux was obtained from the slopes of the amount of tritium permeated vs. time profiles. As the tritium activity in the donor compartment was much higher than in the receiver compartment, the counter diffusion of tritium was neglected. Since the chemical activity difference between the compartments for tritiated water is unity, no labeled water exists in the

Table 3  
Permeability and diffusion coefficient values obtained from tritium tracer experiments

Diacetin concentration (%)	Permeability coefficient ( $\text{cm}^2/\text{h} \times 10^{-3}$ )	
	Average	S.D.
90	0.58	0.56
110	0.74	0.20
130	0.94	0.30
150	1.80	0.30
160	6.60	0.40

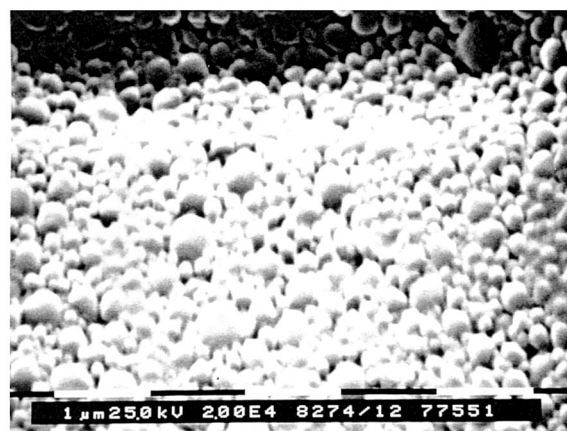


Fig. 5. SEM micrograph for the unplasticized CA pseudolatex showing the spherical nature of the polymer particles.



Fig. 6. Homogeneous film of CA pseudolatex observed under SEM.

receiving compartment at the beginning of the experiment (Lindstedt et al., 1989). Therefore, the permeability coefficients for the membranes can be calculated using the equation

$$Pt = Fh/A \quad (1)$$

where,  $Pt$ , is the permeability for tritiated water;  $F$ , the exchange flux;  $h$ , the thickness of the membrane, and  $A$ , the surface area of the membrane exposed to permeation.

#### 2.2.6. Scanning electron microscopy (SEM)

The surface morphology of unplasticized latex and casted plasticized latex films was examined by a scanning electron microscope (Phillips 505). The coated tablet sections were also examined for the uniformity of the films. The samples were mounted on the aluminum pins, and the liquid samples were dried in an oven at 40°C. All the samples were coated for 70 s under a nitrogen atmosphere with gold in a sputter coater (LADD bench-top sputter coater) and then observed with the scanning electron microscope.

#### 2.2.7. Particle size analysis

The particle size analysis of CA pseudolatex (solids content 10% w/v, pH 8–9) was performed by photon correlation spectroscopy (Particle Sizer, Model BI-90, Brookhaven Instruments Corp., Holtsville, NY). The pseudolatex was suit-

ably diluted to a final concentration of approximately 125  $\mu\text{g/ml}$  in a dust free dilution cell. The samples were then subjected to analysis for particle size and polydispersity of the pseudolatex.

#### 2.2.8. Viscosity measurement

Viscosity and viscoelastic studies were performed using the Haake RV20-CV20 viscometer in combination with PQ45 sensor (plate/plate) system. The viscometer was integrated with an IBM/ps2 model 70 data acquisition and analysis system. The parameters obtained from this study were viscosity ( $\eta$ ), storage modulus ( $G'$ ) and loss modulus ( $G''$ ) as the function of frequency. The applied frequency ranged from 1 to the end value of 9.62 Hz. Three repetitions were performed with a wait time of 3 s/run. The applied strain was 100%. The experiment was carried out at 24.4°C.

#### 2.2.9. CA pseudolatex coating

Atenolol gastrointestinal therapeutic systems (GITS) were coated with CA pseudolatex in laboratory model Uni-Glatt fluidized-bed coater. Following coating, the atenolol GITS were dried at 45°C for 48 h and stored in a closed container at room temperature. After drilling an orifice into drug layer, the tablets were subjected to dissolution using the USP paddle method.

#### 2.3. Preparation of bilayered atenolol osmotic tablets

Bilayered osmotic tablets were prepared as follows: The drug layer was comprised of 100 mg of atenolol, 250–300 mg of Polyox<sup>®</sup> N80, 0–30 mg of Carbopol<sup>®</sup> 934P, and 0.8 mg of magnesium stearate. The osmotic layer was comprised of 200–250 mg of Polyox<sup>®</sup> 303, 0–30 mg of Carbopol<sup>®</sup> 974P, 5–20 mg of sodium chloride, 0.8 mg of magnesium stearate, and 1.4 mg of F D and C red No. 27. Both layers were mixed separately. Bilayered, standard convex tablets of one-half inch diameter were prepared using a carver press (model C) attached to a carver semi-automatic compression accessory (model No 2729). The compression pressure was adjusted so that the average hardness of the tablets after bilayered compression was 7–8 kg. Since the tablets contain

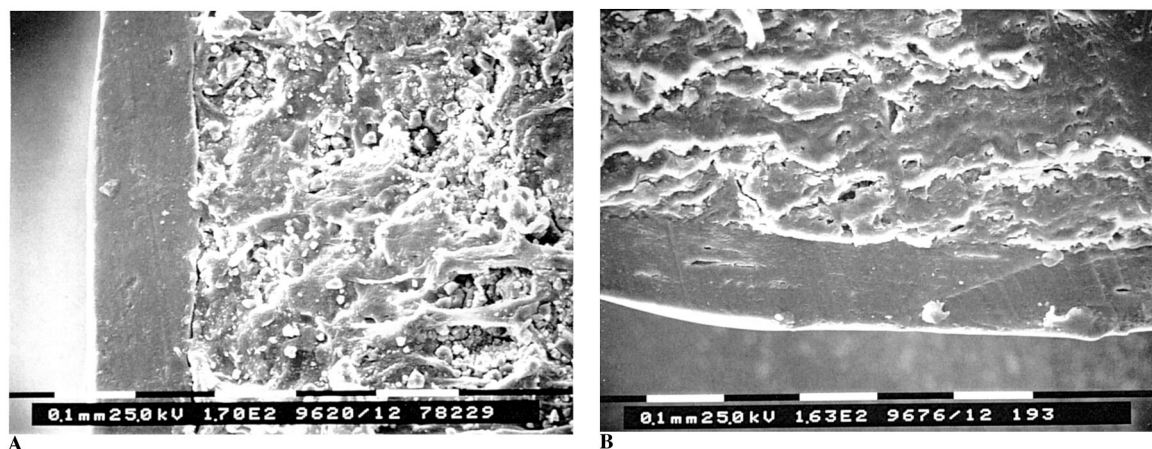


Fig. 7. A and B. SEM micrographs of atenolol GITS cross-sections showing the uniform homogeneous film around the tablet.

highly water swellable polymers, a seal coat was provided with 2% acetic solution of CA prior to pseudolatex coating. The CA pseudolatex had 8.1% w/w solids, and 160% of diacetin was used as the plasticizer based on the solids content. The processing conditions for CA pseudolatex coating are presented in Table 1.

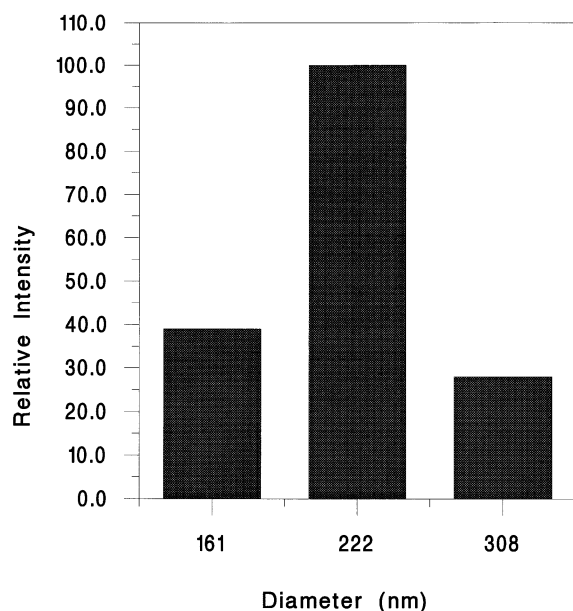


Fig. 8. Particle size distribution of CA pseudolatex.

### 3. Results and discussion

The pseudolatex is characteristically manufactured from the finished polymer itself. The polymer is dissolved in a suitable solvent and emulsified into water phase containing suitable emulsifying agent followed by solvent evaporation. This method has been applied for several polymers (Binschaedler et al., 1986; Vanderhoff et al., 1979; Wu et al., 1990; Bodmeier and Chen, 1991, 1993). CA is insoluble in non-polar solvents because of its high cohesive energy. Most of the solvents used for CA are slightly or completely miscible in water (Binschaedler et al., 1985). Reported organic solvents used in the preparation of CA pseudolatex were aniline, benzyl alcohol, cyclohexanone and a mixture of methylene chloride and methanol (Binschaedler, 1985; Bodmeier and Chen, 1993). They had either high boiling points, resulting in extended evaporation times during stripping or implicated in the formation of very viscous sediments of CA upon standing. Since the CA is soluble in the slightly/completely water miscible solvents ( $\delta = 9.9\text{--}14.7 \text{ (cal cm}^3)^{1/2}$ ), ethyl acetate, a moderately hydrogen bonded ester solvent ( $\delta = 9.9 \text{ (cal cm}^3)^{1/2}$ ) (Burrell, 1989) was used in the CA pseudolatex preparation. Because of its high flash point ( $-3^\circ\text{C}$ ), ethyl acetate was easily stripped from the emulsion.

Diacetin at 160% concentration, based on the solids content of the pseudolatex, was used as a



Table 4  
Mechanical properties of CA psuedolatex films

Diacetin concentration (%)	Tensile (kg/mm <sup>2</sup> )		Elongation (%)		Toughness (mm. kg/mm <sup>3</sup> )		Modulus (kg/mm <sup>2</sup> )	
	Average	S.D.	Average	S.D.	Average	S.D.	Average	S.D.
90	1.120	0.27	1.90	0.94	0.030	0.02	46.60	3.66
110	0.020	0.01	11.80	0.89	0.002	0.01	0.26	0.08
130	0.010	0.00	16.29	3.38	0.001	0.01	0.16	0.07
150	0.009	0.00	23.17	6.90	0.001	0.00	0.08	0.02

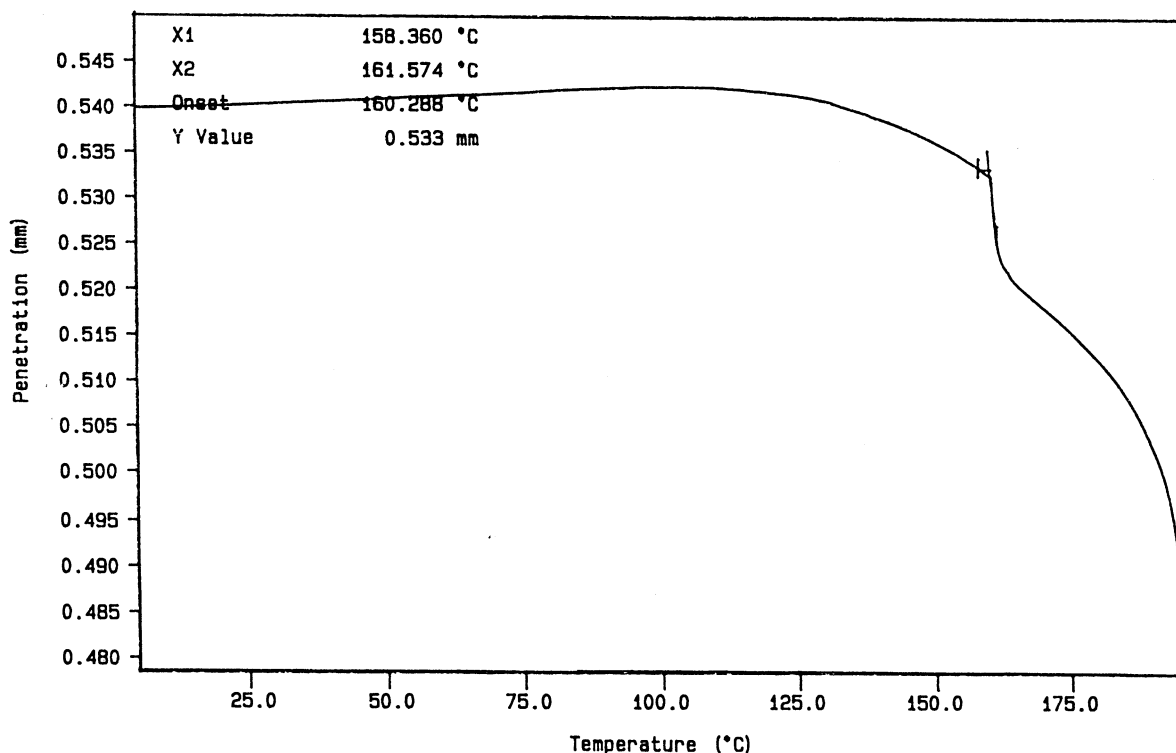


Fig. 9. Thermal mechanical analysis of unplasticized CA pseudolatex. The onset value is the measure of  $T_g$ .

plasticizer in this study. This high concentration should not be of a great concern since at processing temperatures of 60°C outlet temperature, the major content of plasticizer evaporates from the aqueous system and films have good tensile strength (Binschaedler et al., 1987). The residual amount of plasticizer is important for the integrity and the permeability of the resulting film. Literature reports indicated that water miscible plasticizers, such as diacetin produced mechanically

strong films while hydrophobic plasticizer admixture yielded weak membranes that cracked on contact with water (Binschaedler et al., 1987).

### 3.1. Positron annihilation spectroscopy (PAS) experiments

Positron has two possible states; free (delocalized) or positron state (localized) and free (delocalized) or localized positronium (Ps) state, in

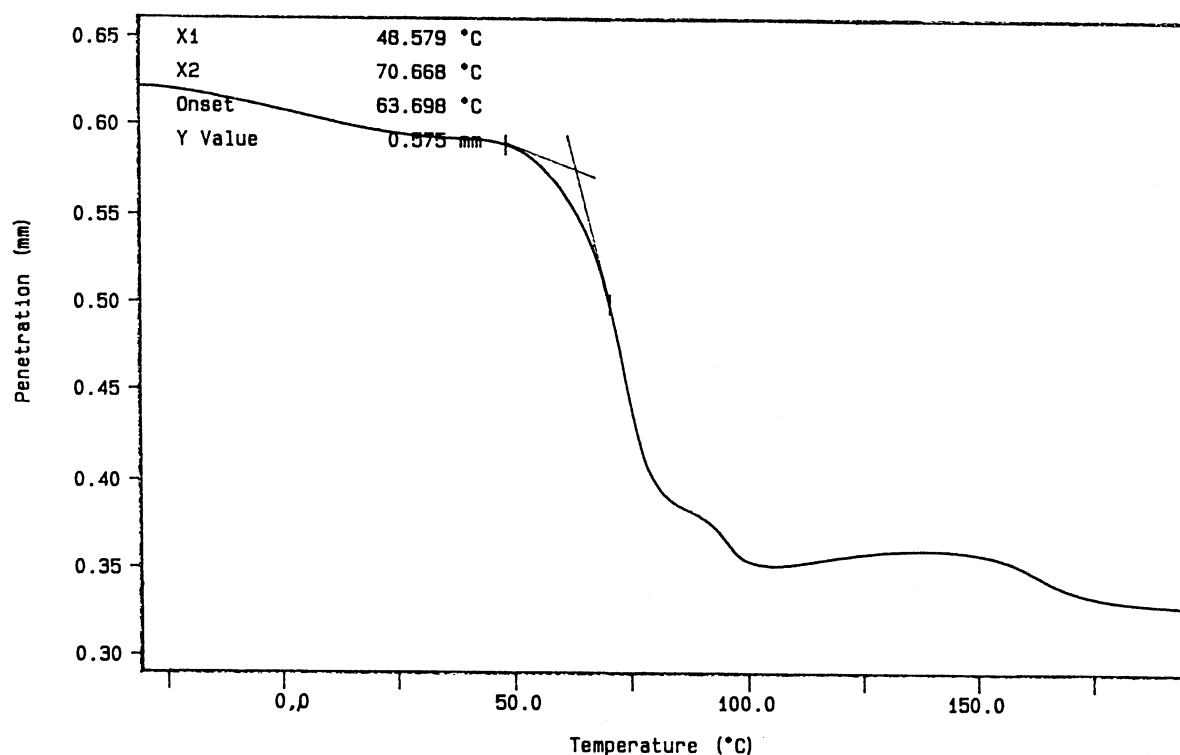


Fig. 10. Thermal mechanical analysis of 90% plasticized CA pseudolatex and the onset value is the  $T_g$ .

polymeric material. The localized sites are free volume spaces and more favorable sites for positron and Ps. The intensity of *o*-Ps state is the measure of free-volume concentration. The average size of the pores was estimated using the Eq. (2) (Jean, 1990).

$$\tau_3^{-1} = 2[1 - R/R_o + (1/2\pi) \sin(2\pi R/R_o)], \quad (\text{ns}^{-1}) \quad (2)$$

where  $R_o = R + \Delta R$  and  $\Delta R = 1.66 \text{ \AA}$ . Pore volume was calculated using  $R_o$  values and are shown in Fig. 3. It can be observed from Fig. 3, that as the life-time  $\tau_3$ , increased the pore volume also increased. The free-volume fraction ( $F_v$ ) can be given by the product of the free-volume size ( $V_f$ ) as derived from  $\tau_3$  and  $I_3$  (Nakanishi et al., 1989).

Therefore,

$$F_v = CV_f I_3 \quad (3)$$

where  $C$  is constant. The relationship between the free-volume fraction ( $F_v$ ) and diacetin concentration is shown in Fig. 4. The values for the above parameters, also shown in Table 2, exhibit a near-linear relationship. Increase in  $F_v$  should also result in increased membrane permeability. The tritium tracer diffusion experiments showed an increase in permeability value, Table 3, when the diacetin concentration increased from 90 to 160%. An increase in free-volume with a corresponding increase in plasticizer concentration has also been shown by other workers (Sinko and Amidon, 1989).

### 3.2. Scanning electron microscopy

The unplasticized pseudolatex observed, Fig. 5, under SEM showed distinct polymer particles with a particle size range in submicron magnitudes. The morphology of the casted films, Fig. 6, showed a homogenous surface appearance. The

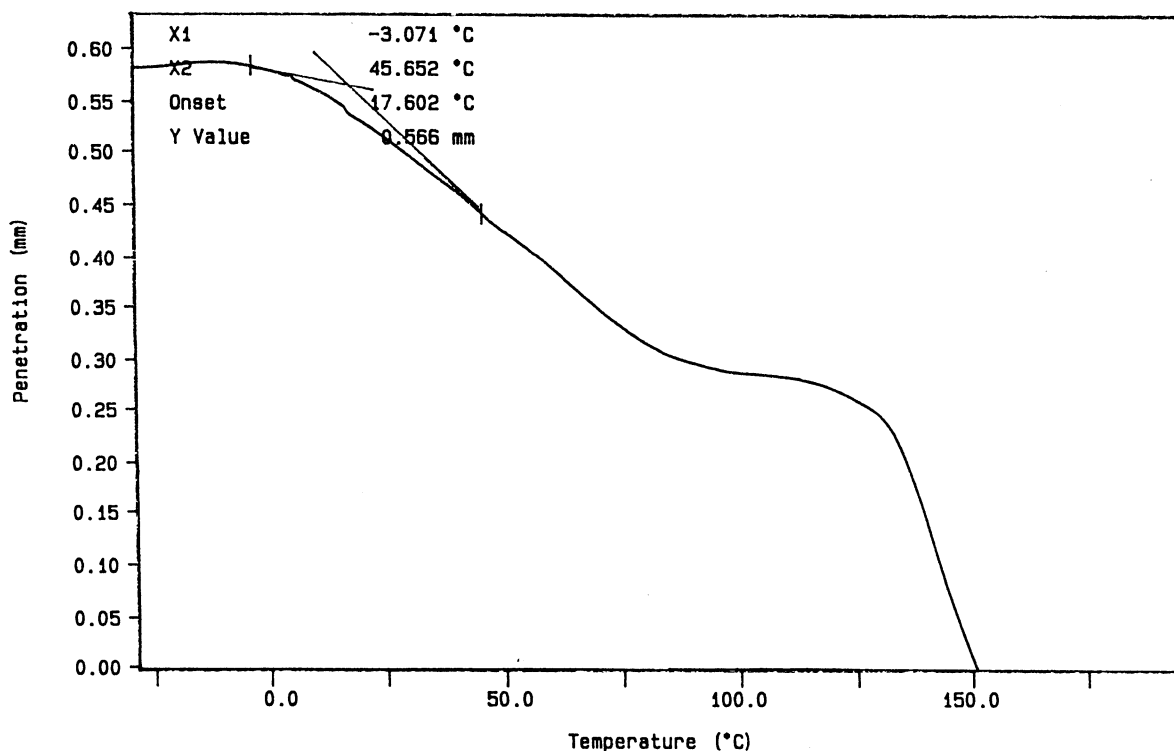


Fig. 11. Thermal mechanical analysis of 110% plasticized CA pseudolatex and the onset value is the  $T_g$ .

formation of strong and homogenous film formation around the osmotic tablets is evident from the SEM photographs, Fig. 7A and B, of the coated tablet sections. Therefore, the experimental CA pseudolatex is effective as an aqueous coating system. The dissolution experiments confirmed the strength and functional performance of the CA pseudolatex films. The process of film formation on solid substrates is continued by evaporation of water and the coalescence of polymer particles into homogenous film. Various theories describe the mechanism of film formation. Dillon et al. proposed that the polymer-water interfacial tension is the main driving force in the coalescence of the polymeric spheres (Dillon et al., 1951). Brown suggested that the capillary forces are responsible for the coalescence of the spheres (Brown, 1956). Vanderhoff et al. demonstrated that both forces are complementary to each other, and also proposed the theory of further gradual coalescence (FGC) during which films become more homogenous upon aging (Vanderhoff et al.,

1966). Besides, the product bed temperature at which the coating system is applied controls the overall end performance of the dosage form. This is more prominent when coating is intended for the controlled release application (Yang and Ghebre-Sellassie, 1990).

### 3.3. Particle size analysis

Particle size analysis of the CA pseudolatex revealed that the mean diameter of particles was 222 nm. with the polydispersity of 0.043. SEM showed (Fig. 5) that these particles are spherical in nature. The thermal convection and Brownian movement of the particles restricts the upper limit to 1  $\mu\text{m}$ . Both forces must be so high that the sedimentation occurs over very long periods of time (Lehmann, 1989). The particle size of the system also plays an important role in film formation. Low particle size of the pseudolatex increases the degree of coalescence as observed in Frenkel's equation (Vanderhoff, 1970):

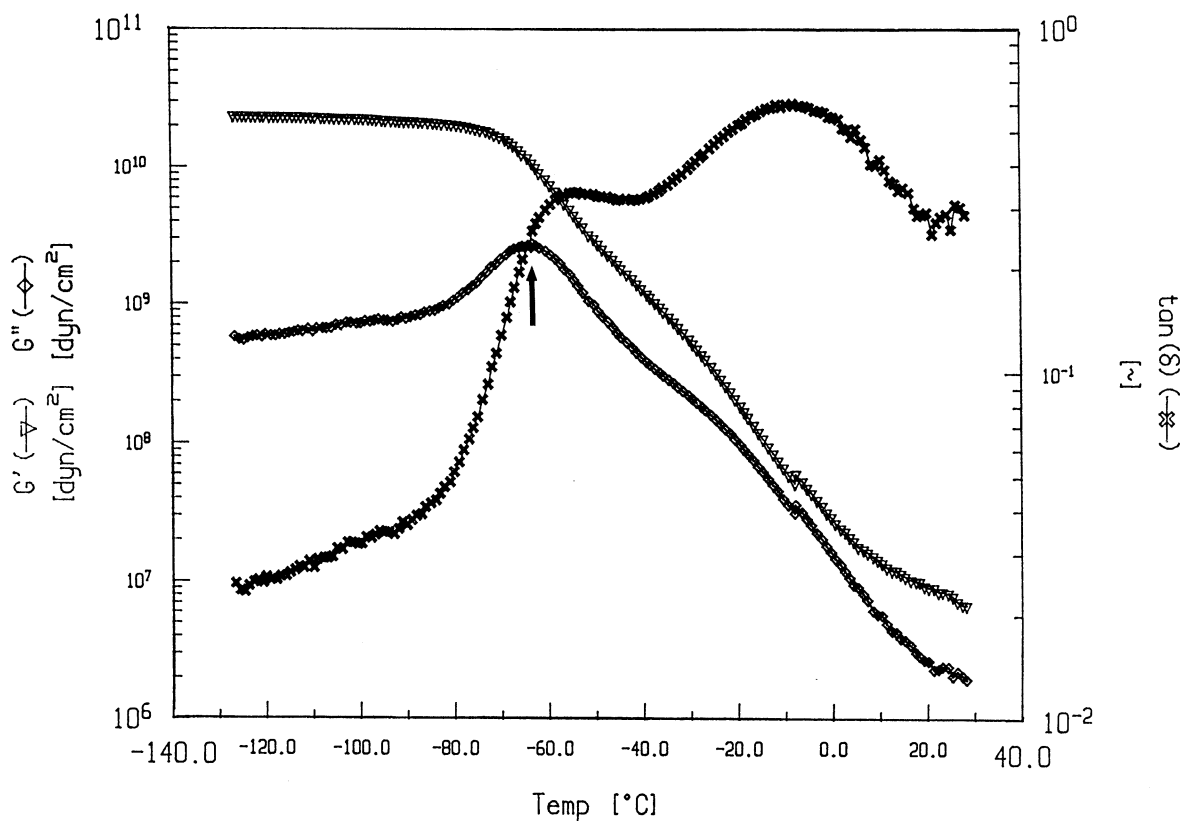


Fig. 12. Dynamic mechanical analysis of 160% plasticized CA pseudolatex.

$$\theta^2 = (3\gamma t)/(2\pi r\eta) \quad (4)$$

where,  $\theta$  is the half angle of coalescence;  $\gamma$  the surface tension;  $t$ , the time;  $r$  the particle radius and  $\eta$  the viscosity. And according to the Laplace–Young equation the capillary forces increase depending on the radius of the particle or the curvature of the aqueous meniscus (Vanderhoff, 1970):

$$P = 2\gamma/r \quad (5)$$

where,  $P$  is the pressure and  $\gamma$  is the surface tension. When the radius of the particles reduces from 1000 to 100 nm, the capillary forces increase 10-fold, and dispersions show better film formation (Lehmann, 1989). Fig. 8 shows the particle size distribution of CA pseudolatex particles in the nanometer size range. The SEM photographs (Fig. 6) show that the films are formed completely

and homogeneously confirming the efficiency of the CA pseudolatex as a coating system.

### 3.4. Viscosity experiments

Viscosity of the unplasticized and plasticized pseudolatex was 22.9 and 35.6 cps, respectively. The increase in viscosity for the plasticized system is obvious from the fact that in the presence of plasticizer, a moderate solvent, the polymer chains tend to relax and form a network structure. The storage modulus ( $G'$ ) and loss modulus ( $G''$ ) values of unplasticized and plasticized pseudolatex also showed an increase from 14.2 to 32.4 mPa and  $-2.67$  to  $22.1$  mPa respectively. This behavior is commonly observed with partly cross-linked polymer molecules (Physical Capillary Viscometer, Instruction Manual, 1991).

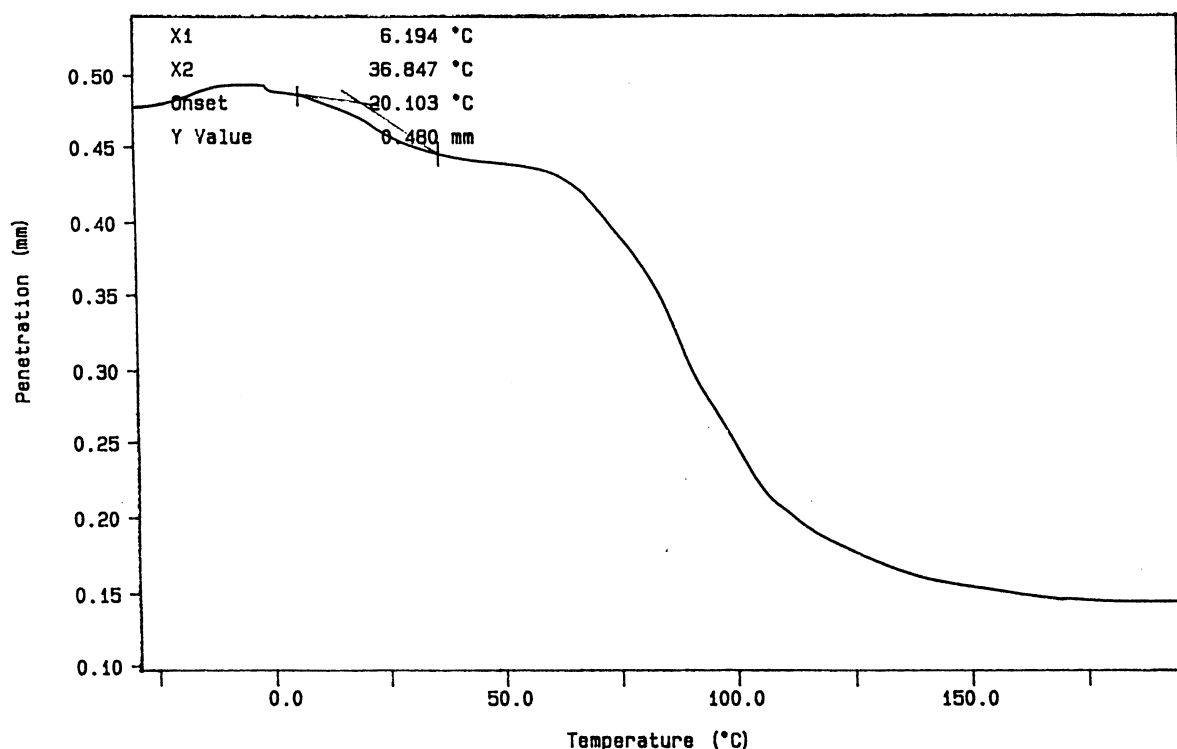


Fig. 13. Thermal mechanical analysis of actual film form tablet surface and the onset value is the  $T_g$ .

### 3.5. Mechanical properties

The mechanical properties of the films which include tensile strength, % elongation, toughness and Young's modulus are presented in Table 4. As the concentration of the plasticizer increased from 90 to 150% the mechanical properties showed a substantial decrease in their values except an increase in the % elongation of the films. Plasticizers modify the physical properties of the polymers to improve film forming behavior. In particular, plasticizers convert a hard, brittle polymer into a softer, more flexible material by reducing the glass transition ( $T_g$ ) and minimum film forming (MFT) temperatures (Lehmann, 1989). The  $T_g$  of the CA pseudolatex were 160°C (unplasticized pseudolatex, Fig. 9), 63°C (90% plasticizer, Fig. 10), 17.6°C (110% plasticizer, Fig. 11), –60°C (160% plasticizer, Fig. 12), and 20.1°C (actual film from tablet surface, Fig. 13). From this observation it is evident that less than 110% of the plasticizer was retained in the films. There-

fore, it can be concluded that a considerable amount of plasticizer evaporated during coating with high inlet and outlet temperatures. The high tensile strength of the film can also be explained by this fact (Binschaedler et al., 1986, 1987). Furthermore, since the heat of vaporization of water is high, and pseudolatex contains 75–80% water, relatively high inlet air temperatures are required to achieve the film formation. This high inlet temperature leaves the tablet bed at the temperature which is sufficient for the homogeneous film formation with 110% plasticization. If the starting plasticizer concentration were 110–120%, the loss during the coating would leave the system with very less plasticizer raising the  $T_g$  above practical coating temperatures. Therefore, high initial plasticizer content is required to achieve good film formation from CA pseudolatex. The MFT for the film containing 160% plasticizer was found to be < 10°C. The coating should be performed at least 10–20°C above the MFT of the pseudolatex so that the drying capacity of the

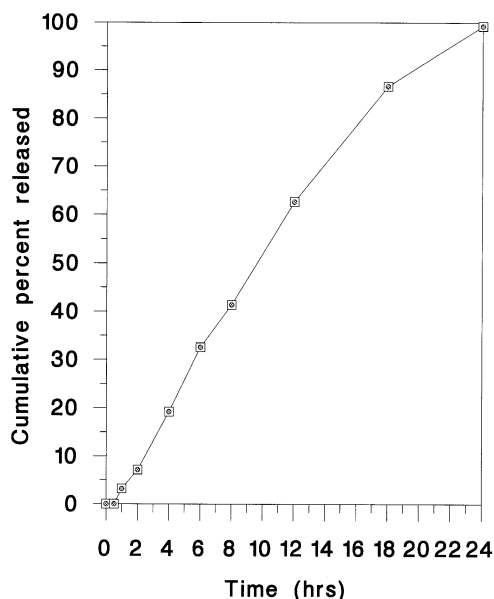


Fig. 14. Representative dissolution profile of atenolol GITS coated with CA pseudolatex.

incoming air is sufficient for fast drying (Lehmann, 1989).

### 3.6. Dissolution experiments

Atenolol GITS coated with the experimental CA pseudolatex yielded a zero-order rate release behavior. It is shown in Fig. 14. This result confirmed the utility of the CA pseudolatex prepared in our laboratory as the membrane provider.

In conclusion, CA pseudolatex was successfully prepared using ethyl acetate as the solvent. The characterization of the pseudolatex revealed that the system possesses suitable properties to be employed as a coating system. The system was successfully applied as a coating material to develop an osmotically controlled drug delivery system.

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