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*Research Article*

# Investigation of the Drug Release and Surface Morphological Properties of Film-Coated Pellets, and Physical, Thermal and Mechanical Properties of Free Films as a Function of Various Curing Conditions

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***Abstract.*** The purpose of the present investigation was to elucidate the influence of curing on different physical properties of Eudragit® NE and RS coating systems. Increased curing times resulted in decreased drug release rates from Eudragit® NE-coated beads. However, an increase in drug release rates was noticed at longer curing times and higher temperatures for the Eudragit® RS coating system. The surface morphological changes of the film-coated beads revealed that there were no visible macroscopic changes as a result of curing. The absence of any ibuprofen melting peak in the DSC thermograms of cured NE and RS coated beads confirmed that there was no surface crystallization of ibuprofen. These results indicated that the increase in drug release rates from RS coated pellets, when subjected to long curing times, resulted from loss of plasticizer. Free films of Eudragit® NE exhibited an increase in tensile strength with increased curing times, whereas Eudragit® RS free films showed a decrease in tensile strength beyond 4 h of curing at 70 and 90 °C. The film thicknesses and weights of free films of Eudragit® RS prepared with triethyl citrate plasticizer were found to change more dramatically with curing than did free films of Eudragit® RS prepared with ibuprofen as the plasticizer. An increase in pore volume was also observed with increased curing times for Eudragit® RS free films. Such changes with curing were shown to be due to the loss of plasticizer molecules, leading to the formation of molecular-scale voids and channels.

**KEY WORDS:** coated beads; curing; Eudragit® NE; Eudragit® RS; film coating.

## INTRODUCTION

Pharmaceutical film coatings have been applied for several purposes. These purposes include odor and taste-masking, improvement of dosage form appearance, protection of the drug core from environmental storage conditions (such as light, oxygen and water vapor), easy identification of drug products for both patients and health care professionals, and control of drug release rate. Reactive components present within the same dosage form can also be separated using polymeric film coating. In recent times, film coating has largely replaced sugar coating since it has several advantages. These advantages include: reduction in processing time, smaller increases in dosage form weight, better control of drug release and improved resistance to chipping (1).

Many polymers used for tablet coating have been formulated into aqueous colloidal dispersions (e.g. latexes and pseudolatexes) in order to overcome the environmental problems associated with the use of organic polymer solutions. But, the use of aqueous dispersions results in a complex mechanism of film formation (2–4). Strict adjustment of both the coating dispersion and the process is generally required to obtain the desired drug release characteristics in a reproducible manner. The complete coalescence of the dispersed polymeric particles must occur to obtain an effective coating of the pharmaceutical dosage form (5).

When the film-coated system is subjected to storage at temperatures above the polymer film's glass transition temperature ($T_g$), the polymer particles coalesce and inter-diffuse to form a homogeneous, continuous and complete film. This process is often referred to as further gradual coalescence or curing (6). Curing takes place to a certain extent during the coating process itself. However, this curing is fairly incomplete. To assure the completion of coalescence, the product is usually exposed to elevated temperatures following coat application, either in the coating machine using a process known as post-coating fluidization (6) or by placing the coated dosage forms into an oven (7,8). Such film properties as cohesion, mechanical strength and water diffusivity are all dependent on the extent of curing. The curing process is dependent on both the time and temperature used during the curing process, as well as the nature and concentration of the plasticizer incorporated into the coating.

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The rate of the curing process is accelerated at elevated temperatures. Post-coating storage temperature (9,10) has been reported to affect the dissolution rates of drugs from coated dosage forms. Researchers have shown that thermal treatment may accelerate (11), decrease (12), or have no effect on drug release (4).

The objective of this study was to determine the relationship between various physical properties and curing conditions for the commercially-available acrylate polymers, Eudragit® NE and Eudragit® RS.

## MATERIALS AND METHODS

### Materials

The materials that were used for the present investigations were all obtained from commercial sources. Ibuprofen was the drug used for the release studies and was obtained from Spectrum Chemical Mfg. Corp. (New Brunswick, NJ, USA). The coating polymers studied were Eudragit® NE and Eudragit® RS, both of which were generously donated by Röhm America, Inc. (Piscataway, NJ, USA). The polymer that was used as a binder for drug layering on non-pareil beads was a cellulosic polymer, Opadry®, which was supplied by Colorcon, Inc. (Chalfont, PA, USA). The plasticizer used for preparing the Eudragit® RS coating dispersion was triethyl citrate (TEC), which was supplied by Morflex, Inc. (Greensboro, NC, USA). Non-pareil beads, size 18–25 mesh, were purchased from Crompton and Knowles Corp. (Mahwah, NJ, USA).

### Methods

*Preparation of Ibuprofen-Loaded Film-Coated Beads*

Approximately 7 g of ibuprofen powder was first weighed. In a separate beaker, Opadry® (18 g) was weighed and added to 150 ml of distilled water. The Opadry® (hydroxypropyl methylcellulose) suspension was agitated with a propeller until the powder was completely dispersed. It is used as a binder and helps in the adhesion of ibuprofen to the bead surface. The previously-weighed ibuprofen was then added slowly into the vortex of the above suspension and the whole suspension was stirred for 2 h. Naked non-pareil beads were loaded into a 6-in., fluidized-bed, Wurster coater. The beads were pre-warmed inside the column for approximately 15 min prior to the initiation of the coating procedure. Coating of the naked non-pareil beads with the aforementioned ibuprofen/Opadry® aqueous dispersion was then initiated. After the drug layering was completed, the beads were dried overnight in a convection oven (30 °C) to evaporate the residual solvent. Known weights of the 16–20 mesh size, ibuprofen-loaded, non-pareil beads (40 g) were loaded into the same Wurster coater.

Fifteen percent (*w*/*w*) Eudragit® NE or Eudragit RS coating dispersions were then prepared. The Eudragit® RS dispersion also contained 10% *w*/*w* (plasticizer/polymer) triethyl citrate as the plasticizer. The coating dispersion was continuously stirred (magnetic stirrer) while it was being sprayed and the spraying rate was maintained at 5 ml/min. The film-coated pellets were cured at 50, 70 and 90 °C for 0.5, 2, 4, 6 and 8 h, respectively.

*Drug Release Studies in Simulated Intestinal Fluid*

*In vitro* dissolution studies were conducted with a USP 23 No. 2 (rotating paddle) dissolution apparatus (VanKel Ind., Cary, NC, USA) at a stirring rate of 55 rpm. The dissolution medium was simulated intestinal fluid (SIF), without pancreatin, prepared according to the USP method. The volume of the dissolution medium in each vessel was 900 ml. One-gram samples of the cured or uncured, Eudragit® NE or RS coated beads ($n$=3) were introduced into the dissolution medium (37 °C). Sample volumes of 5 ml were withdrawn at intervals of 15 min for the first 1 h of drug dissolution. Subsequently, samples were withdrawn every hour until the entire amount of drug was released, or until the cumulative percentage released reached a plateau. The sample volumes (5 ml) withdrawn from the dissolution vessels were replaced with the same volume of the dissolution medium to maintain a constant volume of the dissolution medium. The samples were all filtered using 0.45 μm syringe filters (Pall life sciences, Ann Arbor, MI, USA). The first 2 ml of the filtrate was rejected since it was used to saturate the filter. The remaining 3 ml of the filtrate collected after saturation of the filter was used for analysis. The filtered samples were assayed, either directly or after appropriate dilution with the release medium, by UV spectrophotometry at a wavelength of 222 nm.

*Thermogravimetric Analysis of Coated Beads*

Eudragit® NE coated beads loaded with ibuprofen and cured at 90 °C for various lengths of time were used for this study. Uncured beads of the same coating batch were also used. One gram of each of the cured and uncured bead samples were weighed separately and added to the dissolution vessels (900 ml of SIF each). The dissolution apparatus used was described in USP 23 No. 2 (VanKel Ind., Cary, NC, USA). Dissolution was carried out for 1 h at 37 °C. The beads were then collected from each vessel and patted dry with paper towels. Thermogravimetric analysis (TGA) was performed to determine the water contents inside the film-coated beads after 1 h of dissolution testing in SIF. A Perkin-Elmer thermogravimetric analyzer, Model TGA-7 with TAC 7/DX thermal analysis controller (Waltham, MA, USA), was used. TGA analyses were performed over a temperature range of 25 to 160 °C at a heating rate of 10 °C per minute (nitrogen purge). Weight calibration was accomplished using the 100 mg Class M calibration standard (part no. 0990–8397) provided with the instrument. The Curie-point temperature calibration was performed using an Alumel standard with a magnetic transition temperature of 163 °C.

*Scanning Electron Microscopy of Coated Beads*

Scanning electron microscopy was performed to study the surface morphological changes of Eudragit® NE coated multi-particulate beads before curing and after 6 h of curing at 90 °C. The bead samples were mounted directly onto aluminum stages and were sputter coated with a gold/palladium mixture for 1 min under an argon atmosphere (Pelco Model 3, sputter coater). Scanning electron microscopy was performed using a Hitachi S-2460 microscope (Hitachi

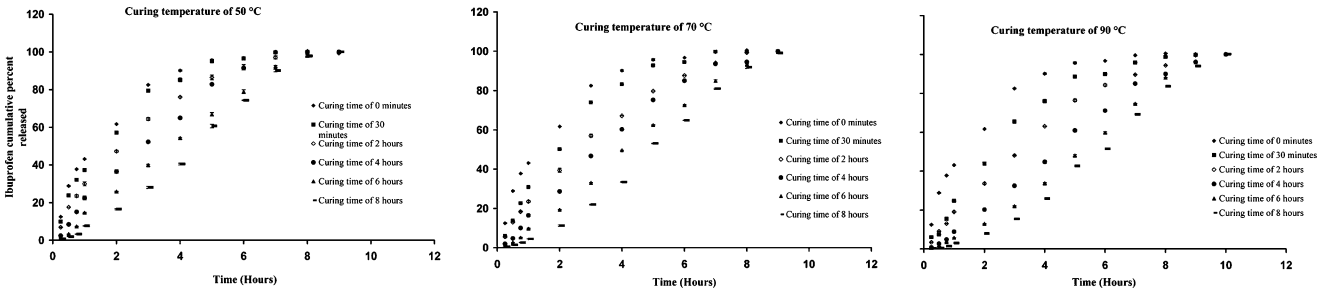


**Fig. 1.** Effect of curing on ibuprofen release rates from Eudragit® NE coated pellets

USA Inc, Madison, WI, USA) at 20 kV. The digitized scanning electron micrographs were stored on a CD-R.

*Differential Scanning Calorimetry to Determine the Physical State of Ibuprofen*

A differential scanning calorimeter, Perkin-Elmer Model DSC-7 with a TAC 7/DX thermal analysis controller, was used to study the effect of curing on the physical state of the ibuprofen located between the non-pareil surface and the film coat. The apparatus was calibrated using the melting transition of indium. Approximately 8–10 mg of the desired sample was placed inside the aluminum sample pan and the pan was sealed by crimping. Thermal analyses were carried out for pure ibuprofen powder and for uncured and cured Eudragit® NE and Eudragit® RS film-coated beads. The studies were performed under a nitrogen purge over a temperature range of 25 to 150 °C. A scanning rate of 10 °C/min was employed.

*Preparation of Polymeric Free Films*

Fifteen percent (*w*/*w*) Eudragit® NE and Eudragit® RS aqueous dispersion was prepared separately using the commercially available 30% aqueous colloidal dispersions of the two polymers. In addition to water, the Eudragit® RS dispersion also contained 1.5 g, or 10% *w*/*w* (plasticizer/polymer) of triethyl citrate (TEC) as the plasticizer. A separate Eudragit® RS coating dispersion that contained 10% *w*/*w* (plasticizer/polymer) ibuprofen as the plasticizer was also prepared. The coating dispersions were all agitated using a magnetic stirrer for at least 8 h prior to use to ensure proper dispersion of the polymer and also complete partitioning of the plasticizer into the polymeric phase of the Eudragit® RS coating dispersion.

Fifteen milliliters of the dispersions were pipetted (separately) into circular, Teflon-coated plates with a diameter of 6 cm. These plates were then dried overnight under ambient conditions to allow film formation. Upon drying, the films were removed from the Teflon plates and cut into square pieces of equal dimensions. The thicknesses of the film specimens were measured using a six-inch electronic digital calipers (NM9560A, Nesco, Amazon, www.amazon.com). The average film thickness was found to be around 0.5 mm. The free films were then cured at 50, 70 and 90 °C and 2, 4, 6, 8, 11 and 24 h. All temperature and time combinations were employed.

*Mechanical Properties of Free Films*

Mechanical evaluation of both cured and uncured free films was performed using a tensile-strength testing apparatus (EnduraTEC, Minnetonka, MN, USA) which was interfaced to a computer. The changes in load and in film displacement with respect to time were fed to the computer with the help of WINTEST software. The films were cut into 4-mm-wide and 40-mm-long strips and the ends of the films were attached to clamps that were screwed to the instrument. Upon clamping, the films were stretched by application of a load of 100 N. The cross-head speed was set at 10 mm/min. Stress at failure, or the tensile strength, was calculated as the maximum load divided by the cross-sectional area of the film prior to stretching (stress=force/area=N/m$^2$). Strain at failure was calculated as the change in length at the time of sample failure divided by the original length, with the quotient multiplied by 100. A minimum of five film samples were used for each curing condition. Average tensile strength and percent elongation values were calculated.

*Differential Scanning Calorimetry to Measure the Glass Transition Temperatures of Free Films*

The glass transition temperatures ($T_g$) of the film samples were measured using a Differential Scanning Calorimeter (Perkin-Elmer DSC-7 system with TAC 7/DX thermal analysis controller. The apparatus was calibrated using the melting transition of indium. The cured and uncured film samples were cut into small pieces, with each piece weighing approximately 8–10 mg. The pieces were individually placed inside aluminum sample pans, which were sealed by crimping. Thermal analyses of the free film samples were performed under a nitrogen purge over a temperature range of −20 to 100 °C. A scanning

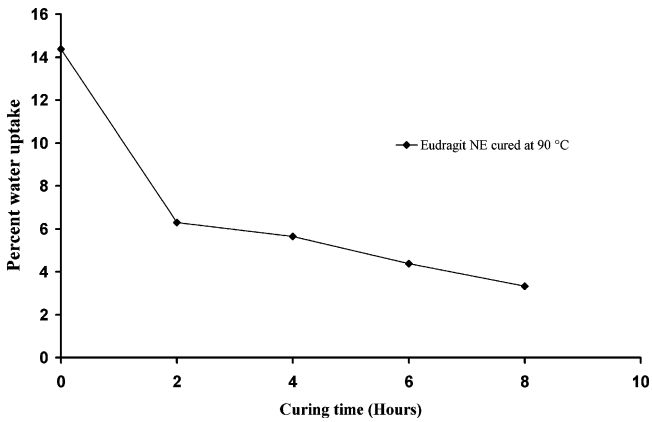


**Fig. 2.** Effect of curing at 90 °C on percent water uptake by Eudragit® NE coated pellets undergoing dissolution for one hour in simulated intestinal fluid

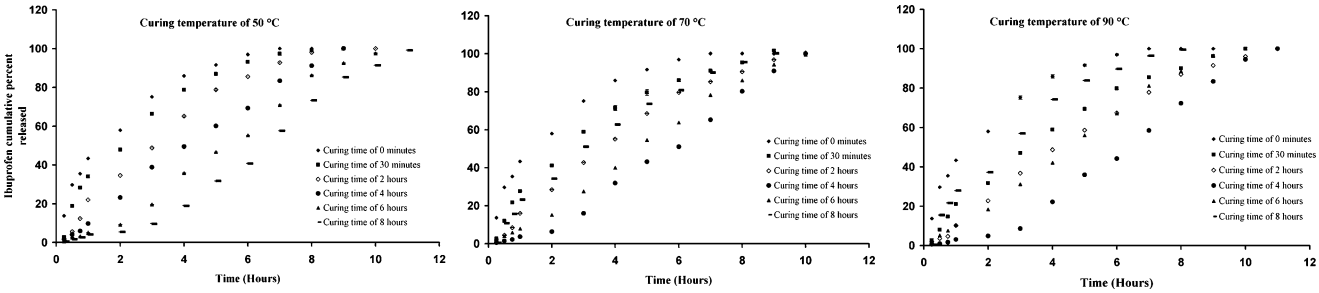


**Fig. 3.** Effect of curing on ibuprofen release rates from Eudragit® RS coated pellets

rate of 10 °C/min was used. The glass transition temperature was calculated from the midpoint of the endothermic curve.

*Physical Characterization of Free Films*

The changes in thicknesses and in weights of the Eudragit® RS free films containing either 10% *w/w* (plasticizer/polymer) triethyl citrate (TEC) or 10% *w/w* (plasticizer/polymer) ibuprofen were measured as a function of curing times. This study was performed on films that were cured at 70 °C. The thicknesses were measured using a 6-in. electronic digital calipers (NM9560A, Nesco, Amazon, www.amazon.com). Measurements were performed at three different points on each film sample and the average was calculated. A Mettler balance (Model 1712, Westbury, NY, USA) was used to measure the weight. Weighing was performed after sample cooling. The change in thickness and weight was then plotted *versus* the curing time in hours.

*Determination of the Pore Volume of the Free Films*

The average pore volumes of Eudragit® RS free films prepared with 10% *w/w* (plasticizer/polymer) triethyl citrate and cured at 90 °C for 4, 6 or 8 h were determined using a Quantasorb instrument (Model QS-16, Quantachrome Corp., Boynton Beach, FL, USA). Nitrogen, the adsorbate gas, and helium, the carrier gas, were supplied by Air Products and Chemicals, Inc. (Allentown, PA, USA). A Quantasorb flow control accessory (Model LMFC-6, Quantachrome Corp.) was used to provide the selected relative pressures of nitrogen. The ambient pressure and temperature were measured using a combination barometer-temperature device (Model 84450186, Sargent-Welch Scientific Co., Skokie, IL, USA). The $N_2$ and He flow rates were adjusted to achieve a relative pressure, $P/P_0$ value of 0.97 for nitrogen.

The free film samples were placed inside a dry sample cell (Model 74005–20, Quantachrome Corp.) and purged under a stream of nitrogen (ambient temperature and pressure) for 24 h prior to analysis. After conditioning of the sample, the sample cell was connected to the sample station and the desired relative pressure of $N_2$ (0.97) was set. A Dewar flask containing liquid nitrogen was then raised to immerse the sample cell in the coolant. After the process of adsorption followed by capillary condensation was complete, the desorption button was depressed, the signal meter was again set to zero using the coarse and fine zero-adjust knobs (if required), the integrator was reset and the Dewar flask was lowered from the sample cell. After desorption of the adsorbed nitrogen was complete, the number of integrator counts was recorded.

The integrator was then reset to zero and a known volume of $N_2$ gas was injected into the Quantasorb using a gas-tight syringe. The quantity of the $N_2$ gas was selected such that the number of integrator counts from this injection would be within 10% of the number of integrator counts for the sample. The number of counts from the known injection was then recorded for the $N_2$ desorption peak. The average pore volume of each film sample was calculated using the following equations:

$$\text{Volume of gas}, V_{\text{desorption}} = A_s / A_{\text{cal}} \times V_{\text{cal}} \quad (1)$$

$A_s$ area of signal for the desorption peak
$A_{\text{cal}}$ area of signal for the calibration injection
$V_{\text{cal}}$ calibration volume

$$\text{Total pore volume}, V_{\text{liquid}} = \left(P_a \times V_{\text{desorption.}} \times V_m\right) / (R \times T) \quad (2)$$

Where,
$V_m$ molar volume of liquid adsorbate; 34.7 $cm^3$/mol for nitrogen
$R$ gas constant; 82.1 atm.$cm^3$/(K.mol)
$T$ ambient temperature (K)

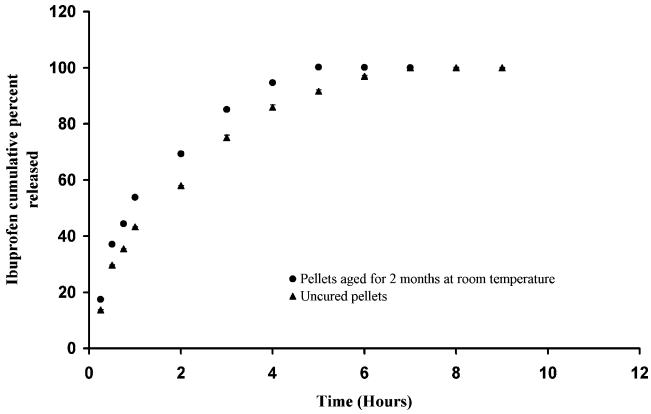


**Fig. 4.** Effect of aging for 2 months at room temperature on the ibuprofen release profile from Eudragit® RS coated pellets

## RESULTS AND DISCUSSION

Film formation from aqueous colloidal polymeric dispersions involves deformation and coalescence of discrete polymer particles so as to form a continuous film. Film formation is a kinetic process and is dependent on both curing time and temperature. Hence, optimal curing can be accomplished by selecting those conditions that result in complete film formation with the minimum exposure to conditions unfavorable to the drug entity.

In this study, the effect of curing on ibuprofen release rates from film-coated beads was investigated in simulated intestinal fluid (SIF). Ibuprofen release profiles in SIF, from NE coated beads cured at 50, 70 and 90 °C, are shown in Fig. 1. A continuous retardation of ibuprofen release rates with increasing curing times was observed. The slower release rates at longer curing times were attributed to the fact that longer curing times resulted in greater coalescence of the polymer particles and the formation of a more continuous and dense film coating. In a previous study it was shown that the release rates were dependent on the membrane thickness, with release being slower from dosage forms with thicker film coatings (13). Those authors varied the film thicknesses by diluting the latex with water while keeping the casting volume constant.

Another interesting observation in this current study was the gradual change in the shape of the release profile with increasing curing times. At longer curing times, the release profiles show an initial lag time, giving way to a sigmoid-shaped ibuprofen release profile. This pattern was evident for all curing temperatures for beads that were cured for 6 and 8 h. This profile can be attributed to the fact that higher curing times result in a more complete and dense film coating. The initial lag time relates to the longer time required for the dissolution medium to diffuse through the film coating.

The longer time required for dissolution medium to diffuse through the film coating was verified by carrying out thermo-gravimetric analyses (TGA) of the NE coated pellets cured at 90 °C for different time periods (Fig. 2). These pellets were subjected to simulated intestinal fluid (SIF) for

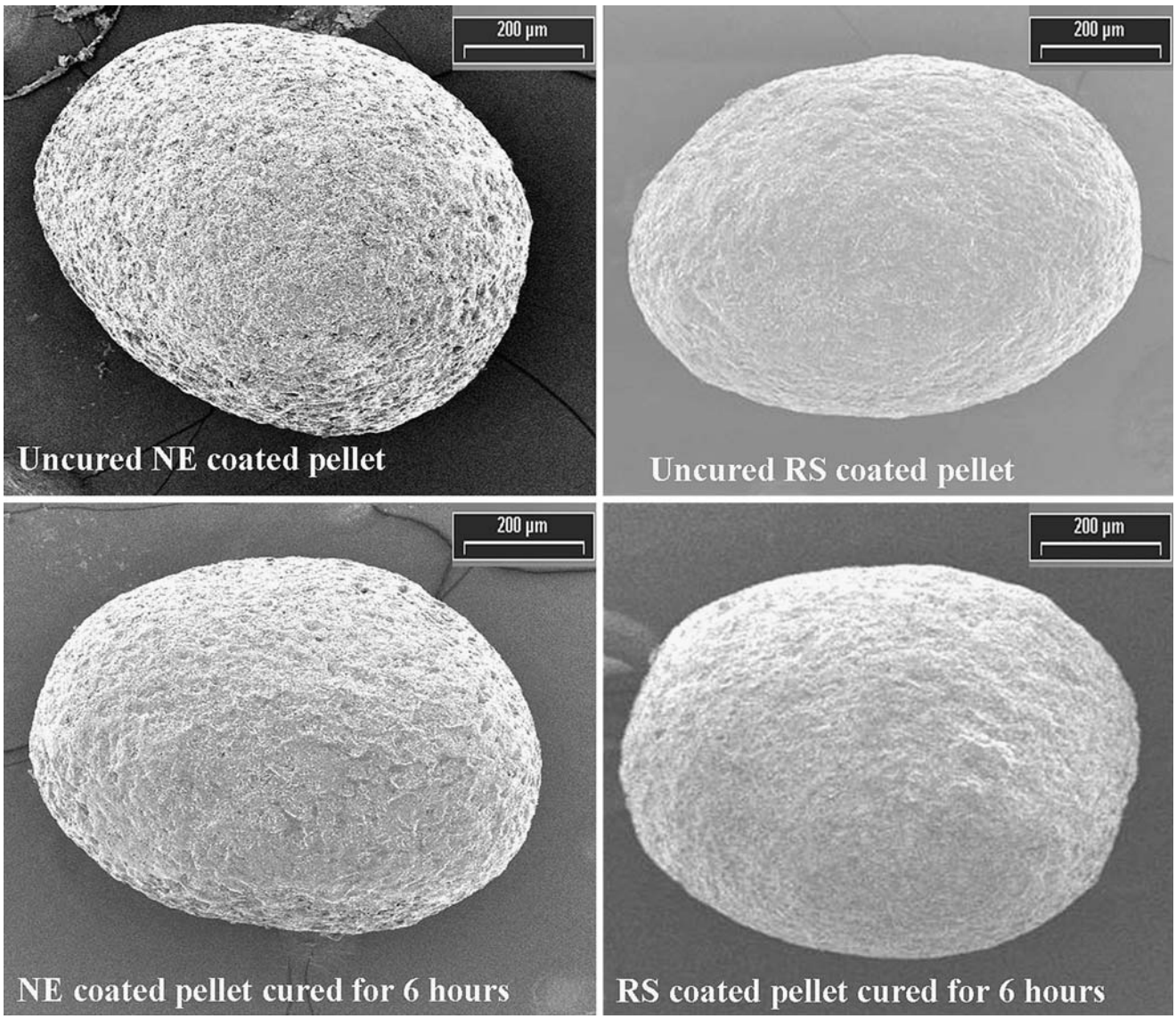


**Fig. 5.** Effect of curing at 90 °C on the surface morphological properties of Eudragit® NE and Eudragit® RS coated pellets

the same amount of time (1 h). This allowed the determination of the water contents of the pellets after exposure to the dissolution medium. From Fig. 2, it can be observed that the total water content for uncured pellets is approximately 14.4% *w*/*w*, and that this value decreases to approximately 3.3% *w*/*w* for pellets cured for 8 h at 90 °C. From the results, it can be suggested that pellets cured for longer times will have imbibed less water one hour after immersion than pellets cured for shorter times.

The ibuprofen release profiles from Eudragit® RS coated beads cured at 50, 70 and 90 °C are shown in Fig. 3. The drug release pattern for bead samples cured at 50 °C follows a similar trend to that observed with Eudragit® NE coated beads. However, the release patterns for Eudragit® RS coated pellets cured at 70 and 90 °C were quite different from the 50 °C results. The release rates showed an initial decrease, which was followed by an increase for curing times of 6 and 8 h. Such changes could result from curing beyond the system's optimal curing condition. In order to confirm this hypothesis, the Eudragit® RS coated pellets were subjected to aging studies (2 months) at room temperature. The drug release rate from the aged pellets, was compared to the

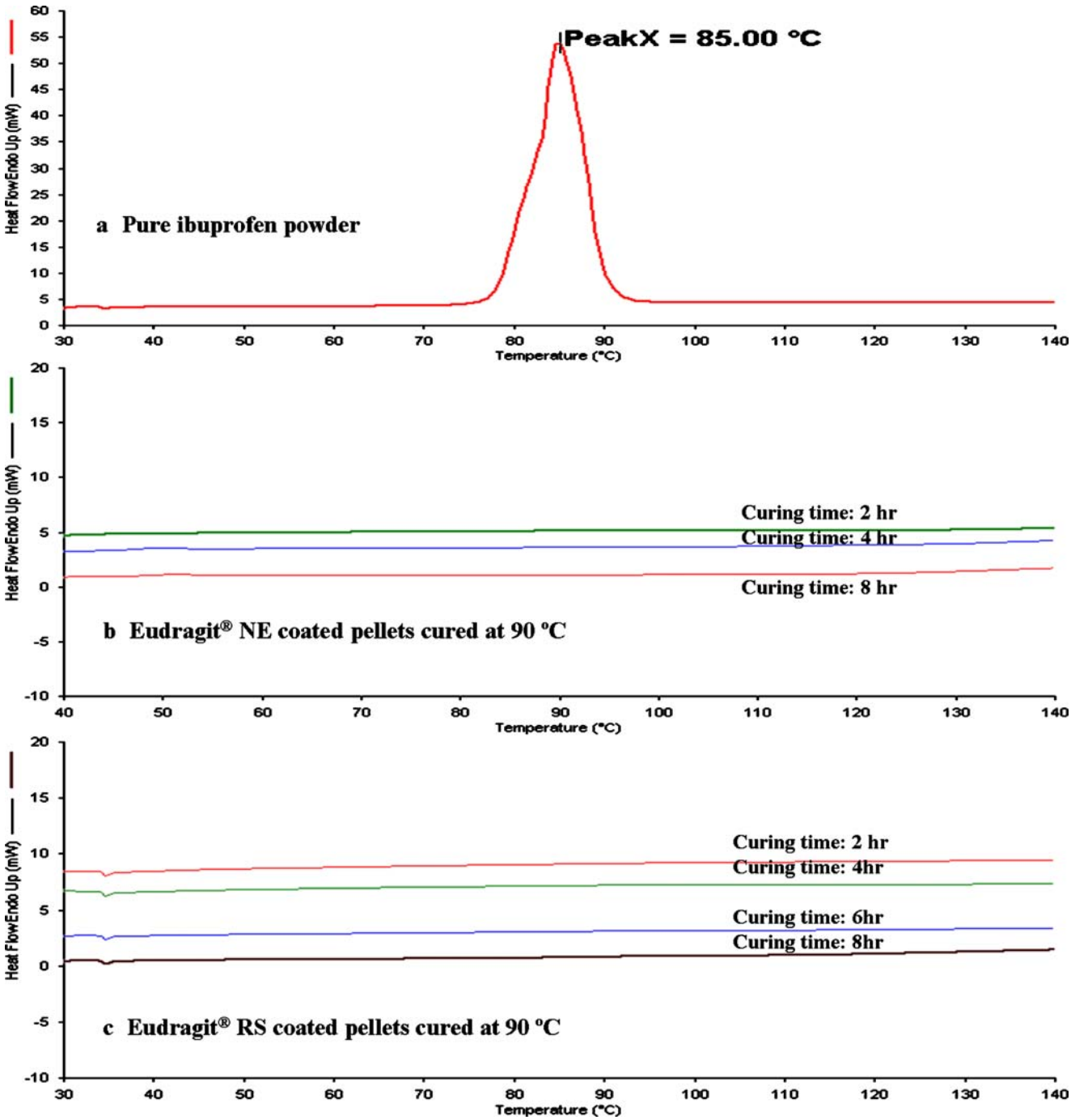


**Fig. 6.** DSC thermograms of **a** Pure ibuprofen powder; **b** Eudragit® NE coated pellets cured at 90 °C and; **c** Eudragit® RS coated pellets cured at 90 °C

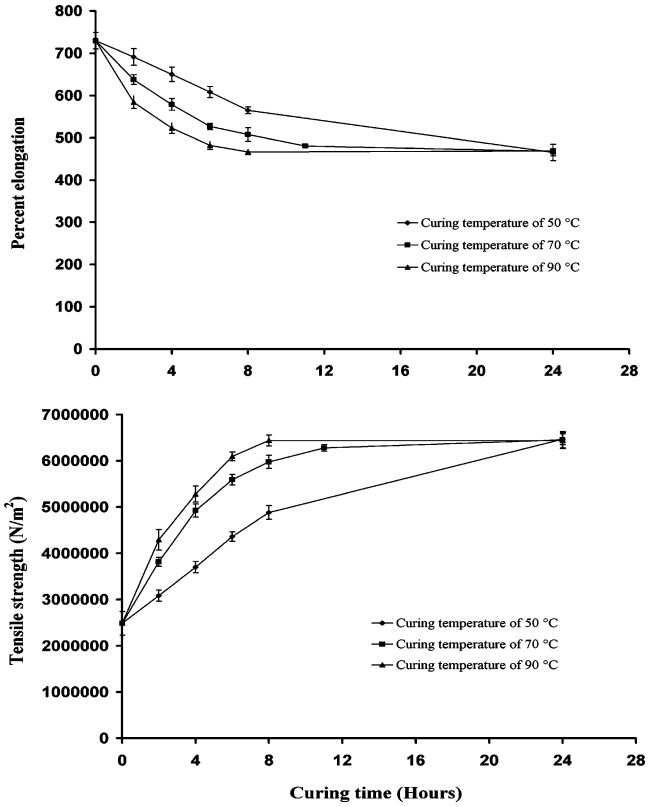


**Fig. 7.** Effect of curing on percent elongation and tensile strength of Eudragit® NE free films

release rate from the uncured pellets (Fig. 4). When pellets are aged at room temperature there will be some amount of polymer chain movement during the aging process. As a result, there is going to be some degree of polymer film coalescence. Therefore, a decrease in the drug release rate should be observed from aged pellets when compared to uncured pellets. Instead, a slight increase in the ibuprofen release rate is seen for the RS-coated pellets that were subjected to aging. This is possible only if a less dense film, presumably due to an increase in film porosity, occurs as a result of the aging process.

In previous studies, researchers have indicated that the increase in the drug release rate as a result of over curing could result from partitioning of the drug into the film coating (11). It was speculated that the foregoing could lead to the formation of drug crystals on the surfaces of the film-coated pellets, which would result in higher drug release rates. Observation of the surfaces of the cured pellets by SEM and analysis of the physical state of ibuprofen within the film-coated pellets by DSC were performed by these authors to evaluate the potential for ibuprofen to partition into the coat. The micrographs for the uncured and cured Eudragit® NE and Eudragit® RS coated pellets are shown in Fig. 5. From the micrographs, it can be determined that there were no visible macroscopic changes in the surface morphologies of the film-coated pellets as a result of curing. Essentially, the curing process promotes polymer-chain inter-diffusion in the coat, which "patches up" small cracks and pores. SEM micrographs of the cured RS coated pellets do not show the presence of any ibuprofen crystals on the surfaces of the film-coated pellets. Thus, the higher release rates did not occur due to partitioning of the drug into the film coating with subsequent surface crystallization.

The physical state of ibuprofen in the coated pellets was also examined as a function of curing. Pellets subjected to different curing conditions were analyzed. The ibuprofen melting peak was identified using the DSC thermogram of the pure drug powder (Fig. 6a). The DSC thermogram for the naked pellets did not show any peaks within the same range. A Wurster coater was used to layer the naked pellets with ibuprofen dispersed in Opadry®. The process of solvent evaporation is so fast with this system that crystallization on the surfaces of the naked pellets is not possible. Hence, prior to film coating with Eudragit® NE or RS, the drug is molecularly dispersed within the internal drug/Opadry® coat. If the curing of NE or RS coated pellets results in partitioning of ibuprofen into the film coat and its subsequent crystallization on the outer surface of the film coat, an ibuprofen melting peak would be observable. The absence of any drug melting peak in the DSC thermogram for cured Eudragit® NE coated pellets (Fig. 6b) or in the DSC thermogram for cured Eudragit® RS coated pellets (Fig. 6c) confirms that there was no surface crystallization of ibuprofen. From these results, it can be inferred that the increase in the ibuprofen release rate from Eudragit® RS coated pellets, when subjected to long curing times, resulted from some phenomenon related to the loss of plasticizer. In order to confirm this fact, further characterizations of free films were carried out.

Film coatings that exhibit high mechanical strengths and percent elongations are the most suitable candidates for

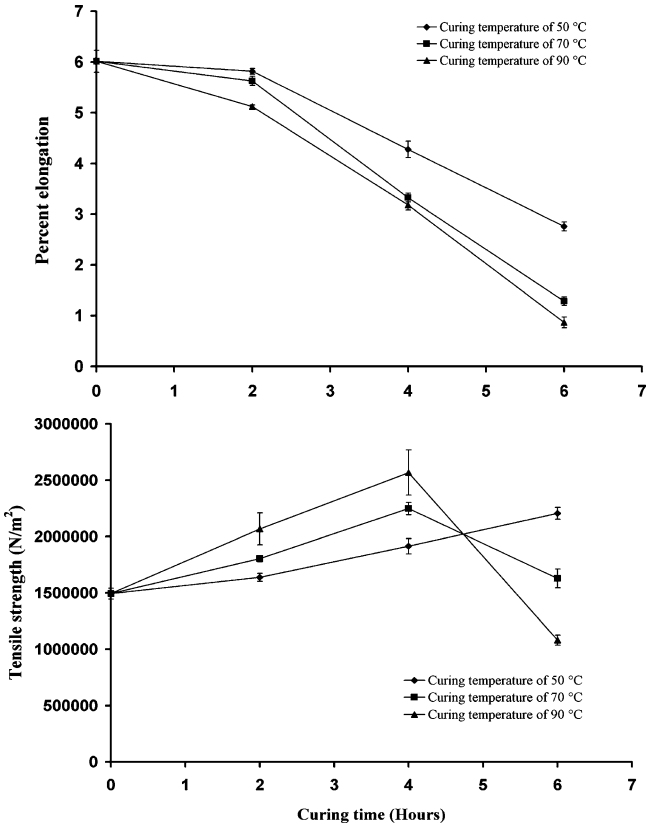


**Fig. 8.** Effect of curing on percent elongation and tensile strength of Eudragit® RS free films

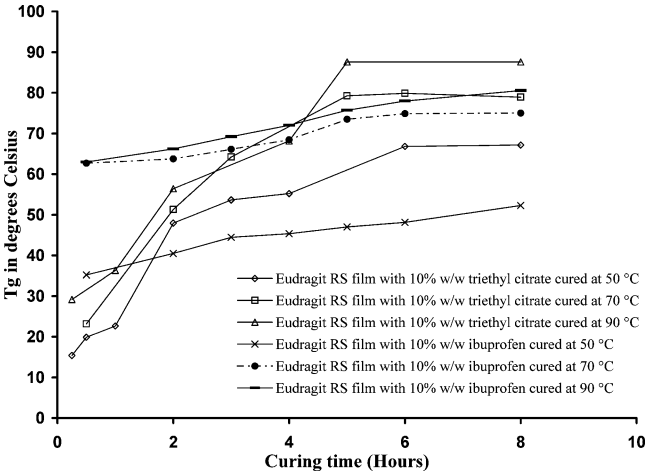


**Fig. 9.** Effect of curing on glass transition temperatures of Eudragit® RS free films prepared using 10% *w/w* ibuprofen and 10% *w/w* triethyl citrate as the plasticizers

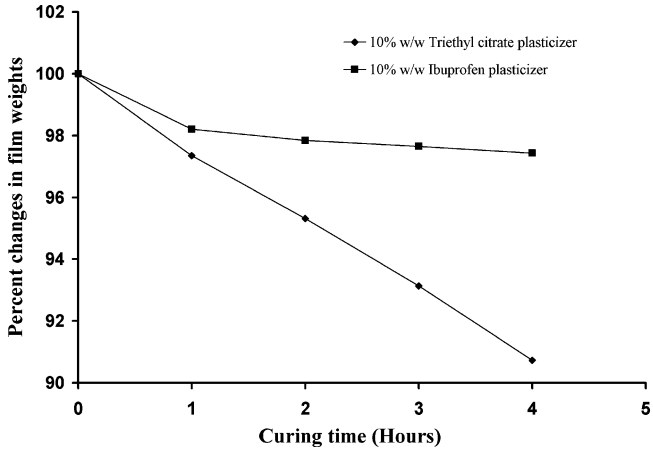


**Fig. 11.** Effect of curing at 70 °C on percent changes in film weights of Eudragit® RS free films prepared using 10% *w/w* ibuprofen and 10% *w/w* triethyl citrate as plasticizers

tablet coating. Curing can result in extensive structural changes within a polymeric film coating by inducing coalescence of the polymer particles. This coalescence will lead to the formation of tougher and stronger films. The influence of curing on the mechanical properties of Eudragit® NE and RS free films was investigated as a function of curing (Figs. 7 and 8). For the Eudragit® NE free films, the tensile strengths increased to a plateau value and the percent elongations at failure decreased to a plateau value. This occurred within 8 h of curing at a curing temperature of 90 °C, within 11 h at a curing temperature of 70 °C, and within 24 h at a curing temperature of 50 °C. The rate of change of the mechanical properties was observed to be faster at higher curing temperatures.

Curing not only causes structural changes but also results in moisture loss from the film samples. Moisture acts as a plasticizer and can help in reducing inter-molecular attractions between the polymer chains. Hence, its loss causes an increase in tensile strength and a decrease in percent elongation of the film specimens (14). Higher curing temperatures have also been shown to increase the percent tensile strengths of ethylcellulose pseudolatex coating systems (9). The changes in mechanical properties that were observed for Eudragit® NE film samples with curing is thus a result of both structural changes and moisture loss.

It can be observed (Fig. 8) that Eudragit® RS film samples reached 1.3% and 2.8% elongation after being cured for 6 h at 70 and 50 °C, respectively. The tensile strengths of the films showed a gradual increase with increasing curing time at 50 °C. But, at curing temperatures of 70 and 90 °C, the tensile strengths of the film samples showed an initial increase, but, in each case, reached a maximum value within 4 h of curing. After the maximum value, there was a sudden decrease.

It has been shown (15) that a decrease in the tensile strength value with curing correlated to increased coating defects. It has also been shown that a decrease in the plasticizer content within the polymeric film samples resulted in a decrease in the percent elongation and a corresponding increase in the tensile strength values (9, 16). From the foregoing observations and the results obtained in this study, it can be hypothesized that film formation was completed, or the best curing possible under these conditions was achieved, within the first 4 h of curing at 70 and 90 °C for the Eudragit® RS film samples. Further curing resulted in extensive loss of plasticizer (triethyl citrate), leading to an increase in the glass

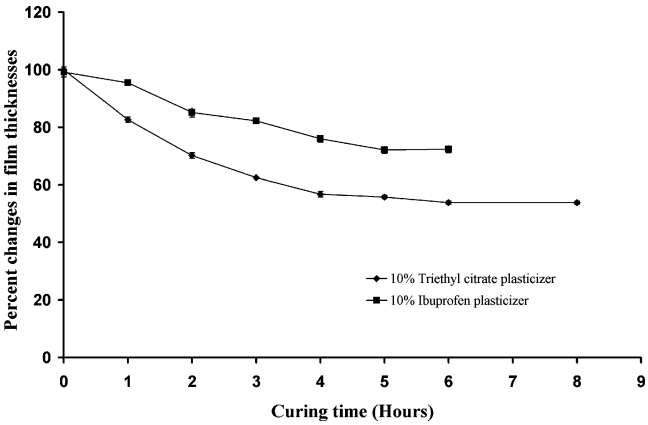


**Fig. 10.** Effect of curing at 70 °C on percent changes in film thicknesses of Eudragit® RS free films prepared using 10% *w/w* ibuprofen and 10% *w/w* triethyl citrate as plasticizers

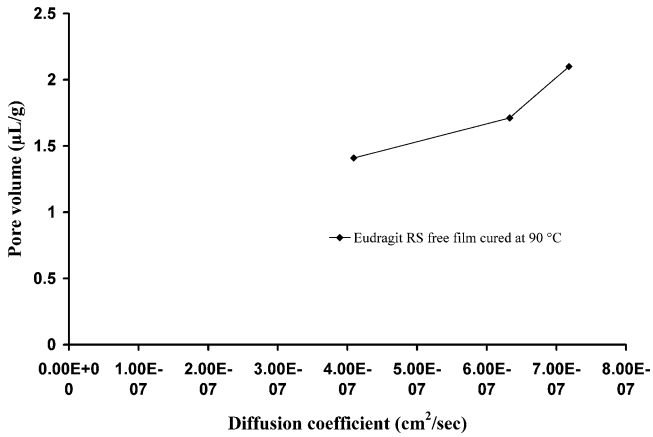


**Fig. 12.** Effect of curing at 90 °C on the pore volumes of Eudragit® RS free films

transition temperature ($T_g$) as previously shown by these authors (17). The increase in $T_g$ rendered the film samples brittle and weak.

Studies were also done to compare the effects of curing on the $T_g$ values of RS free films prepared separately using either triethyl citrate (TEC) or ibuprofen as the plasticizer. The results are shown in Fig. 9. When ibuprofen was used as the plasticizer, the change in Tg value was caused mainly by the evaporation of excess moisture during the curing process. But, in case of TEC, the change in $T_g$ was much more dramatic and was caused by the evaporation of both excess moisture and TEC.

Curing of RS free films prepared with TEC also resulted in greater changes in percent film thicknesses (Fig. 10) and percent film weights (Fig. 11) compared to RS free films prepared with ibuprofen as the plasticizer. These data are consistent with the changes that were observed in the glass transition temperatures of Eudragit® RS film samples as a function of curing. The total loss in weight after 4 h of curing at 70 °C for TEC containing films was 9% *w*/*w* compared to 3% *w*/*w* for ibuprofen containing films. The extra 6% loss for the TEC system could be attributed to loss of TEC.

Plasticizer loss could also lead to the formation of molecular pores and voids within the polymeric film coatings that could act as an alternate path for the passage of drug from film-coated pellets. This could have resulted in the higher rate of drug release that was observed for the Eudragit® RS coated pellets cured for longer times at higher curing temperatures. The formation of molecular-sized pores as a result of excessive film curing and plasticizer evaporation was also demonstrated by FTIR studies performed by these authors (17). This conclusion was further investigated by measuring the change in pore volume of Eudragit® RS free films prepared with triethyl citrate. The pore volume was calculated from the nitrogen desorption data following adsorption at a $P/P_0$ of 0.97 using the Quantasorb sorption apparatus. The average pore volume was found to be 1.41 μl/g after 4 h of curing, 1.71 μl/g after 6 h of curing and 2.10 μl/g after 8 h of curing at 90 °C (Fig. 12). The continuous increase in pore volume with increasing curing time results from the increased plasticizer loss.

## CONCLUSION

The curing process affects the microstructure of the polymeric film coating, thus significantly influencing its properties. As expected, the kinetics of the curing process were faster at higher curing temperatures. An optimal curing condition for the Eudragit® NE coating system could be achieved at all curing temperatures, whereas the Eudragit® RS coating system could not be cured to its optimal curing condition, because of excessive loss of plasticizer. The result was a less uniform and more brittle film.

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