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Non-traditional plasticization of polymeric films

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Abstract

The objective of this study was to investigate the influence of methylparaben, ibuprofen, chlorpheniramine maleate and theophylline on the thermal and mechanical properties of polymeric films of Eudragit® RS 30 D. The effects of methylparaben and ibuprofen in the film coating on the rate of drug release from Eudragit® RS 30 D coated beads were also studied. The physical and mechanical properties of the cast films and coated beads were investigated using thermal analysis, tensile testing, X-ray diffraction analysis and dissolution testing. The results demonstrated that the glass transition temperature of the Eudragit® RS 30 D decreased with increasing levels of methylparaben, ibuprofen and chlorpheniramine maleate in the film.Theophylline exerted no influence on the thermal properties of the polymer. The higher levels of the ibuprofen and methylparaben incorporated into the film resulted in a decrease in the tensile strength of the film. The decrease in Young's modulus of Eudragit® RS 30 D coated beads was attributed to an increase in the flexibility of the polymeric films when the level of methylparaben or ibuprofen in the polymeric dispersion was increased. The dissolution data demonstrated that the rate of release of the ibuprofen from coated beads was decreased by increasing the amount of ibuprofen and methylparaben in the polymeric film coating.

Keywords: Chlorpheniramine maleate; Eudragit® RS 30 D; Ibuprofen; Methylparaben; Non-traditional plasticizer; Plasticized polymeric film

1. Introduction

Plasticizers are necessary for almost all polymers that are currently used for film coating of tablets and beads. Plasticizers reduce the brittleness, improve flow, impart flexibility, and increase toughness, strength, tear resistance, and impact resistance of the polymer. Although there are many plasticizers used in the chemical industry, only a few plasticizers have been approved for pharmaceutical applications due to environmental and/or human health concerns attributed to plasticizer toxicity.

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For polymeric solutions and dispersions used in film coating, a plasticizer will increase the flexibility or distensibility of the polymeric material. It will also function as a film-forming aid by reducing the glass transition temperature (T_g) of the polymer, thereby promoting the coalescence of the latex particles. The degree of plasticization of a polymer is dependent to a large extent on the amount of plasticizer in the film and the interactions between the plasticizer and the polymer. Gutierrez-Rocca and McGinity (1994) concluded that the efficiency of a plasticizer was related to its chemical structure and the interaction between its functional groups with those of the polymer. Careful selection of the type and amount of plasticizer ensures a uniform and reproducible coated product. The deformation of polymeric lattices under specified conditions is one of the most important steps in the film formation process. A sharp increase in mobility of the polymer chains occurs at temperatures higher than the T_g (Okhamafe and York, 1988). The relationship between T_g, minimum film forming temperature (MFT) and fluidized-bed processing conditions for film coating is well documented (Lippold et al., 1989; Gilligan and Li, 1991; Fukumori, 1994). Plasticizers can also modify the physicochemical and mechanical characteristics of the film, and influence the permeability rate of certain molecules (Jenquin et al., 1992). By increasing the amount of plasticizer in the polymeric coating, the rate of drug release is generally reduced since a greater degree of coalescence is afforded by larger amounts of plasticizer (Goodhart et al., 1984; Hutchings and Sakr, 1994). The effects of plasticization are the result of the plasticizer's ability to weaken polymeric intermolecular attractions thus allowing the polymer molecules to move more readily, which increases the flexibility of the polymer. Increasing the amount of plasticizer could lead to an increase in free film elongation and a decrease in tensile strength and Young's modulus (Gutierrez-Rocca and McGinity, 1994; Hutchings et al., 1994). A strong interaction between a drug and a polymer has been reported to significantly influence drug release through a polymeric film (Bodmeier and Paeratakul, 1989; Jenquin et al., 1990, 1994). Other researchers have addressed the influence of preservatives, surfactants and drugs on the plasticization of proteins and polymers (Frisbee and McGinity, 1994; O'Donnell et al., 1997). The plasticizing properties of methyl-

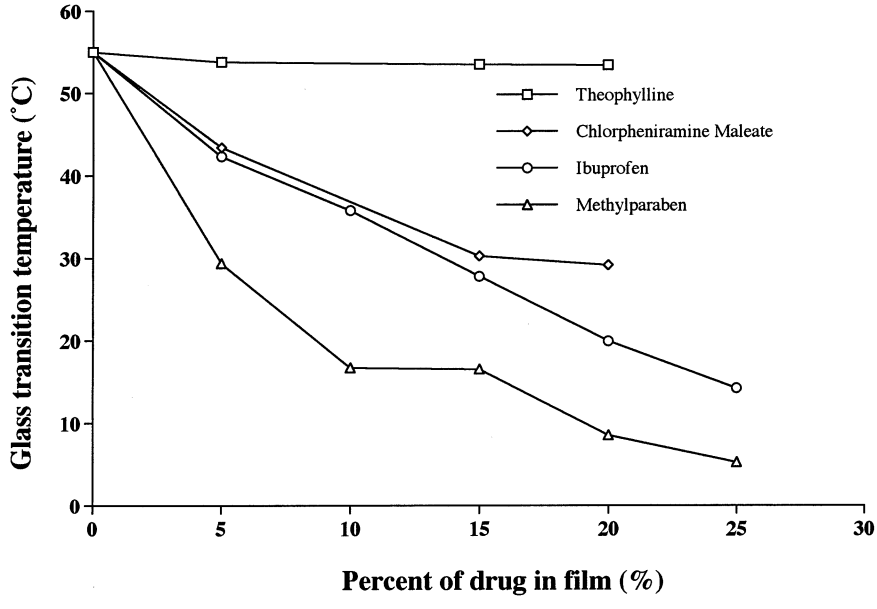

Fig. 1. The effect of different drugs and methylparaben on the glass transition temperature of Eudragit® RS 30 D films.

Table 1
Influence of methylparaben levels in the polymeric film on the mechanical properties of ibuprofen beads (1.4 mm, diameter) coated with Eudragit® RS 30 D ($n = 20$)

Percentage of methylparaben in films (%, w/w)	Tensile strength (MPa) (mean ± S.D.)			Young's modulus (Mpa) (mean ± S.D.)		
	5% RS 30 D coating	10% RS 30 D coating	15% RS 30 D coating	5% RS 30 D coating	10% RS 30 D coating	15% RS 30 D coating
5	6.96 ± 0.88	7.99 ± 1.11	9.95 ± 1.24	93.9 ± 7.2	98.3 ± 8.6	110.9 ± 8.5
10	6.71 ± 0.67	7.43 ± 0.98	9.46 ± 1.22	83.5 ± 8.4	94.9 ± 7.9	106.8 ± 9.9
15	6.39 ± 0.74	6.88 ± 1.05	8.81 ± 1.08	82.2 ± 8.6	82.6 ± 7.4	104.9 ± 6.2

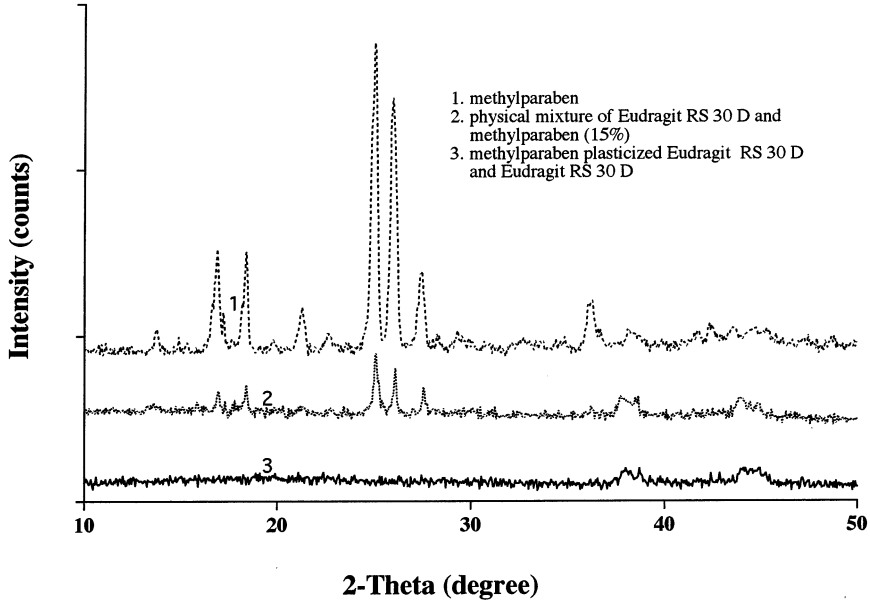

Fig. 2. X-ray diffraction patterns of methylparaben and Eudragit® RS 30 D.

paraben and propylparaben in a pseudolatex dispersion of zein were reported by O'Donnell et al. (1997).

In the current study, methylparaben and several drugs, including ibuprofen, chlorpheniramine maleate (CPM) the theophylline were investigated for their influence on the thermal and mechanical properties of polymeric films of Eudragit® RS 30 D. The mechanism of drug plasticizer interaction with the polymer was investigated using X-ray diffraction. In addition, the influence of methylparaben and ibuprofen present in the film coating

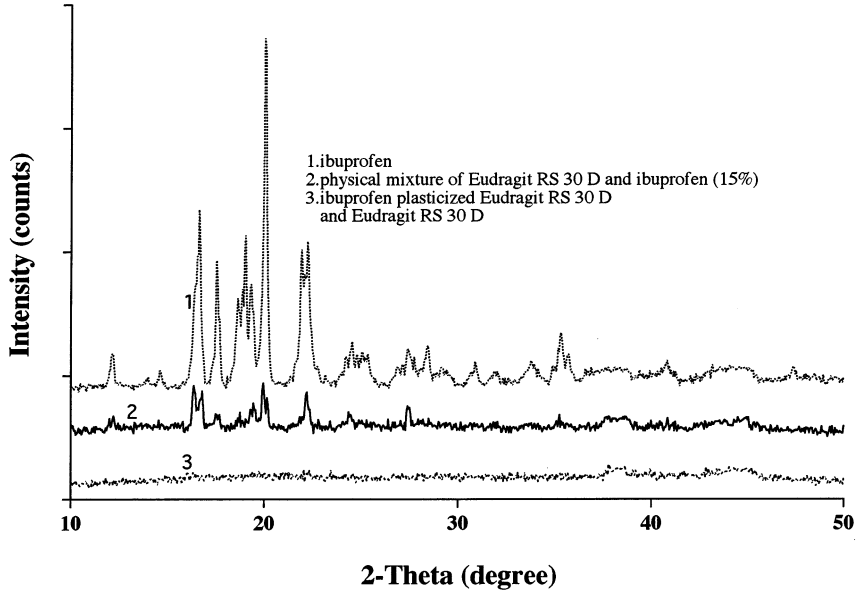

Fig. 3. X-ray diffraction patterns of ibuprofen and Eudragit® RS 30 D.

on the rate of drug release from Eudragit® RS 30 D coated beads was studied.

2. Materials

Eudragit® RS 30 D is a 30% (w/w) aqueous latex of poly (ethylacrylate methylmethacrylate trimethylammonioethyl methacrylate chloride). (Hüls America, Somerset, NJ). Ibuprofen was obtained from Francis S.P.A. (Italy). Chlorpheniramine Maleate (CPM) and methylparaben were purchased from Chemical Mfg. (Gardena, CA). Theophylline was purchased from Sigma (St. Louis, MO). Microcrystalline Cellulose (Avicel PH 101) was donated by FMC Corp (Princeton, NJ).

3. Methods

3.1. Film preparation

The polymer dispersions were equilibrated with either methylparaben or one of the model drugs for 4 h prior to casting on a teflon surface mounted on a level glass plate (casting area = 14.5×14.5 cm; casting volume = 65 ml; total solids content = 8 g). These additives were included in the dispersion at 0, 5, 10, 15, 20 and 25% by weight of dry polymer. The films were dried in an oven at 50°C and 30% relative humidity for 48 h. The dried films were peeled from the teflon surface, cut into 9 cm^2 test sections with a razor blade, and stored at 25°C and 0% relative humidity for 48 h prior to thermal and X-ray analysis. Dried films were analyzed for uniformity of drug content at four random sites in the film.

3.2. Thermal analysis of films

The thermal properties of the films were evaluated using a differential scanning calorimeter (Modulated DSC, TA Instruments, New Castle, DE). Film samples of 10–15 mg were accurately weighed into aluminum pans and then sealed. The samples were tested under a nitrogen atmosphere at a heating rate of 10°C/min, over a temperature range of −20 to 80°C.

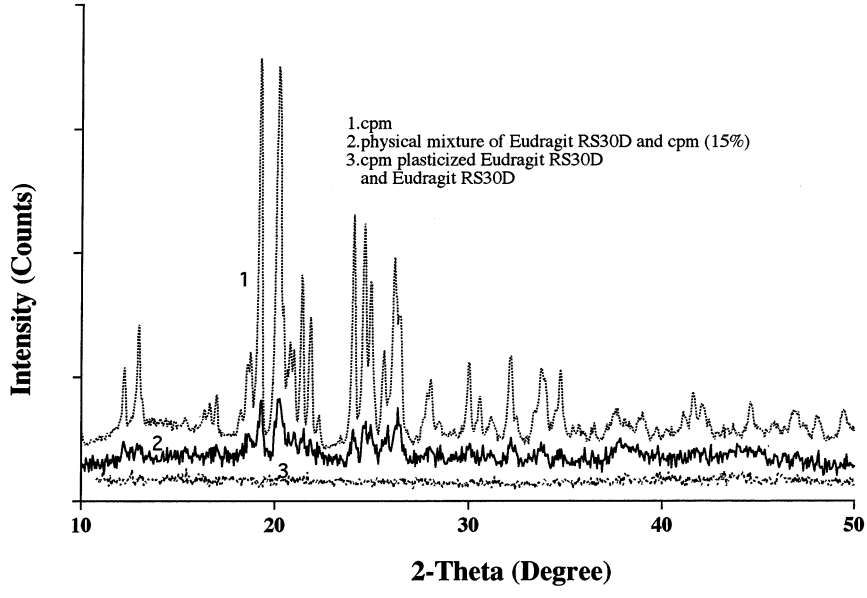

Fig. 4. X-ray diffraction patterns of chlorpheniramine maleate and Eudragit® RS 30 D.

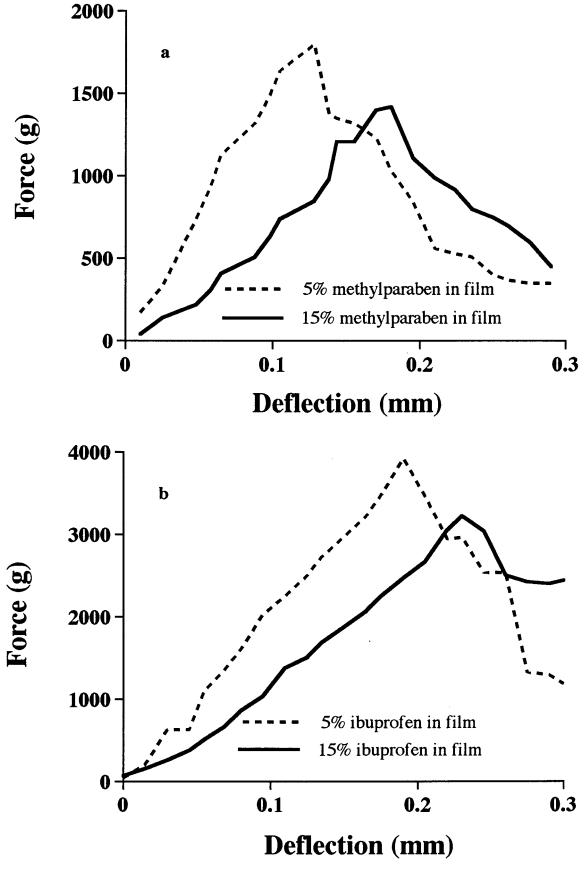

Fig. 5. Force-deflection profiles from single beads coated with 15% weight gain of Eudragit® RS 30 D containing different levels of methylparaben (a) or ibuprofen (b), using the Chatillon digital test equipment.

3.3. X-ray diffraction analysis

The powder X-ray diffraction profiles were determined using a Philips vertical scanning diffractometer (type 42273, Philips Electronic Instrument, Mount Vernon, NY)

The samples were exposed to CuKα radiation under 35 kV and 20 mA over the 2-theta range from 10° to 50° at increments of 0.5°. The diffraction patterns for the drug, polymer, drug-polymer mixtures and drug plasticized polymers were obtained. The cast films were ground into fine powder before analysis. Physical mixtures of drugs (15%) and Eudragit® RS 30 D (85%) were prepared by grinding the polymer with the additives.

3.4. Bead preparation

A dry powder blend of microcrystalline cellulose (Avicel PH 101) and ibuprofen in a 9:1 ratio was mixed for 20 min using a twin-shell blender. Purified water was added in the wet massing process. The moistened mass was extruded using a LCI Benchtop Granulator (LCI, Charlotte, NC). The rotation speed of the impeller was controlled at 25 rpm.

The extrudates were spheronized using a Caleva Model 120 Spheronizer (G.B. Caleva, Dorset, England) by setting the spheronization speed and residence time at 1000 rpm and 15 min, respectively. The wet spheronized beads were then dried at 40°C for 48 h.

3.5. Film-coating beads

The acrylic coating suspensions were prepared by adding water to the commercially available Eudragit® RS 30 D polymeric dispersion to decrease the solids content to 20%. The pH of the acrylic dispersion was 4.92. The additives (model drug or methylparaben) were present at the 5, 10 or 15% level (based on the dry polymer weight). Ibuprofen-containing beads, 14–20 mesh, were coated with the aqueous coating dispersions in a fluid-bed coater (Uni-Glatt Laboratory Unit, Glatt Air Technique, NJ). A 300-g batch of beads was placed in the fluid-bed coater and prewarmed for 10 min prior to the spraying. Inlet bed temperatures were held between 35 and 40°C. The atomizing air pressure was 2.0 kg/cm^2. The Eudragit® RS 30 D dispersion containing each additive was applied at a rate of 2.0 g/min. The aqueous dispersion was stirred continuously throughout the coating process. To promote further coalescence of the polymeric film and to assure that the distribution of the non-traditional plasticizer was homogeneous, the coated beads were spread and tray-dried at 40°C for 48 h in an air circulated oven. The dried beads were then stored over a silica gel desiccant at 0% relative humidity and 25°C prior to further testing.

Table 2
Influence of ibuprofen levels in the polymeric film on the mechanical properties of beads coated with 15% Eudragit® RS 30 D ($n = 20$)

Percentage of ibuprofen in films (%, w/w)	Tensile strength (Mpa) (mean ± S.D.)		Young's modulus (Mpa) (mean ± S.D.)	
	1.4 mm diameter	2.0 mm diameter	1.4 mm diameter	2.0 mm diameter
5	13.06 ± 0.65	12.94 ± 0.77	142.7 ± 9.1	128.2 ± 7.3
10	12.76 ± 0.70	12.60 ± 0.66	139.1 ± 7.9	127.2 ± 5.6
15	12.01 ± 0.48	12.05 ± 0.82	134.4 ± 6.6	114.5 ± 6.8

3.6. Mechanical analysis of coated beads

The stress-strain profiles and the mechanical properties, including tensile strength and Young's modulus, were determined for individual beads using a Chatillon® TCD-200 tension/compression tester (Chatillon, Greensboro, NC) equipped with a DFGS50 force gauge. The force gauge was fitted with a circular steel plate which served as the upper platen. Beads were placed on a lower stationary platen. The upper platen was lowered at a rate of 2.5 mm/min. A personal computer (Leading Edge, Westborough, MA) recorded the force (kg), measured by the gauge, and the displacement (mm) every 0.01 mm that the platen moved (Wang et al., 1996; Felton et al., 1996). Twenty beads, with a particle size of 1.4 and 2.0 mm in diameter, of each bead formulation were selected for testing. The force-deflection data obtained from a personal computer connected to the Chatillon® tension/compression tester were mathematically converted to stress-strain profiles. The tensile strength of the film at the fracture point was determined using the Hiramatsu–Oka equation (Hiramatsu and Oka, 1966). The Young's modulus was calculated from the linear portion of the stress-strain curve.

3.7. Mechanical properties of film

The mechanical properties of the films containing a non-traditional plasticizer were evaluated using an Instron (Model 4201, Instron, Canton, MA). The rectangular film specimens (8 × 1.3 cm) were held in place with pneumatic grips. The initial length of the film specimens was 50 mm, and the extension speed was 10 mm/min. The stress-strain curves were recorded for each sample, and the tensile strength at break, elongation, and elastic modulus were calculated.

3.8. Drug release studies

The USP XXIII Method II (paddle) was used to investigate the dissolution properties of ibuprofen in 900 ml of medium from coated beads at 37°C over a 24 h period. The medium was agitated at 100 rpm and samples were taken at specified time intervals and analyzed spectrophotometrically (ibuprofen at 221 nm and methylparaben 290 nm) for drug content. The dissolution medium consisted of 50 mM sodium phosphate buffer at pH 7.4. Drug release profiles were determined using 5, 10 and 15% methylparaben or ibuprofen in the coating film as a percentage of the dried polymer weight.

Table 3
The mechanical properties of Eudragit® RS 30 D films containing different levels of methylparaben ($n = 6$)

Percentage of methylparaben in films (%, w/w)	Tensile strength (Mpa) (mean ± S.D.)	Elongation (%) (mean ± S.D.)	Young's modulus (Mpa) (mean ± S.D.)
15	8.62 ± 1.24	12 ± 2	73.6 ± 13.6
20	2.13 ± 0.53	241 ± 59	6.15 ± 1.99
25	0.44 ± 0.31	360 ± 33	1.59 ± 0.29
30	0.17 ± 0.03	692 ± 266	0.27 ± 0.08

3.9. Solubility of methylparaben, ibuprofen, and chlorpheniramine maleate in Eudragit® RS 30D

Each drug was equilibrated with 50 ml of Eudragit RS 30D dispersion at room temperature for 24 h with stirring. The dispersion was then centrifuged to obtain a clear supernatant liquid and a polymer sediment. To determine the saturated solubility in the supernatant liquid, the aqueous phase was analyzed for drug content by UV spectroscopy after appropriate dilution with purified water. To determine the solubility of each drug in the latex dispersion, drug was added in small increments to the latex dispersion. When the equilibrated solubility in the supernatant had reached a steady state after 24 h of gentle agitation, the solubility of the drug in the Eudragit® RS 30D was determined.

4. Results and discussion

4.1. Thermal analysis of films

The effect of a plasticizer on the glass transition temperature (T_g) of a polymer is a specific measure of plasticizer efficiency since the glass transition temperature is a function of chain mobility. The purpose of a plasticizer is to increase chain mobility. The effect of the methylparaben and three model drugs on the glass transition temperature of Eudragit® RS 30 D films is shown in Fig. 1. The glass transition temperature for Eudragit® RS 30 D was seen to decrease with increasing levels of methylparaben, ibuprofen and chlorpheniramine maleate (CPM) in the film. However, high levels of theophylline in the film displayed no influence on the glass transition temperature of the polymer. The profiles demonstrated that methylparaben is a most effective plasticizer for the acrylic resin copolymer. O'Donnell et al. (1997) reported earlier on the plasticizing property of methylparaben on the protein zein. Films containing the ibuprofen and chlorpheniramine maleate demonstrated higher T_g values compared to films containing the methylparaben. Both drugs displayed a decrease in the T_g, however the effect was not as dramatic as with the methylparaben. Theophylline was shown to exert no effect on the thermal properties of the acrylic polymer.

The calculated value for Eudragit® RS 30D was reported by Wang et al. (1997) to be 19.2 $(J/cm^3)^{1/2}$. The solubility parameter of methylparaben was calculated to be 24.4 $(J/cm^3)^{1/2}$ (Martin et al., 1984) and 28.6 $(J/cm^3)^{1/2}$ for theophylline (Adjei et al., 1984). The values for ibuprofen and chlorpheniramine maleate were 19.0 $(J/cm^3)^{1/2}$ and 21.5 $(J/cm^3)^{1/2}$, respectively, when calculated by the Van Krevelen method (Van Krevelen, 1990). Theophylline was the only compound that did not plasticize the polymer. In order to obtain good miscibility between two components, Sears and Touchette (1982) reported that the solubility parameters should be the same or differ by less than ± 6.3 $(J/cm^3)^{1/2}$. The solubility parameter for theophylline was 9.4 $(J/cm^3)^{1/2}$ greater than the calculated value for the polymer.

4.2. X-ray diffraction analysis

The profiles in Figs. 2–4 illustrate the X-ray diffraction patterns for the Eudragit® RS 30 D film, the additives, physical mixtures of Eudragit® RS 30 D with methylparaben and the model drugs, and drug-plasticized Eudragit® RS 30 D films. The Eudragit® RS 30D polymer is amorphous due to the absence of complete stereoregularity and the presence of bulky side groups. Stereoregularity or symmetry is essential for a polymer to be crystalline (McCrum et al., 1988). Amorphous polymers contain randomly entangled chains. Such an irregular molecular structure prevents crystallization. The crystallinity of methylparaben, ibuprofen and CPM was clearly demonstrated by their unique X-ray diffraction patterns. The diffraction pattern from a physical mixture of 15% drug, methylparaben, ibuprofen or CPM, with pure polymer contained sharp diffraction peaks corresponding to the crystallinity of each additive present in the mixture. The presence of diffraction peaks in the physical mixture of additives (15%) with the Eudragit RS® 30 D polymer demonstrated that the presence of undissolved crystalline drug dispersed in the matrix displayed specific diffraction peaks when exposed to the X-ray. The diffraction patterns from cast

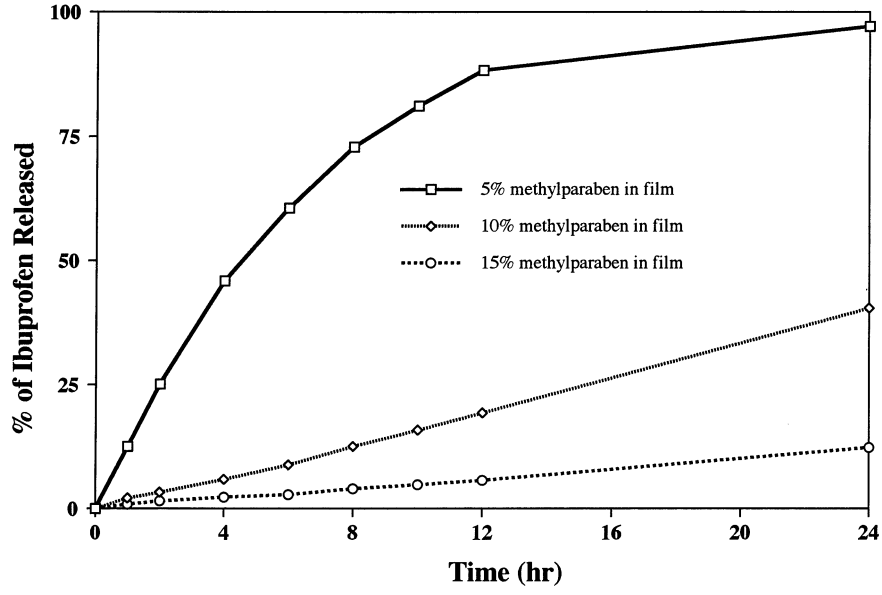

Fig. 6. Dissolution profiles of ibuprofen beads coated with Eudragit® RS 30 D containing different levels of methylparaben in the coating film ($n = 3$).

Eudragit® RS 30 D films containing the additives are also displayed in Figs. 2–4. These profiles contain no peaks associated with the crystalline drug molecules. These diffraction patterns were identical to those of the pure polymer, suggesting that the drug was either dissolved in the polymer or present in an amorphous state within the polymeric matrix.

Several theories that have been proposed to explain the flexible properties imparted by plasticizers on polymeric materials (Sears and Touchette, 1990). In general, the mechanism of plasticization effects is considered to be a decrease in the cumulative intermolecular forces along the film polymer chains (Banker, 1966). Crystallinity of a film structure promotes intermolecular forces, thus increasing the rigidity and brittleness of the film. The addition of methylparaben, ibuprofen or CPM enhanced plasticization, and resulted in a highly amorphous polymer film structure due to the disordered placement of the polymer chains in the film matrix. This mechanism was proposed earlier by Heinamaki et al. (1994). The X-ray diffraction profile of cast films of Eudragit® RS 30 D containing theophylline demonstrated the crystallinity of the drug as well as the immiscibility of the drug for the polymer. These data are in agreement with the T_g findings for the theophylline-containing films.

4.3. Mechanical analysis of coated beads

Compression testing of the coated beads was conducted using a Chatillon digital force gauge and test stand. This equipment was previously described in detail by Wang et al. (1996) and Felton et al. (1996). The force and the deflection measurement were recorded on a computer during the test. Typical force-deflection profiles of individual beads coated with Eudragit® RS 30 D in which methylparaben or ibuprofen was employed as a non-traditional plasticizer are shown in Fig. 5(a) and (b), respectively. Increasing the amount of additive in the film led to a reduction of the maximum force and an increase in the deformation at fracture values. All polymer-drug formulations demonstrated a significant increase in the flexibility of the polymeric films when the level of methylparaben or ibuprofen in the polymer dispersion was increased. In the postpeak stage of

the profiles, the force decreased gradually to zero, since the coated beads distorted elastically prior to film fracture. A stable deformation process was indicated by the linear segment in the profiles where crack formation was initiated. The Young's moduli were derived from these linear segments by linear regression.

The tensile strength at break was determined for individual beads coated with Eudragit® RS 30 D using methylparaben or ibuprofen as a plasticizer for the brittle polymer. The tensile strength was calculated from the Hiramatsu–Oka equation as described previously by Wang et al. (1996). For uncoated beads, the tensile strength was 5.26 ± 0.97 MPa, which was significantly lower than the tensile strength of the coated pellets. As seen in Table 1, the tensile strength increased as the Eudragit® RS 30 D coating level was increased, while a decrease was seen as the methylparaben in the film was increased. This is in agreement with the findings of Lin et al. (1991) and Hutchings et al. (1994) who suggested that increasing plasticizer content led to a reduction in tensile strength. Similar results were obtained when ibuprofen was employed as the plasticizer as shown in Table 2. The tensile strength decreased as the ibuprofen content in the film was increased. However, there was no significant change in the tensile strength as a function of particle size of the coated beads.

The Young's modulus of elasticity represents the hardness, flexibility and stiffness of a polymer. Stiffness is used to describe the capacity of a material to resist deformation in the elastic range. The higher modulus values are associated with films having greater stiffness while lower modulus values represent softer films. Results from the physical-mechanical studies with the Eudragit® RS 30 D polymer coated beads demonstrated that the addition of the methylparaben or ibuprofen resulted in a decrease in Young's modulus as the level of methylparaben or ibuprofen added to the Eudragit® RS 30 D was increased, as shown in Tables 1 and 2. The decrease in the Young's modulus was due to a lowering of the T_g and an increase in elasticity of the polymer due to the presence of the ibuprofen in the acrylic polymer. Interestingly, for the Eudragit® RS 30 D coated beads containing methylparaben as the plasticizer, the Young's modulus was found to be dependent on the coating level. The higher coating level resulted in a higher Young's modulus, however, when 15% of methylparaben was employed as the

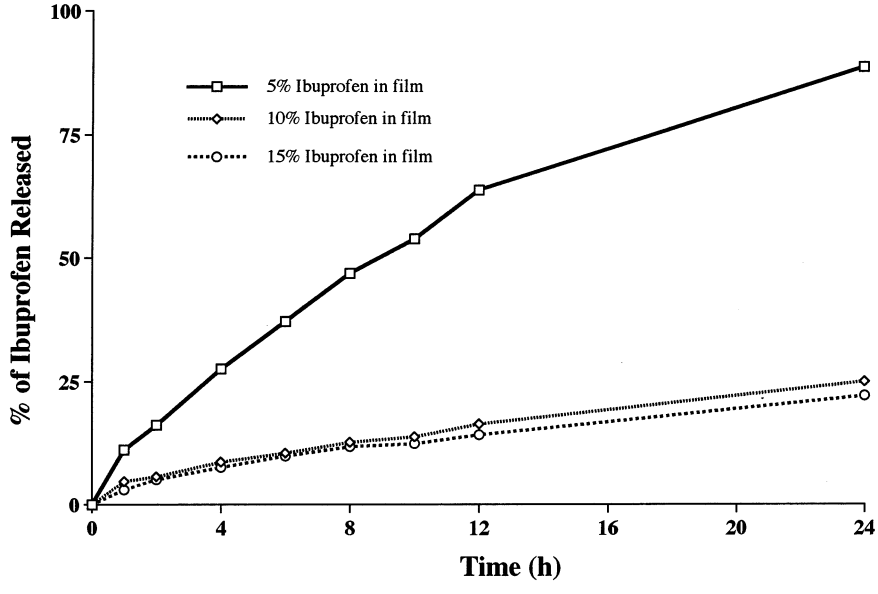

Fig. 7. Dissolution profiles of ibuprofen beads coated with Eudragit® RS 30 D containing different levels of ibuprofen in the coating film ($n = 3$).

plasticizer, the Young's moduli for 5 and 10% of Eudragit coating level were similar, as shown in Table 1. Furthermore, the Young's moduli of the Eudragit® RS 30 D coated beads also decreased as the particle size was increased, regardless of the concentration of ibuprofen in the polymer, as exhibited in Table 2. The origination of Young's modulus may be traced back to the intermolecular interactions at the molecular level. The distance of separation between the molecules should also be considered. (Roberts and Rowe, 1991; Wang et al., 1996).

Eudragit® RS 30 D contains ammonium and ester groups that are capable of interacting with other molecules by hydrogen bonding, as well as electrostatic and dispersion forces. The ibuprofen, CPM and methylparaben have the ability to interact with the copolymer by the same forces. Hydrogen bonding between the Eudragit® RS 30 D polymer and each additive may weaken the interchain hydrogen bonding within the polymer itself. These results were supported by the results of the X-ray diffraction patterns displayed in Figs. 2 and 3. The incorporation of methylparaben or ibuprofen in the Eudragit® RS 30 D dispersion changed the crystalline status of both the methylparaben and ibuprofen in the acrylic film.

4.4. Mechanical properties of film

The effect of methylparaben on the plasticization of the acrylic polymer was investigated by adding increasing amounts of methylparaben (15–30% w/w based on the dry polymer, with increments of 5% w/w) to the Eudragit® RS 30 D latex dispersion. The mechanical properties of the Eudragit® RS 30 D films are shown in Table 3. The addition of higher amounts of methylparaben to Eudragit® RS 30 D resulted in significant changes in the mechanical properties, making the polymer softer and more flexible. Films containing 30% w/w methylparaben were very soft and weak due to excessive plasticization of the polymer. Polymer films that were 5 cm in length were employed in these studies rather than 10 cm films as described in the test procedure based on the American Society for Testing and Material D882-75d method. The shorter films were studied due to the significant influence that the non-traditional plasticizer demonstrated on the elongation of the acrylic film. The elongation of the acrylic film containing 30% w/w methylparaben was found to increase by nearly seven fold. Films containing 10–20% w/w methylparaben demonstrated suitable toughness and flexibility as a film-coating material. As a result of the decrease in tensile strength and the increase in elongation, the Young's modulus of Eudragit® RS 30 D films decreased with increasing methylparaben concentration in the films. These results demonstrated that methylparaben was an efficient plasticizer for Eudragit® RS 30 D.

4.5. Drug release studies

Higher levels of plasticizer in a polymeric film cause a greater degree of coalescence for a given set of processing conditions and are generally associated with a reduction in the rate of drug release. The dissolution profiles of ibuprofen beads coated with Eudragit® RS 30 D containing methylparaben or ibuprofen as the plasticizer are shown in Figs. 6 and 7, respectively. For ibuprofen beads coated with Eudragit® RS 30 D containing methylparaben as a non-traditional plasticizer, the rate of drug release decreased when the methylparaben levels were increased from 5 to 15% based on the drug polymer weight (Fig. 6). The trends observed for methylparaben and ibuprofen are in agreement with results in the literature for the plasticization of films where triethyl citrate, acetyl triethyl citrate, tributyl citrate, or glyceryl monostearate were used as the plasticizer (Banker and Peck, 1981; Goodhart et al., 1984; Amighi and Moes, 1996). When ibuprofen was used to plasticize the acrylic polymer, increasing the amount of the drug in the film from 5 to 10% led to a decrease in the rate of drug release. However, increasing the concentration of ibuprofen in the film coating from 10 to 15% led to little change in the release profile (Fig. 7). When the ibuprofen in the film was increased beyond a certain saturation point, there was no further enhancement of film formation and no change in the drug release profile.

Plasticizers can be classified as being either water-soluble and/or water-insoluble. Water-soluble plasticizers dissolve in the aqueous medium and then partition into the colloidal polymeric nanoparticles, while insoluble plasticizers are emulsified in the aqueous phase of the dispersion and then partition into the polymer particles (Dillon et al., 1953). During plasticization of the polymeric dispersion, the ibuprofen, methyl paraben and chlorpheniramine maleate partitioned into the colloidal polymer particles and softened the polymer, thus promoting particle deformation and coalescence to form a film upon drying. The solubilities of ibuprofen, methylparaben and chlorpheniramine maleate in the Eudragit® RS 30 D dispersion were determined to be 16.6, 10.8 and 477 mg/ml, respectively. The solubility of theophylline was not determined due to the flocculation of the latex that followed the addition of the theophylline to the Eudragit® RS 30 D dispersion.

In conclusion, the glass transition temperature of the Eudragit® RS 30 D decreased with increasing levels of methylparaben, ibuprofen and CPM in the film. No change in T_g was found with theophylline. X-ray diffraction studies demonstrated that the methylparaben, ibuprofen and CPM were soluble in the film and then became incorporated within the polymeric network, functioning as a plasticizer for the Eudragit® RS 30 D. Increasing the percentage of the ibuprofen and methylparaben incorporated in the film resulted in a decrease in the tensile strength and Young's modulus of Eudragit® RS 30 D coated beads. The dissolution data demonstrated that the rate of drug release was reduced by increasing the amount of the non-traditional plasticizers, ibuprofen and methylparaben, in the polymeric film coating.

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