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Plasticizer uptake by aqueous colloidal polymer dispersions used for the coating of solid dosage forms[1]

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Abstract

The extent and rate of distribution of water-soluble (triethyl citrate, triacetin) and water-insoluble plasticizers (acetyltriethyl citrate, acetyltributyl citrate, tributyl citrate, diethyl phthalate, dibutyl phthalate) between aqueous and polymer phases in colloidal polymer dispersions were characterized by association coefficients and rate constants. A separation scheme and a high performance liquid chromatography (HPLC)-analysis were used to quantify the amount of plasticizer dissolved/emulsified in the aqueous phase and in the colloidal polymer particles as a function of plasticization (mixing) time. The rate of plasticizer uptake was a function of formulation factors such as the type and concentration of the plasticizer, and the type and solids content of the polymer dispersion. The plasticization time had a minimal effect on the rate of uptake of water-soluble plasticizers, while it had a strong effect on the uptake of water-insoluble plasticizers. The rate of the uptake depended on the water solubility of the plasticizer while the association coefficient reflected the polymer–plasticizer interaction. The rate at which plasticizers were taken up by the polymer was correlated to the film formation of the plasticized dispersions. © 1997 Elsevier Science B.V.

Keywords: Aquacoat®; Aqueous colloidal polymer dispersion; Coating; Controlled drug release; Ethyl cellulose; Eudragit®; Plasticizer

1. Introduction

Plasticizers cause changes in the physicomechanical properties of polymers, such as reductions in the glass transition temperature and in tensile strength and an increase in elongation and flexibility of the polymer film. With aqueous colloidal polymer dispersions (latexes or pseudola-

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[1] Dedicated to Professor Dr H. Rupprecht, Universität Regensburg, Germany for his 60th birthday.

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texes), plasticizers are also added to reduce the minimum film formation temperature (MFT) below the coating temperature to allow coalescence of the colloidal polymer particles in a homogeneous film (Lehmann, 1989; Steuernagel, 1989). Besides these major functions, plasticizers can be used as additives to influence the drug release (Hennig and Kala, 1986; Hutchings and Sakr, 1994) and the adhesion of the polymeric film to the substrate (Lin et al., 1991; Felton and McGinity, 1996).

Plasticizers can be divided into water-soluble and -insoluble plasticizers. Water-soluble plasticizers are dissolved, while insoluble plasticizers have to be emulsified in the aqueous phase of the polymer dispersions. During plasticization of the polymer dispersions, the plasticizer partitions into the colloidal polymer particles and softens them thus promoting particle deformation and coalescence into a film upon drying. Plasticizer partitioning in colloidal polymer dispersions has been studied by only a few researchers (Dillon et al., 1953; Morton et al., 1954; Hoy, 1973; Sutter, 1987; Iyer et al., 1990; Bodmeier and Paeratakul, 1994a). Dillon et al. presented a model for the plasticization of synthetic paint latexes in terms of a three-phase system. After addition of a water-insoluble plasticizer to the latex, the plasticizer could be dissolved or emulsified in the aqueous phase or it could be dissolved in the polymer particles (Dillon et al., 1953).

The plasticization time—the time between the addition of the plasticizer to the polymer dispersion and the coating step, is a critical process variable, especially with water-insoluble plasticizers. Sufficient time should be allowed for the plasticizer uptake by the colloidal polymer particles, otherwise liquid plasticizer droplets would be sprayed onto pellets or tablets. This could result in an inhomogeneous distribution of the plasticizer in the coating film. As a consequence, the plasticizer could redistribute in the coating upon aging, resulting in possible stability problems such as changes in drug release properties. Changes in drug release observed during the curing (thermal treatment at elevated temperatures) of coated dosage forms are generally attributed to the better coalescence of the colloidal polymer particles (Bodmeier and Paeratakul, 1991a, 1994b). During curing, plasticizers could also redistribute in the polymeric film.

Commercial suppliers of polymer dispersions often recommend a relatively short plasticization time of 1/2–1 h irrespective of the solubility of the plasticizer. Conflicting results were reported for a dibutyl sebacate–ethyl cellulose dispersion. Iyer et al. reported the uptake of dibutyl sebacate by the commercial ethyl cellulose pseudolatex, Aquacoat®, to be complete within 30 min irrespective of the amount of plasticizer used (Iyer et al., 1990), while Sutter reported the presence of visible dibutyl sebacate droplets in the same polymer dispersion after 1 week (Sutter, 1987; Lippold et al., 1989).

In previous studies, a separation method (Bodmeier and Paeratakul, 1994a) and a high performance liquid chromatography (HPLC)-technique (Bodmeier and Paeratakul, 1991b) were developed, which allowed the quantification of the plasticizer in the aqueous and polymer phases of colloidal polymer dispersions. The objective of this study was to determine the rate of plasticizer uptake by the colloidal polymer particles and to relate the results to the film formation of plasticized polymer dispersions upon drying at elevated temperatures. The aqueous polymer dispersions (ethylcellulose–Aquacoat®; acrylic polymers—Eudragit® RS and L 30 D) and the plasticizers (citrate or phthalate esters) investigated are widely used in the film coating of pharmaceutical solid dosage forms.

2. Materials and methods

2.1. Materials

The following chemicals were obtained from commercial suppliers and were used as received: Aquacoat® (aqueous dispersion of ethylcellulose) (FMC Corporation, Newark, DE); Eudragit® L 30 D [aqueous dispersion of poly (ethyl acrylate–methacrylic acid) copolymer], Eudragit® RS 30 D [aqueous dispersion of poly (ethyl acrylate–methyl methacrylate–trimethyl ammonioethylmethacrylate chloride) copolymer with a ratio of

1:2:0.1] (Röhm, Darmstadt, Germany); hydroxypropyl methylcellulose (Methocel E5, Colorcon), PEG 4000 (BASF, Germany); diethyl phthalate (DEP), dibutyl phthalate (DBP), glyceryl triacetate (triacetin) (Eastman Kodak, Rochester, NY); triethyl citrate (Citroflex®-2; TEC), acetyltriethyl citrate (Citroflex® A-2; ATEC), tributyl citrate (Citroflex®-4; TBC), acetyltributyl citrate (Citroflex® A-4; ATBC) (Morflex Chemicals, Greensboro, NC); methanol (Mallinckrodt Specialty Chemicals, Paris, KY); double-distilled water.

2.2. Methods

A previously developed separation method (Bodmeier and Paeratakul, 1994a) and a HPLC-assay (Bodmeier and Paeratakul, 1991b) were used to characterize the distribution of plasticizers between the aqueous and polymer phases of the colloidal polymer dispersions. The plasticizers (225–900 mg) were mixed with the diluted polymer dispersions (15 g, solids content = 15% w/w) in a beaker using a magnetic stirrer ($n = 2$). At predetermined time intervals, the plasticized dispersions were separated as described below.

Polymer dispersions plasticized with a water-soluble plasticizer (TEC or triacetin) were ultracentrifuged (45 000 rpm, 60 min, 22°C; Beckman Ultracentrifuge L5-50) to obtain a clear supernatant and the polymer in the sediment. The centrifugation time of 60 min and of 15 min in the case of water-insoluble plasticizers has to be added to the plasticization time since plasticizer uptake probably also occurred during centrifugation. The aqueous phase was analyzed for the plasticizer content by HPLC after appropriate dilution with the mobile phase. The polymer sediment was freeze-dried for 24 h and was further vacuum-dried for 24 h to obtain the polymer powder. The dried polymer powder (200–500 mg) was accurately weighed and dissolved in methanol (10–14 ml) followed by the addition of water (6–10 ml) to precipitate the polymer. The extraction samples were ultracentrifuged (45 000 rpm, 30 min, 22°C) to separate the polymer prior to appropriate dilution of the supernatant with the mobile phase and analysis by HPLC. The measured amounts of the plasticizer in the polymer and in the aqueous phase were adjusted by the amount of plasticizer dissolved in the residual water in the polymer phase as determined by the weight loss during freeze- and vacuum-drying.

Polymer dispersions plasticized with water-insoluble plasticizers were centrifuged at 3000 rpm for 15 min in order to separate the emulsified plasticizer droplets from the remaining colloidal polymer particles. Because of the higher specific gravity of the plasticizer, the emulsified plasticizer was in the bottom layer of the centrifuged samples. The colloidal polymer particles did not settle at this centrifugation speed. The remaining portion of the polymer dispersion was then assayed for combined plasticizer content dissolved in the aqueous phase and in the polymer particles. This portion was accurately weighed (1–2 g) and dissolved in methanol (14–19 ml) prior to appropriate dilution with the respective mobile phase or addition of water to precipitate the polymer. The extraction samples were ultracentrifuged, if necessary, to obtain a clear supernatant prior to injection into HPLC. The emulsified portion was dissolved in methanol (50–100 ml) followed by dilution with the mobile phase and injection into the HPLC. For the plasticizer uptake studies, the amount of plasticizer recovered in the remaining portion of the polymer dispersion represented the plasticizer which was dissolved in the aqueous phase and in the polymer phase. This amount was subtracted from the total amount of plasticizer incorporated in order to obtain the amount of plasticizer emulsified. The percentage of emulsified plasticizer (% w/w of total plasticizer added) was then plotted as a function of time to express the profile of plasticizer uptake by the colloidal polymer particles. The measured amounts of plasticizer did not vary by more than 7% for both water-soluble or water-insoluble plasticizers.

The rate constant, k, characterizing the plasticizer uptake was obtained by plotting log (emulsified plasticizer remaining in the aqueous phase) vs. plasticization time. The linear portion of the curve was determined by linear regression analysis. The negative slope obtained from the regression analysis was the rate constant of plasticizer uptake by the polymer phase.

Table 1
The association coefficients of plasticizers in different aqueous polymer dispersions (solids content of polymer dispersion, 15% w/w; level ofplasticizer, 20% w/w)

Plasticizer	Aqueous polymer dispersion		
	Aquacoat®	Eudragit® RS 30 D	Eudragit® L 30 D
Water-soluble			
Triethyl citrate	5.70	4.09	5.27
Triacetin	3.14	3.00	2.98
Water-insoluble			
Acetyltriethyl citrate	32.26	33.21	10.92
Acetyltributyl citrate	38.75	41.68	1.39
Dibutyl sebacate	40.35	41.68	8.48
Diethyl phthalate	37.96	33.87	18.02
Dibutyl phthalate	34.51	32.11	1.96
Tributyl citrate	47.30	36.26	1.64

In analogy to partitioning experiments with drugs, an 'association coefficient' was calculated to characterize the plasticizer distribution in the colloidal polymer dispersions. The association coefficient, *K*, was calculated as the ratio of the concentration of the plasticizer in the polymer phase to the concentration in the aqueous phase. With water-insoluble plasticizers, the plasticizer concentration in the aqueous phase included the dissolved and emulsified portion.

The following variables affecting the rate of plasticizer uptake into the colloidal polymer particles were investigated: plasticizer concentration, 10–40% w/w, in increments of 10%; solids content of the polymer dispersion: 10–25% w/w, in increments of 5% w/w, type of plasticizer (water-soluble: TEC, triacetin; water-insoluble: ATEC, ATBC, DBP, DEP, TBC), type of aqueous colloidal polymer dispersion (Aquacoat®, Eudragit® RS and L 30 D).

The solubility of the plasticizers in water was determined by shaking excess plasticizer with water for 48 h at 22°C ($n = 2$). The mixture was centrifuged at 3000 rpm for 15 min and the clear phase was then analyzed by HPLC for the plasticizer content.

To correlate the effect of plasticization time with the film formation, the plasticized polymer dispersions (3–4 ml) were cast after a predetermined plasticization time into aluminum dishes (6 cm in diameter, American Scientific Products, McGaw Park, IL) and dried in an oven at 40°C for 24 h. The plasticization times corresponded to those in the uptake studies and were in the range of 5 min to 7 days. The film formation of the plasticized dispersions was classified into the following categories:

(−)	no film formation, films were cracked into small pieces
(±)	partial film formation, films were partly continuous and partly cracked
(o)	partial film formation with exudation or phase separation of the plasticizer
(+)	complete film formation, films were continuous throughout

3. Results and discussion

In a previous study, the extent of plasticizer distribution between the aqueous phase (dissolved or emulsified) and the polymer phase of the ethyl cellulose dispersion, Aquacoat®, was determined (Bodmeier and Paeratakul, 1994a). The extent of the plasticizer distribution for Aquacoat and two other widely used polymer dispersions, Eudragit RS® 30 D and L 30D, can be summarized by an 'association coefficient' (Table 1). The association coefficient reflects the affinity of the plasticizer for the polymer of the colloidal polymer dispersion. A large value indicates extensive partitioning into the colloidal particles, while a small value is indicative of a poor plasticizer compatibility or affinity for the polymer.

In this study, emphasis is on the rate of plasticizer uptake by the polymer particles after plasticizer addition to the polymer dispersion. The rate at which the plasticizer partitions into the colloidal particles determines the amount of plasticizer taken up by the polymer after a certain plasticization time. The rate of plasticizer uptake thus affects the film formation process and therefore the quality of the resulting film or coating.

With water-soluble plasticizers such as triethyl citrate (TEC) or triacetin, the distribution of the plasticizer was not affected by the plasticization time (Fig. 1). The distribution pattern of triethyl citrate and triacetin in the ethylcellulose pseudolatex, Aquacoat®, remained unchanged after a plasticization time of 5 min (plus centrifugation time as mentioned in the experimental section). The rapid attainment of equilibrium was due to the relatively high water solubility of the plasticizers (TEC, 55.4 mg/ml; triacetin, 77.8 mg/ml). Triethyl citrate was equally distributed between the polymer and aqueous phase. The higher amount of triacetin in the aqueous phase can be explained with its higher water solubility and the lower association coefficient (Table 1). The rapid plasticizer uptake was in agreement with the film formation data where a complete film formation of the plasticized dispersion occurred at a very early stage of plasticization when compared to the water-insoluble plasticizers, i.e. after 5 min of mixing (data not shown). With regard to the coating of solid dosage forms with polymer dispersions plasticized with water-soluble plasticizers, large amounts of the plasticizer are dissolved in the aqueous phase and are not taken up by the colloidal polymer particles prior to the coating. The dissolved plasticizer will be sprayed on the solid substrate together with the plasticized polymer particles. During drying, the polymer dispersion becomes more concentrated; the plasticizer further partitions into the polymer phase and should be homogeneously distributed in the coating film, if the plasticizer is compatible with the polymer.

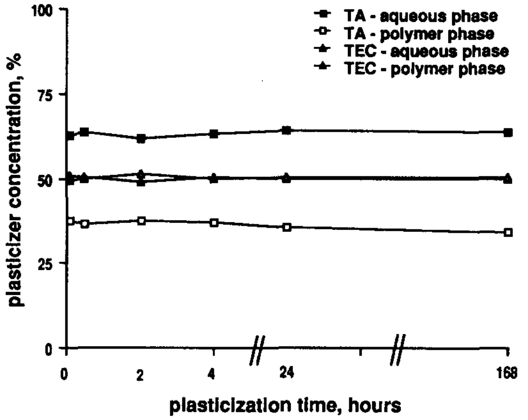

Fig. 1. Effect of plasticization time on the distribution of triethyl citrate (TEC) and triacetin (TA) in aqueous and polymer phases of Aquacoat® (solids content of the polymer dispersion = 15% w/w; plasticizer concentration = 20% w/w based on polymer).

In contrast to water-soluble plasticizers, the uptake rate of water-insoluble plasticizers was more time-dependent and was influenced by a number of formulation factors. When emulsified in the polymer dispersion, a water-insoluble plasticizer is primarily present in either the polymer phase or in emulsified form in the aqueous phase and, because of the low water solubility, only a minor portion is dissolved in the aqueous phase. In order to be taken up by the polymer particles, the plasticizer has to dissolve from the emulsified droplets in the aqueous phase and then partitions from the aqueous phase into the polymer phase. Because of the low water solubility, the rate of the plasticizer taken up by the polymer particles corresponds to the rate of plasticizer lost from the emulsified phase. The uptake rate was therefore expressed by the rate at which the emulsified plasticizer disappeared from the aqueous phase (into the polymer phase). The effect of the plasticizer (ATBC) concentration on the ATBC uptake by Aquacoat® as a function of plasticization time is shown in Fig. 2. The ATBC uptake was fastest with 10% w/w ATBC and then decreased with increasing ATBC concentration. Table 2 shows the rate constants determined at each plasticizer concentration by linear regression analysis. The

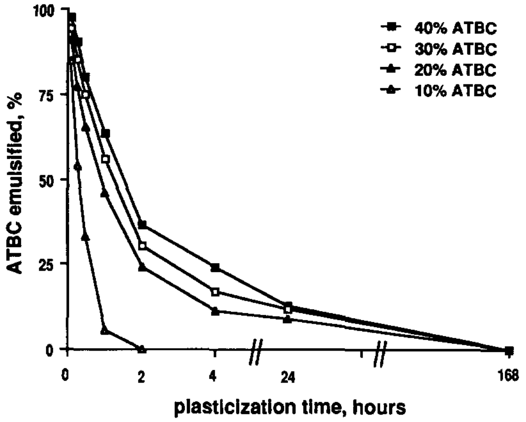

Fig. 2. Effect of acetyltributyl citrate concentration (ATBC, % w/w based on polymer) on the plasticizer uptake in Aquacoat® (solids content of the polymer dispersion = 15% w/w).

rate constant, *k*, was highest with the 10% w/w level while similar values were obtained with the 20, 30, and 40% w/w levels. The similar rate constants above 20% could indicate that the dissolution process from the emulsified plasticizer droplets and not the plasticizer uptake by the polymer particles is the rate limiting step.

After 24 h plasticization, emulsified ATBC droplets were still detectable at ATBC concentrations in excess of 10% w/w. The emulsified plasticizer droplets gradually disappeared and could no longer be detected after 1 week of mixing. With extremely high plasticizer concentrations (50–70% w/w), however, the plasticizer was not absorbed completely and the plasticizer–polymer masses could be observed as large rubber-like sediments after 24 h of plasticization. The plasticizer probably dissolved the colloidal particles at higher plasticizer concentrations.

In order to study the effect of plasticization time on the film formation of plasticized colloidal dispersions, the data obtained from plasticizer uptake experiments were correlated to the film formation of the respective plasticized dispersions dried at 40°C (Table 3). At a plasticizer concentration of 10% w/w, films did not form because of an insufficient amount of plasticizer. The concentration of plasticizer generally recommended by the supplier is in the range of 20–30% w/w based on polymer solids. When the ATBC concentration was increased to 20% w/w or higher, more and more plasticizer existed in the aqueous phase as emulsified droplets. Since the drying of the polymer dispersions into a film during coating in a fluidized bed is instantaneous, the drying of the cast polymer dispersions over a time period of 24 h was not representative of the drying process during coating. The continued plasticizer partitioning from the emulsified droplets into the colloidal polymer particles during the drying period could result in misleading film formation data. To exclude this effect, the plasticized dispersions were centrifuged to separate the emulsified plasticizer from the polymer dispersion prior to casting the pseudolatex; the results are shown in brackets. When emulsified plasticizer droplets were excluded, the film formation occurred later and after a similar plasticization period (2–4 h) irrespective of the amount of plasticizer incorporated. This implied that, after the same plasticization time, the colloidal particles could take up similar absolute amounts of plasticizer from the aqueous phase. The absolute amounts of ATBC taken up by the polymer phase (polymer solids = 2.25 g) at the plasticization time at which film formation occurred were calculated to be 225 mg (no film formation), 409 mg (8 h), 561 mg (4 h), 572 mg (2 h) at the 10, 20, 30, and 40% w/w plasticizer level, respectively. This corresponded to absorbed plasticizer contents in the polymer phase of 10.0, 18.2, 24.9, 25.4% w/w of polymer. The results indicated that ATBC must be taken up by the polymer phase at a level of approximately 18% w/w in order for the film formation to occur. This is close to 20% level recommended by the supplier. At the level of 10% w/w ATBC added, the amount of plasticizer was insufficient even though it was taken up completely.

The effect of the solids content of the pseudolatex (10–25% w/w, a range normally used for film coating) on the plasticizer uptake at a constant ATBC concentration of 20% w/w (based on the polymer) is shown in Fig. 3. The plasticizer uptake increased with increasing solids content of the pseudolatex, the uptake being complete after 2 h with the most concentrated pseudolatex (25% w/w). The result was in agreement with earlier findings where the extent of diffusion of dibutyl

Table 2
Effect of type and concentration of the plasticizers and solids content of the polymer dispersions on the rate constant of plasticizer uptake

Polymer dispersion (solids content, % w/w)		Plasticizer (level, % w/w)		Rate constant, (h^{-1})
Aquacoat®	(15)	ATBC	(10)	0.98
			(20)	0.29
			(30)	0.26
			(40)	0.23
Aquacoat®	(10)	ATBC	(20)	0.19
	(15)			0.29
	(20)			0.44
	(25)			1.26
Aquacoat®	(15)	ATBC	(20)	0.29
		ATEC	(20)	1.26
		DBP	(20)	0.38
		DEP	(20)	1.35
		TBC	(20)	0.80
Eudragit® RS 30 D	(15)	ATBC	(20)	0.59
Eudragit® L 30 D	(15)	ATBC	(20)	0.01

sebacate, another water-insoluble plasticizer, was found to be the highest when a concentrated pseudolatex system was used (Bodmeier and Paeratakul, 1994a). In addition, less concentrated dispersions were obtained by dilution of the concentrated dispersion with water. The colloidal ethyl cellulose particles are stabilized with sodium lauryl sulfate (0.4% w/w based on the aqueous phase). Dilution with water resulted in a lower surfactant concentration and therefore in a lower solubility of the water-insoluble plasticizer. The solubility of acetyltributyl citrate depends on the surfactant concentration because of solubilization. The plasticizer had a higher solubility in the concentrated dispersions and was therefore taken up faster. The effect of pseudolatex solids on the film formation is shown in Table 4. The results were consistent with the uptake profile and the calculated rate constants (Table 2).

The effect of the plasticizer type is shown in Fig. 4. The rate constants could be ranked in the order of DEP > ATEC > TBC > DBP > ATBC (Table 2). The rate constants corresponded to the water solubilities of the plasticizers, with diethyl phthalate being more soluble than dibutyl phthalate and tributyl citrate and acetyltriethyl citrate being more soluble than acetyltributyl citrate. This indicated that the dissolution process of the plasticizer from the emulsified droplets was the rate limiting step. In addition to the solubility in the aqueous phase, the association coefficients took into account the affinity of the plasticizer for the polymer and characterize the final distribution between the polymer and aqueous phase (Table 1). The polymeric films of the DEP-plasticized dispersion could be formed after 15 min of plasticization (Table 5) at which 320 mg of DEP (per 2.25 g polymer) corresponding to 14.2% w/w plasticizer were absorbed. The film formation of dispersions plasticized with ATEC, TBC, and DBP occurred after 30 min, 1 and 2 h, respectively, with 357 mg (15.9% w/w), 348 mg (15.5% w/w), and 370 mg (16.4% w/w) of the plasticizer being absorbed.

The ATBC uptake rate was determined with different polymer dispersions (Fig. 5). The rate constant was highest with Eudragit® RS 30 D followed by those of Aquacoat® and Eudragit® L 30 D, as shown in Table 1. The plasticized Eudragit® RS 30 D showed a noticeable increase in viscosity particularly after the first hour of plasticization. The viscosity increase of the pseudolatex could be an indication of extensive plasticizer–polymer interactions, which became apparent at

Table 3
Effect of acetyltributyl citrate (ATBC) concentration and of plasticization time on the film formation of Aquacoat® (solids content of polymer dispersion, 15% w/w)

Plasticization time	ATBC concentration, % w/w of polymer			
	10	20	30	40
5 min	—	—	—	—
15 min	—	—	—	±(−)
30 min	—	—	±(−)	+(−)
1 h	—	—	+(−)	+(−)
2 h	—	±(−)	+(−)	+(+)
4 h	—	+(±)	+(+)	+
8 h	—	+(+)	+	+
24 h	—	+	+	+
72 h	—	+	+	+
7 days	—	+	+	+

(−) no film formation, films were cracked into small pieces.
(±) partial film formation, films were partly continuous and partly cracked.
(+) complete film formation, films were continuous throughout.
( ) symbols in brackets indicate the film formation of centrifuged dispersions after emulsified plasticizer was removed.

Table 4
Effect of solids content of the polymer dispersion and of plasticization time on the film formation of Aquacoat® (acetyltributyl citrate concentration, 20% w/w ofpolymer)

Plasticiziation time	Solids content of polymer dispersion, % w/w			
	10	15	20	25
5 min	—	—	—	—
15 min	—	—	—	—
30 min	—	—	—	±(−)
1 h	—	—	±(−)	+(±)
2 h	±(−)	±(−)	+(±)	+(+)
4 h	+(±)	+(±)	+(+)	+
8 h	+(+)	+(+)	+	+
24 h	+	+	+	+
72 h	+	+	+	+
7 days	+	+	+	+

(−) no film formation, films were cracked into small pieces.
(±) partial film formation, films were partly continuous and partly cracked.
(+) complete film formation, films were continuous throughout.
( ) symbols in brackets indicate the film formation of centrifuged dispersions after emulsified plasticizer was removed.

the stage where most of the plasticizer (approximately 80% of plasticizer added) had already diffused into the polymer. In contrast to Eudragit® RS 30 D, the ATBC uptake of Eudragit® L 30 D levelled off and plateaued after 1 h. More than 80% w/w of the total plasticizer incorporated was not absorbed by the polymer after 24 h and remained in the dispersion as emulsified droplets. The film formation correlated well with the plasticizer uptake data (data not shown). The film

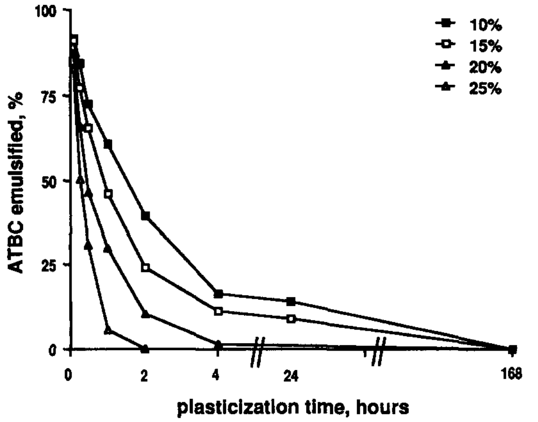

Fig. 3. Effect of solids content of the polymer dispersion on the plasticizer (acetyltributyl citrate) uptake in Aquacoat® (plasticizer concentration = 20% w/w based on polymer).

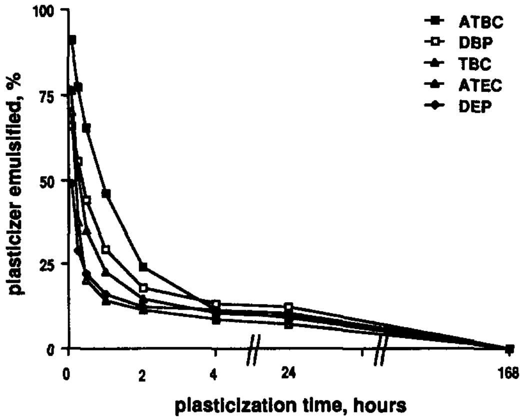

Fig. 4. Effect of the type of plasticizer on the plasticizer uptake in Aquacoat® (solids content of the polymer dispersion = 15% w/w; plasticizer concentration = 20% w/w based on polymer).

Table 5
Effect ofplasticizer type and of plasticization time on the film formation of Aquacoat® (solids content of polymer dispersion, 15% w/w; plasticizer concentration, 20% w/w ofpolymer)

Plasticization time	Plasticizer				
	ATBC	ATEC	DBP	DEP	TBC
5 min	—	±(±)	—	±(±)	±(−)
15 min	—	+(±)	−(−)	+(+)	±(−)
30 min	—	+(+)	±(−)	+	+(±)
1 h	—	+	+(±)	+	+(+)
2 h	+(−)	+	+(+)	+	+
4 h	+(±)	+	+	+	+
8 h	+(+)	+	+	+	+
24 h	+	+	+	+	+
72 h	+	+	+	+	+
7 days	+	+	+	+	+

(−) no film formation, films were cracked into small pieces.
(±) partial film formation, films were partly continuous and partly cracked.
(+) complete film formation, films were continuous throughout.
( ) symbols in brackets indicate the film formation of centrifuged dispersions after emulsified plasticizer was removed.

formation of Eudragit® L 30 D dispersion plasticized with ATBC was not obtained because of plasticizer exudation/phase separation. The phase separation indicated the incompatibility between the two components and, hence, the ineffectiveness of ATBC for this particular enteric polymer.

In conclusion, the rate of plasticizer uptake depended on the type and concentration of plasticizer and the type of the polymer dispersion. The plasticization time had no effect on the distribution behaviour of water-soluble plasticizers, while the distribution water-insoluble plasticizers was strongly affected by the plasticizaiton time. The plasticizer uptake couldf be related to the film formation of the plasticized polymer dispersions.

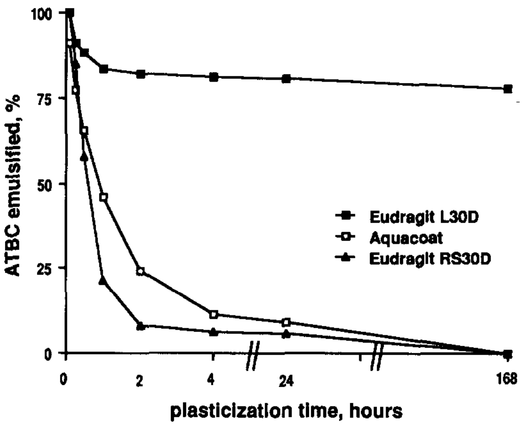

Fig. 5. Effect of the type of aqueous colloidal polymer dispersion on the plasticizer (acetyltributyl citrate) uptake (solids content of the polymer dispersion = 15% w/w; plasticizer concentration = 20% w/w of polymer).

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