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Research paper

Tackiness of acrylic and cellulosic polymer films used in the coating of solid dosage forms

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Abstract

The objective was to determine the tackiness of acrylic and cellulosic polymer films in order to make predictions on the tackiness (agglomeration) of coated dosage forms during coating and curing. Force-displacement curves of the detachment process of two polymeric films were used as a measure of tackiness. Various polymers (cellulosic (Aquacoat®) and acrylics (Eudragit® RS 30D, L 30D, NE 30D)), plasticizers (triacetin, triethyl citrate, tributyl citrate, acetyltributyl citrate) and anti-tacking agents (talc and glyceryl monostearate) were investigated. The order of tackiness for films prepared from the different aqueous polymer dispersions was in order of Eudragit® NE 30D > RS 30D > RL 30D > Aquacoat®. The tackiness increased with increasing plasticizer concentration due to the softening of the polymer. A correlation between the minimum film formation temperature and the tackiness was observed, however, no correlation between the tackiness and the lipophilicity of the plasticizer was seen. Talc and glyceryl monostearate (GMS) reduced the tackiness of the films significantly, with GMS being effective at much lower concentrations. Curing of Eudragit® RS 30D-coated theophylline beads at temperatures higher than 40°C resulted in an irreversible agglomeration of the beads and damage of the coating upon separation of the beads. This resulted in a faster release than with uncured beads. Blending the beads with talc just prior to the curing step eliminated the agglomeration and therefore film damage, even at a curing temperature of 60°C. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Adhesion; Aqueous polymer dispersion; Coating; Curing; Ethylcellulose; Eudragit®; Mechanical properties; Polymer films; Tackiness

1. Introduction

The tackiness of polymeric films is important for the coating of solid dosage forms and for the subsequent curing step (post coating thermal treatment). During coating with cellulosic or acrylic polymers, an unwanted, and sometimes irreversible agglomeration of several beads or, in the worst case, of the complete batch, can occur, especially at higher product temperatures and higher plasticizer content in the coating [1,2]. Plasticizers are often added to aqueous colloidal polymer dispersions to reduce the minimum film formation temperature [3]. This can result in 'sticky' coatings. A fine balance has to be found between sufficiently high temperatures and non-agglomeration.

Beads coated with aqueous polymer dispersions are often cured at elevated temperatures after the coating to enhance the coalescence of the polymer particles in a homogeneous film in order to avoid aging effects [4,5]. The curing can either be performed directly in the coating equipment or in an oven. The curing temperatures usually exceed the product temperature during coating (60°C vs. 35–40°C), and sticking/picking and agglomeration becomes especially apparent at the higher curing temperatures.

Many studies have investigated the mechanical [6–9] or adhesive [10–13] properties of polymeric films. Several guidelines describe standardized methods for the determination of the mechanical or adhesion properties of polymers. The ASTM or DIN 53455/53457 guidelines describe the measurement of tensile properties [14,15]. The peel

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adhesion test defines the conditions for the evaluation of the adhesion properties of films to a substrate [11]. The test film is pulled from the substrate at a 180° angle while recording the required force. Additional methods to determine the adhesion of polymer film coats on substrates like tablets have been developed [16].

Only little work has been reported on determining the adhesion, tackiness or sticking behavior of acrylic and cellulosic polymer films to each other. For coating applications, a low tackiness is desirable. A polymer formulation with a low tackiness shows less tendency for film coating defects, it results in an easier handling of the coating process and it also reduces the process time.

The objective of this study was to develop a method, which is suitable to measure the tackiness of cellulosic and acrylic polymer films, and to use this method to evaluate the influence of the type of polymer, of the type and concentration of plasticizer and of anti-tacking agents on the sticking behavior of the polymer films. The method should be suitable to give a qualitative prediction of the tackiness of various polymer formulations during coating or curing.

2. Materials and methods

2.1. Materials

The following chemicals were used as received: Aquacoat® (FMC c/o Lehmann and Voss and Co., Hamburg, Germany), Eudragit® RS 30D, RL 30D, L 30D, or NE 30D (Röhm GmbH, Darmstadt, Germany), triethyl citrate (TEC; Citroflex-2), acetyltributyl citrate (ATBC; Citroflex A-4), tributyl citrate (TBC-Citroflex-4) (Morflex Chemical Co., Greensboro, NC, USA), glyceryl triacetate (triacetin; Eastman Kodak Co., Rochester, NY, USA), Imvitor® 900 (glyceryl monostearate (GMS); Hüls AG, Witten, Germany), talc (Merck, Darmstadt, Germany), polysorbate 80 (Tween® 80; ICI c/o Atlas Chemie, Essen, Germany), theophylline beads (18–20 mesh, 94% drug content, Klinge Pharma GmbH, München, Germany).

2.2. Preparation of the polymer films

The aqueous polymer dispersions were plasticized for 2 h (TEC or triacetin) or 72 h (with the lipophilic plasticizers ATBC or TBC) (20–40% w/w based on the mass of polymer) in order to achieve a complete uptake of the plasticizer by the polymer particles. Talc (25% or 50% w/w based on the mass of polymer) or glyceryl monostearate (GMS) (5% or 10% w/w based on the mass of polymer) in the form of a 2% w/v emulsion in an aqueous 0.08% w/v Tween 80 solution were added to the plasticized polymer dispersion in order to investigate their ability to reduce tackiness. Finally, the polymer dispersion was adjusted to a polymer content of 12.5% w/w by dilution with deionized water prior to casting on a Teflon protective overlay (Bytac® Type VF-81, Norton Performance Plastics Co., Akron, OH, USA) mounted on a leveled glass plate (area of casting 19.0 × 19.0 cm^2; standard conditions: casting volume 113 ml; total polymer content 14 g; approximate film thickness 300 μm ($n = 6$; foil thickness gauge, Model 497, Erichsen, Hemer, Germany). The films were dried in an oven (Heraeus T 6120, Hanau, Germany) for 48 h at 40°C and 50% relative humidity before storage for 1 h at 23°C and 52% relative humidity.

The dried films were peeled from the Teflon surface and cut into 2.5 × 9.0 cm^2 sections. Two test films were then put congruently on top of each other. One end of the test films was separated by a double-sided Teflon tape placed between the two films prior to storage for 3 h at 50% relative humidity at various temperatures and under different weights. After this treatment, the two films were cooled to room temperature (23°C ± 2°C) for 1 h at 52% relative humidity. A rigid tape was attached on the outer sides of the test films in order to avoid elongation of the polymer film during testing.

2.3. Determination of the tackiness of acrylic and cellulosic films

The test specimens were placed with one end of each polymer film in two clamps (width 2.5 cm) of an Instron® Model 4466 (Instron Wolpert GmbH, Ludwigshafen, Germany) as schematically illustrated in Fig. 1. The upper clamp, which was attached to a driving load cell (500 N maximum load), was then driven upwards at a crosshead speed of 15 mm/min, while the lower clamp remained in the original position. The force needed to separate the polymer films was recorded. The average value was obtained from the constant force portion of the force vs. displacement diagram. Five to 10 test specimens were tested for each experiment.

2.4. Preparation of coated theophylline beads

Eudragit® RS 30D was plasticized with triethyl citrate (20% w/w, based on the mass of the polymer) for 2 h.

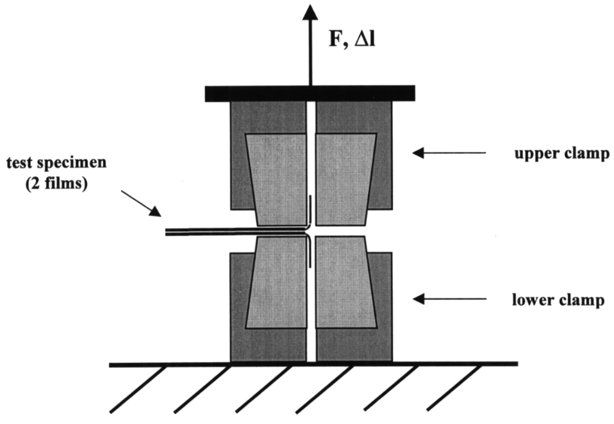

Fig. 1. Schematic diagram of the experimental set-up for the determination of force (F) and displacement (Δl) curves (tackiness) of polymeric films.

Glyceryl monostearate (5% w/w based on the mass of the polymer) was added as an anti-tacking agent in the form of a 2% w/v emulsion in an aqueous 0.08% w/v Tween 80 solution. The polymer content of the final dispersion was adjusted to 15% w/w by dilution with water.

The polymer dispersion was sprayed (nozzle diameter 1.2 mm, atomization pressure 1.8 bar) onto 600 g of theophylline beads in a fluidized bed coater (GPCG 1, Wurster insert, Glatt GmbH, Binzen, Germany) (product temperature 30–33°C, air volume 80 m^3/h, spray rate 2–7 g/min) to a polymer weight gain of 7.5% w/w. The coated beads were placed in glass petri-dishes and cured at different temperatures (RT, 40°C, 50°C or 60°C) and for different time periods (1, 8 or 24 h). The beads were then stored in closed, light-protected glass vials until further experimentation.

2.5. In vitro release studies

The USP XXIII rotating paddle method (VanKel 700 and VK 800, VanKel 650a, Vankel, Edison, NJ, USA, 900 ml, 0.1 N HCl, 37°C, 100 rpm, $n = 3$) was used to study the drug release from coated beads. The samples (3 ml, not replaced) were withdrawn at predetermined time intervals and theophylline was detected spectrophotometrically at 270 nm (UV-2101PC, Shimadzu Europa GmbH, Duisburg, Germany).

3. Results and discussion

In this study, a method to determine the tackiness of cellulosic and polymeric films was developed. In preliminary experiments, the weight applied to the dried films and the temperature were varied in order to optimize the preparation of the test specimen (Fig. 2). A glass plate covering the film sections was loaded with different weights up to 500 g. A weight of 125 g was chosen for further experiments due to the lowest standard deviation calculated from the corresponding force values (Fig. 2A,B). The investigated temperature ranged from 40°C to 60°C with increments of 10°C. A temperature of 40°C provided the lowest variation in force values and was therefore chosen for all following experiments (Fig. 2C). In addition, at higher weights and temperatures, some films could not be separated.

A typical force vs. displacement diagram is shown in Fig. 3. Usually, the profile could be divided into three phases. In the beginning, a steep increase in force was recorded resulting in a maximum force. At this point, the films were just prior to detaching from each other. This first phase was followed by a slight decrease in force followed by the last phase with a constant force. This last phase represented the detachment of the films from each other. The recorded force values in the last phase of the diagram were averaged and taken as a measure of the tackiness of the polymer films.

Next, various polymers commonly used for the coating of solid dosage forms were evaluated. Aquacoat® was selected as the cellulosic polymer formulation and Eudragit® RS 30D, RL 30D and NE 30D as acrylic polymer formulations. Fig. 4 shows the influence of the type of polymer on the tackiness of films containing 30% plasticizer (TEC or ATBC). The order of the tackiness was NE 30D $>$ RS 30D $>$ RL 30D $>$ Aquacoat. Eudragit® NE 30D films required the highest force for detachment, which was indicative of the highest tackiness. Eudragit® NE 30D has a low minimum film formation temperature and does not require the addition of plasticizers. It is known to give highly flexible films and agglomeration problems during coating [9,17]. The tackiness was higher for films plasticized with the hydrophilic plasticizer, triethyl citrate, when compared to films plasticized with the lipophilic plasticizer, acetyltributyl citrate. This was especially evident with Eudragit® RS, which is also known to result in agglomeration problems if used without anti-tacking agents. Eudragit® RL films had lower values when compared to the Eudragit® RS films. This could possibly be explained with the number of quaternary ammonium groups, which is twice as high in Eudragit® RL when compared to Eudragit® RS. Aquacoat® films were easy to separate from each other and provided the lowest tackiness. Aquacoat® films are brittle and show only little elongation [9].

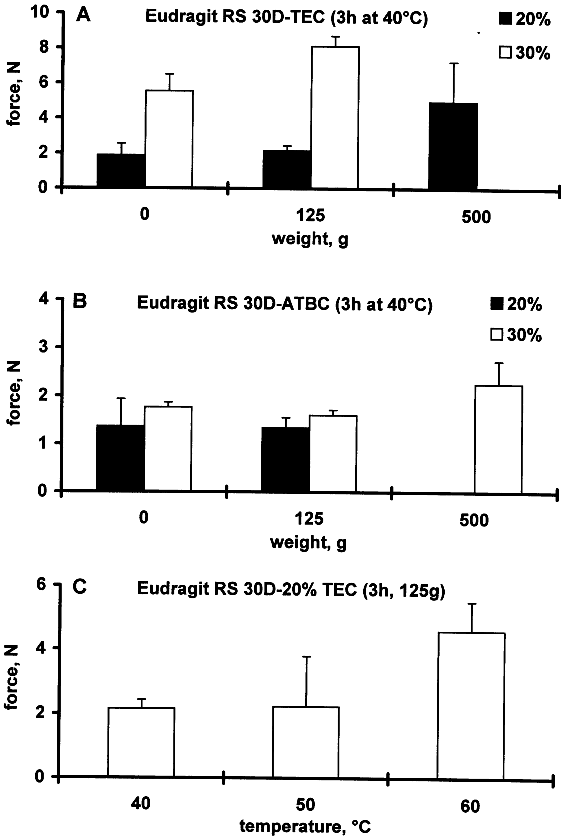

Fig. 2. Effect of the weight (A,B) and temperature (C) on the tackiness of Eudragit® RS 30D films.

The effect of the type and concentration of the plasticizer on the tackiness of Eudragit® RS 30D films is shown in Fig. 5. Higher plasticizer levels might be necessary for applications, where more flexible coatings are required, for example, for the compression of coated beads. As expected, increasing the plasticizer concentration from 20%, which represents the recommended plasticizer concentration for Eudragit® RS 30D coating formulations [18], to 30%, increased the tackiness of Eudragit® RS 30D regardless of the incorporated plasticizer. This behavior was less significant with the lipophilic plasticizer, ATBC. ATBC resulted in the lowest detachment values and the tackiness was also not affected by the plasticizer concentration in the investigated range.

With increasing plasticizer levels, the minimum film formation temperature (MFT) of the acrylic polymer dispersions decreases and correlates to the tackiness of the dried polymer films. The MFT values for the investigated plasticized Eudragit® RS 30D dispersion have been published [17]. For example, a MFT of 10°C has been reported for Eudragit® RS 30D plasticized with 20% ATBC and a MFT of 5°C for Eudragit® RS 30D plasticized with 20% TEC. Lower MFT-values corresponded to higher detachment values, indicative of a higher tackiness. A correlation between the MFT and the tackiness was seen for the investigated plasticizers, however, no correlation between the lipophilicity of the plasticizer and the tackiness was obvious.

Anti-tacking agents are added to the coating formulation to avoid agglomeration or picking problems during the coating step. Traditionally, talc is used as an anti-tacking agent at concentrations up to 100% based on the polymer [19]. The high amount of additive is also present in the final coating and therefore can affect the drug release or mechanical properties negatively. In addition, high amounts of suspended pigments can result in nozzle clogging and sedimentation. As an alternative to talc, glyceryl monostearate (GMS) has shown great promise as an anti-tacking agent. It can be used at a much lower concentration and can be added to the polymer dispersion as an emulsion, thus avoiding potential sedimentation problems [20].

With regard to the tackiness of Eudragit® L 30D films (plasticized with 40% TEC), 5% GMS was as effective as 50% talc (Fig. 6). The reduction in tackiness of talc-containing films could not be improved by increasing the concentration from 25% to 50%. The effectiveness of GMS as anti-tacking agent was also shown with Eudragit® RS 30D formulation plasticized with 30% TEC or ATBC (Fig. 7). A strong anti-tacking effect was seen with films plasticized with TEC. The force necessary to separate the film sections decreased from 8 N for GMS-free films to less than 1 N for GMS-containing films. Increasing the GMS concentration from 5% to 10% did not result in a further reduction of the tackiness. For films plasticized with ATBC, this tendency was less significant due to the already lower force values for GMS-free films.

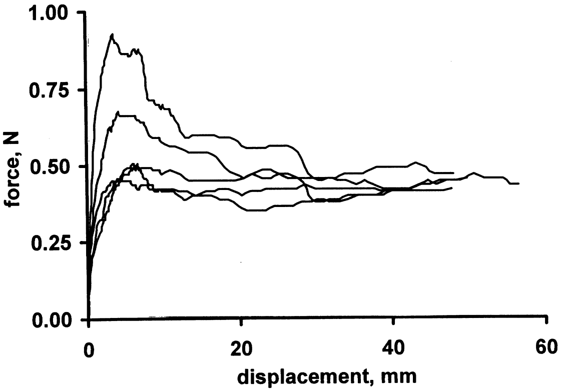

Fig. 3. Typical force vs. displacement diagram ($n = 5$).

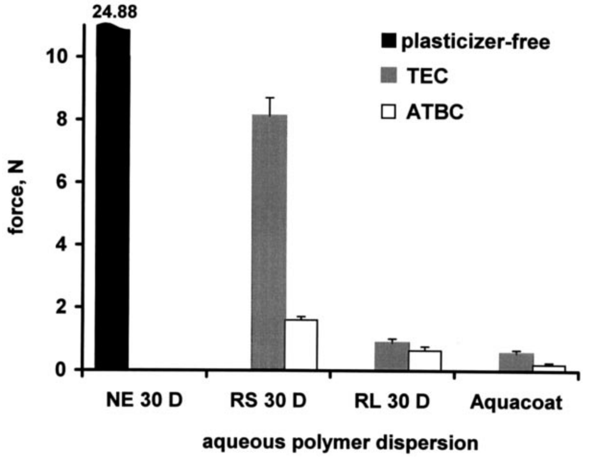

Fig. 4. Effect of the type of polymer dispersion on the tackiness of polymer films plasticized with 30% plasticizer (triethyl citrate or acetyltributyl citrate).

The same trend was also observed with Eudragit® NE 30D films (Fig. 8). The lower values obtained with additive-free films compared to the corresponding values given in Fig. 4 were caused by the different temperature applied during the preparation step of the test specimens. The temperature used during application of the weight on the two films was 20°C for the experiments shown in Fig. 8, otherwise, a temperature of 40°C (like in Fig. 4) was used. As expected, the force values were lower at lower preparation temperatures. The results with Eudragit® NE 30D films in

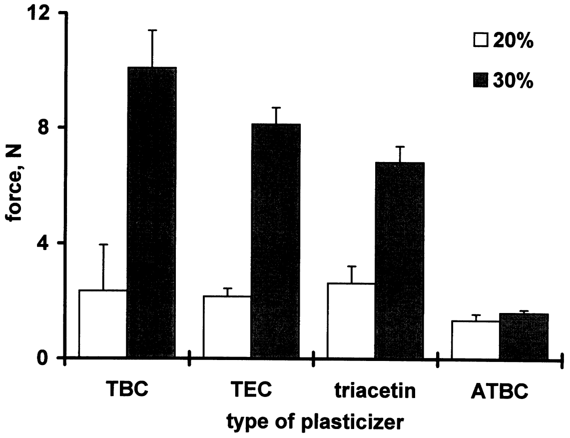

Fig. 5. Effect of the type and concentration of the plasticizer on the tackiness of Eudragit® RS 30D films.

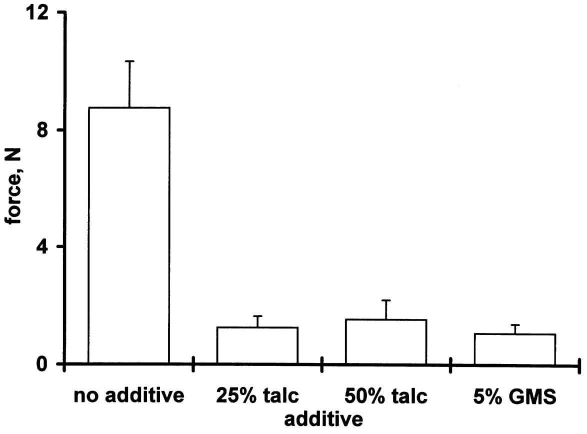

Fig. 6. Effect of anti-tacking agents on the tackiness of Eudragit® L 30D-55 films plasticized with 40% triethyl citrate.

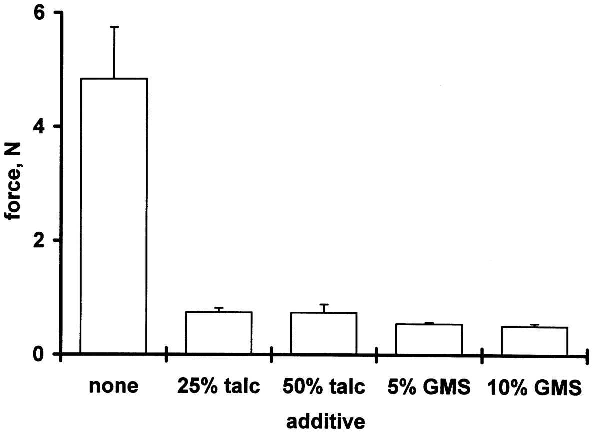

Fig. 8. Effect of anti-tacking agents on the tackiness of Eudragit® NE 30D films.

Fig. 8 confirm the results seen with the two other acrylic polymer dispersions (Figs. 6 and 7). The incorporation of the anti-tacking agents lead to a decrease in tackiness, with GMS being more efficient than talc. An increase in anti-tacking agent did not reduce the detachment values further.

Eudragit® RS containing formulations are known to cause sticking problems during the coating and curing step. In order to correlate the results of the tackiness test with the sticking of coated beads, theophylline beads were coated with plasticized Eudragit® RS 30D and were oven-cured in glass-dishes at different temperatures prior to determining the in vitro drug release. Curing at 40°C did not result in sticking problems, the beads were free-flowing and were not sticking to the petri-dish or to each other. This curing temperature, however, was too low to cause complete coalescence of the colloidal polymer particles into a homogeneous film, as shown by a rapid drug release. Curing of Eudragit® RS 30D-coated theophylline beads at a temperature higher than 40°C resulted in the fusion of the beads into a cake, no individual beads remained. It was not possible to remove the cured beads from the petri-dish without damaging the coating. The fusion of the beads into a cake was time- and temperature-dependent, an irreversible fusion of the beads was obtained after 8 h at 50°C and after only 1 h at 60°C.

In order to overcome the sticking problems during curing, talc was evaluated as an anti-tacking agent. In this case, talc was not added to the aqueous polymer dispersion prior to the coating of the beads, but was blended with the coated beads just prior to curing (2% w/w talc based on the mass of the beads). The release data of uncured and cured beads with and without talc are shown in Fig. 9. Curing the beads for 1 or 8 h resulted in an increase in drug release when compared to the release of uncured beads. This unexpected increase was caused by the mechanical damage done to the coated beads during the separation of the fused ‘bead cake’ into individual beads. Blending the coated beads with talc prior to the curing avoided the

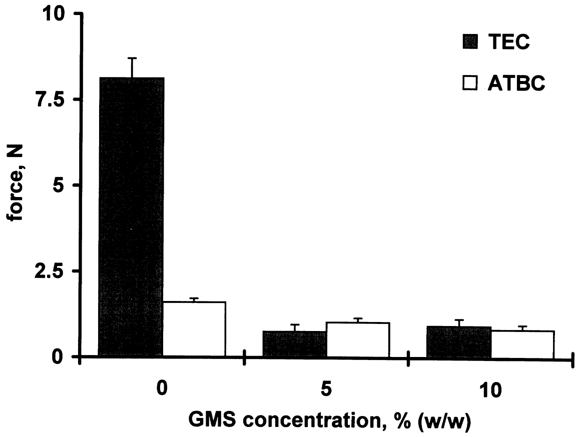

Fig. 7. Effect of the glyceryl monostearate concentration on the tackiness of Eudragit® RS 30D films containing 30% plasticizer (triethyl citrate or acetyltributyl citrate).

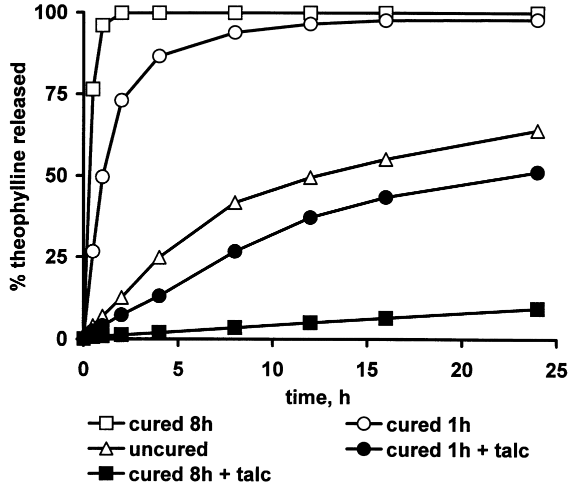

Fig. 9. Effect of the talc addition to theophylline-Eudragit® RS 30D-coated beads prior to curing at 60°C on the drug release.

fusion into a cake, the beads remained free-flowing after the curing and therefore the coating was not mechanically damaged. Curing of the talc-treated beads resulted in the expected decrease in drug release because of the enhanced coalescence of the colloidal polymer particles. The talc addition to the coated beads avoided the agglomeration during curing.

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