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Research paper

Characterization of the film formation of the dry coating process

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Abstract

As the film formation of the dry coating process differs completely from conventional coating methods it is of certain interest to define a parameter like the minimum film formation temperature (MFT) used for aqueous dispersion based processes in order to describe an efficient film formation. Film formation occurs mainly during the curing step following the coating phase. Therefore, the film formation of the dry coating process was analyzed with regard to the two process parameters influencing film formation, namely curing temperature and time.

Theophylline pellets were coated using the enteric polymer HPMCAS and TEC/Myvacet® as plasticizer composition. The polymer and the plasticizer were applied to the pellets simultaneously, except for the beginning of the coating step when the plasticizer has been sprayed 30 s before powder feeding was started. The coated pellets were cured for five different time periods at eight different temperatures. Drug release was determined in 0.1 N HCl. Their surface and cross-sectional morphologies were examined by scanning electron microscopy. The glass transition temperature of the obtained films as well as of the polymer plasticizer mixture obtained by casting a film using an organic solution of the coating components was determined by thermomechanical analysis.

At higher curing temperature and/or extended curing time an enhancement of acid resistance is observed. The glass transition temperature of the coating mixture was determined to be 51.7 ± 3.3 °C. It is close to the temperature needed for film formation. Enteric resistant pellets are obtained after curing for 0.75 h at 55 °C. However, enteric resistance was achieved as well slightly below the glass transition temperature at 45 °C applying long curing periods of at least 12 h. This may be caused by the plasticizer gradient along the coat which is caused by spraying the plasticizer 30 s before starting powder feeding. This results in a higher plasticizer concentration of the inner layers of the coat relatively to the outer ones. Due to this film formation starts at the inner layers even below the glass transition temperature. As the plasticizer diffuses to the outer layers during curing according to the plasticizer gradient, film formation proceeds.

Keywords: Dry coating; Glass transition temperature; Film formation; Curing

1. Introduction

Film formation of polymer coatings is crucial with respect to the functionality of pharmaceutical coatings of oral dosage forms like enteric resistance or modified release. Consequently, the coating technology has developed steadily in the last decades.

The first coatings applied to solid oral dosage forms were organic solvent based coatings. Film formation using organic polymer solutions is easily achieved due to the dissolved polymer that after deposition builds the film on the substrate surface by undergoing sol to gel transition as the organic solvent evaporates. Upon evaporation, the polymer molecules approach each other and finally form a homogeneous film with a high degree of polymer chain interpenetration [1]. However, the use of organic solutions holds various disadvantages, such as low polymer concentration, which is limited by the viscosity of the solution. Furthermore, the toxicity of the solvent requires its recovery combined with high costs and environmental concerns.

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Thus, using aqueous polymer dispersions is of current interest and often solvent based coatings are replaced by aqueous dispersion based coatings. The film formation of aqueous polymer dispersions using latex or pseudolatex materials is driven by the evaporation of water and subsequent coalescence of the polymer particles [2]. The process of film formation using aqueous polymer dispersions is usually divided in three phases [3,4]. Phase I is the evaporation of water. The density of the dispersion increases until the colloidal particles come into contact with each other and, subsequently, form close-packed arrays. The particles then undergo deformation to polyhedra [5] without interparticle spaces in phase II, induced by an increase in temperature above the minimum film formation temperature (MFT), one of the most important parameters of film formation from aqueous dispersion based coatings. It is defined to be the minimum temperature at which a cast film becomes crackless and clear [6]. Below this temperature, the dried dispersion appears opaque and powdery [2]. Increasing the temperature above the glass transition temperature (T_g) in stage III, the boundaries between the particles disappear through interdiffusion of polymer chains developing a continuous film without distinguishable particles [7]. The micromechanical process of the coalescence is still not completely analyzed, however, several models are discussed in the literature. Dillon et al. [8] explained the film formation mechanism introducing the dry sintering hypothesis which postulates that the surface tension of the polymer is the driving force accompanied by viscous flow and particle deformation. An analogous mechanism based on the polymer–water interfacial tension was suggested by Vanderhoff et al. [9] known as wet sintering. An alternative theory was developed by Brown [10] termed the capillary theory. Capillary forces exerted by the liquid facilitate the deformation of the particles in the interstitial capillary system between particles during drying.

Film formation of aqueous polymer dispersions usually takes several minutes up to hours depending on film thickness and environmental conditions [11]. Therefore, the temperature has an important effect on the rate of polymer diffusion and film formation [5,12]. Recently Siepmann et al. reported that additional to heat, humidity enhances film formation of HPMCAS coatings. Furthermore film formation was shown to be dependent on the particle size of the polymer [13]. Additionally, it is described in the literature that film formation begins at the upper surface of the coating and proceeds from top to bottom progressively during drying or rather curing [14].

The film formation of solvent free coating processes occurs mainly during the curing step [15]. The dry coating process can be divided in two phases, the coating and the curing phases. During the coating phase polymer powder and plasticizer are added separately but simultaneously to the pellets and adhere on their surface achieving a homogeneous application of the coating material onto the pellets. During the curing step film formation is achieved by an increase in temperature [16]. Before the curing step, the coating consists mainly of adhered polymer particles and agglomerates. Obara et al. suggested to spray a small amount of water to the coated spheres triggering film formation by acting as a plasticizer [17]. Film formation can be achieved without water by adjusting higher curing temperatures, thereby decreasing the polymer's melt viscosity, a major resisting force for film formation [18]. Film formation can be further enhanced by increasing the plasticizer concentration [19]. Recently, studies of Terebesi et al. [20] showed that different plasticizers also affect the film formation. Since dry coating is conducted without any dispersion media it may be assumed that the film formation follows the theory of dry sintering. However, the application of liquid plasticizer has to be considered influencing the film formation by temporarily building capillary forces between the polymer particles before the plasticizer will have been taken up by the polymer. Nevertheless, the film formation of the dry coating process with its key parameters for achieving functional film formation is not described in the literature.

Since the film formation of the dry coating process differs considerably from conventional coating methods, the aim of the study is to define a parameter like the minimum film formation temperature (MFT) of aqueous dispersion based processes for obtaining an efficient film formation during dry coating.

As film formation is supposed to take place during the curing step, parameters influencing the curing process namely curing temperature and time were especially considered. In previous studies the coating and the curing step were performed in the rotary fluid bed. In this study, the pellets were coated in the fluid bed and afterwards cured in an oven in order to ensure that the different cured samples underwent the same coating conditions. Film formation was characterized by scanning electron micrographs and drug release studies. Thermomechanical analysis was performed in order to determine the glass transition temperature (T_g) of dry coated films on the coated spheres and of cast films obtained using an organic solution of the coating components.

2. Materials and methods

2.1. Materials

Theophylline pellets were donated by Klinge Pharma (München, Germany) and hydroxypropyl methylcellulose acetate succinate (HPMCAS, AQOAT®) as enteric film former was provided by Shin-Etsu Chemical Co. (Niigata, Japan). As liquid plasticizers triethyl citrate (TEC, Jungbunzlauer Ladenburg GmbH, Ladenburg, Germany) and acetylated monoglyceride (AMG, Myvacet®, 9-45K, Quest International, Zwijndrecht, The Netherlands), acting as well as wetting agent, were used.

2.2. Methods

2.2.1. Preparation of coated pellets

The process was conducted in a rotary fluid bed (Glatt Rotor-GPCG-1.1, Glatt GmbH Binzen, Germany) with a three way nozzle aligned to the direction of the fluid bed movement. HPMCAS powder was quantitatively passed through a powder feeder (K-Tron Soder K-CL-24-KT20, K-Tron, Gelnhausen, Germany) to the three way nozzle and was applied together with the plasticizer composition (TEC/Myvacet®; 35:15) through the nozzle (Fig. 1).

The coating process took 23 min and was carried out using a batch size of 1.0 kg, adjusting the following parameters: inlet temperature: 26–28 °C, product temperature: 25–26 °C, outlet temperature: 24–25 °C, air flow rate: 70 m^3/h, powder feed rate: 11 g/min, plasticizer feed rate: 3.5 g/min. The coating level was 25% calculated by the weight of the pellets. Immediately following the coating process the coated pellets were oven-cured at different temperatures starting with 25 °C and increasing the temperature by 10 °C steps up to 95 °C (Memmert universal oven U, Memmert GmbH+Co.KG, Schwabach, Germany). The curing time was varied between 0.75, 3, 6, 12, and 24 h. Additionally, samples of coated but uncured pellets were prepared. The process was performed in triplicate.

2.2.2. Drug release studies

The in vitro drug release of the coated pellets was carried out according to the USP XXIX rotating paddle method (Sotax AT6, Sotax GmbH, Lörrach, Germany). The dissolution was studied at 37 ± 0.5 °C in 750 ml of 0.1 N HCl (pH 1) for 120 min using 40 mg pellets in each vessel. The drug release was analyzed spectrophotometrically at 272 nm using a continuous flow-through system attached to the UV spectrophotometer (Lambda 2, Perkin-Elmer, Rodgau-Juegesheim, Germany). The mean and standard deviation of four samples is given.

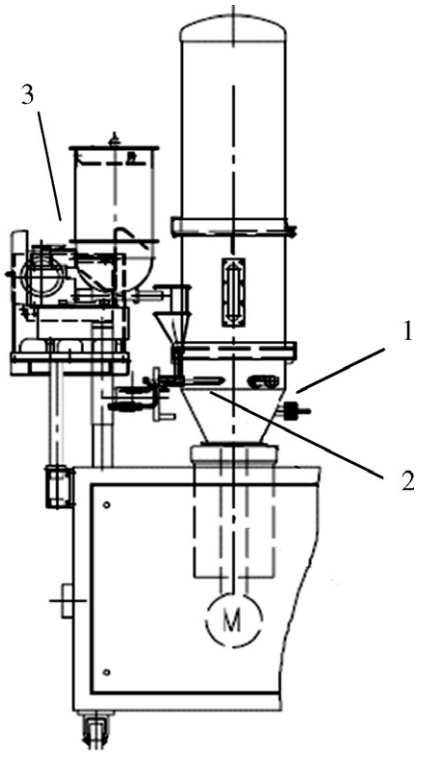

Fig. 1. Schematic of a rotary fluid bed: (1) rotor, (2) three way nozzle, (3) powder feeder.

2.2.3. Thermal analysis

The glass transition temperature (T_g) of dry coated pellets was obtained by thermomechanical analysis (Mettler TMA40 with Star^e-Software, Mettler Toledo, Giessen, Germany). Sample preparation was accomplished by adjusting the pellets in a sample holder (Fig. 6). The analysis was carried out under nitrogen atmosphere between −20 and 120 °C at a heating rate of 10 °C/min. The determination of the samples' T_g was performed in triplicate.

2.2.4. Surface/cross-sectional morphologies

Pellets and broken pellets of the dry coating process uncured and cured at different temperatures for different time periods were sputter coated with gold for 240 s (Agar Manual Sputter Coater, Agar Scientific Ltd., Stansted, Essex, England). Afterwards the samples were examined by observing their surface and cross-sectional morphologies with a scanning electron microscope (LEO VP 1430, Carl Zeiss NTS GmbH, Oberkochen, Germany).

2.2.5. Preparation of polymeric films

Films consisting of 75% (w/w) HPMCAS and 25% (w/w) plasticizer were obtained from casting organic solution of the coating components. For the polymeric films a 10% HPMCAS solution was prepared by dissolving HPMCAS in acetone and mixed with the plasticizers which consisted of TEC (70% (w/w)) and Myvacet® (30% (w/w)).

Both liquids were combined, poured out in PTFE – Petri dishes and dried. The obtained films were used for thermomechanical analysis in order to determine the T_g.

3. Results and discussion

Generally, film formation of the plasticized polymer particles is expected to occur already at temperatures below the pure polymer's glass transition temperature. This is caused by the plasticizer reducing the polymer's T_g which results in elevated mobility and softness of the polymer molecules. Thus, the film formation temperature should be lower in comparison to the glass transition temperature of the pure polymer. In contrast to conventional coating processes using aqueous polymer dispersions no water with plasticizing quality is in use. Though, due to the absence of water no temporarily plasticizing effect exists. Nevertheless, it has to be kept in mind that the liquid plasticizer may temporarily exert capillary forces as long as it is not taken up completely by the polymer powder. However, the capillary forces exerted by the plasticizer are assumed to be of minor

importance in comparison to aqueous dispersion based processes. Especially during the curing phase following the coating phase, when the plasticizer is assumed to have penetrated completely into the polymer particles, the temporary capillary forces disappear and film formation proceeds under different driving forces. Since the dry coating process is carried out without any solvent, respectively, dispersion media, and no plasticizer is left, it can be assumed that film formation conforms to the dry sintering theory of polymers. Dillon et al. [8] introduced this theory where film formation occurs due to viscous flow and particle deformation. Caused by the viscoelastic behavior of polymers, applied stress induces a combined response of elastic deformation and viscous flow [6]. Considering the decreased viscosity and modulus of the polymer particle by the plasticizer the deformation and the resulting film formation is facilitated since a softer polymer is able to deform and flow easier than a harder one [21]. In order to induce the viscous flow and film formation the applied temperature needed is supposed to be close to the T_g of the polymer [22].

In order to investigate the viability of this hypothesis, theophylline pellets were coated using the enteric polymer HPMCAS and TEC/Myvacet® as plasticizer composition in the ratio of 75% (w/w) HPMCAS/25% (w/w) plasticizer. The polymer and the plasticizer were applied to the pellets simultaneously, except for the beginning of the coating phase when the plasticizer has been sprayed 30 s before powder feeding was started. As the film consisting of 75% (w/w) HPMCAS and 25% (w/w) plasticizer obtained from a cast organic solution of the coating components exhibited a T_g of 51.7 ± 3.3 °C, the influence of curing temperatures between 25 °C and 95 °C on enteric resistance was investigated. Additionally, the influence of curing time was studied. Drug release was determined in 0.1 N HCl. Surface and cross-sectional morphologies of the pellets were examined by scanning electron microscopy. The glass transition temperature of the obtained films was determined by thermomechanical analysis.

3.1. Influence of process conditions and coating temperature

During the coating phase of the dry coating process the product temperature was adjusted as low as possible (25 °C) in order to prevent premature film formation. At the beginning the plasticizer has been sprayed 30 s before the feeding of the dry polymer was started. This ensures the wetting of the pellets' surface facilitating the adhesion of the polymer to the surface of the substrate and the cohesion of the polymer particles with each other. Regarding the scanning electron micrographs (SEM) (Fig. 2a) a continuous layering can be detected after 10 min applying the coating material. When the application is accomplished (Fig. 2b) the layer of the cohered particles is twice the thickness as after 10 min. Furthermore, the material layer shows partial film formation of the inner layers. This might be caused by the higher plasticizer concentration on the substrate surface leading to an enhanced softening of the polymer particles of the inner layers with respect to the outer ones. Additionally, capillary forces emerging from the plasticizer prior to its uptake into the polymer particles may play a role as well. Capillary forces are known as one driving force for film formation [23] (Fig. 2b). Once the plasticizer is penetrated into the polymer particles the capillary forces are negligible. Another reason may be simply a longer residence time of the inner layered polymer particles which results in enhanced film formation of the inner layers in comparison to the outer ones due to the known time dependence of film formation.

However, the film obtained after the coating step does not result in enteric resistance, which has been shown in previous studies [16] caused by poor film formation. In this context it has to be pointed out that by using SEM it might not be possible to differentiate whether film formation is sufficient to achieve enteric resistance or whether it is not.

3.2. Influence of curing temperature and curing time

As described in the literature [3,12] and as shown above an additional curing phase is needed in order to achieve functional film formation. As mentioned before the main parameters influencing the curing process are curing temperature and time.

In order to determine the curing conditions needed for film formation the coated pellets were cured at different temperatures and time intervals. The influence of curing temperature on film formation is shown by comparing the drug release of coated pellets which were cured at different temperatures (Fig. 3). Prior to dissolution the coated pellets were cured 0.75 h at eight temperatures starting with 25 °C and increasing in 10° steps up to 95 °C. By an increase in curing temperature an enhancement of acid resistance can be observed. Consequently, the drug release of cured pellets was decreasing from 52.4 ± 2.9% at 25 °C to 1.6 ± 0.1% at 75 °C. Due to the stickiness of the film at higher curing temperatures the film may have been damaged during sample preparation prior to dissolution leading to irregular drug releases between 65 °C and 95 °C curing temperature.

With respect to the requirements of enteric coated articles according to USP XXIX an enteric resistance can be observed after 0.75 h curing at 55 °C and above, which is in perfect accordance to the expectation that enteric resistance should be obtained by curing close to the T_g. The drug release at 55 °C curing temperature was 6.7 ± 2.0%. Considering the obtained results film formation is shown to improve by increasing the curing temperature which also is confirmed by scanning electron micrographs.

The micrographs reveal that the surface of pellets cured at lower temperatures is rough and that the film is porous (Fig. 4a–d). Film thickness of pellets cured at 25 °C seems to be similar to uncured pellets. Nevertheless, film formation is superior to uncured pellets according to the results obtained by dissolution studies. Once more it has to be pointed out that the determination of the quality of film

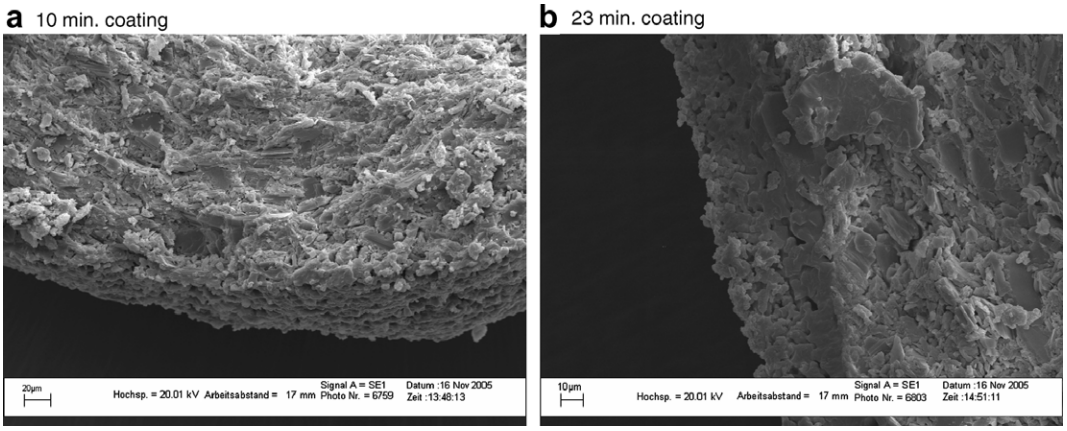

Fig. 2. Scanning electron micrograph of dry coated pellets during the coating phase after 10 min and after 23 min.

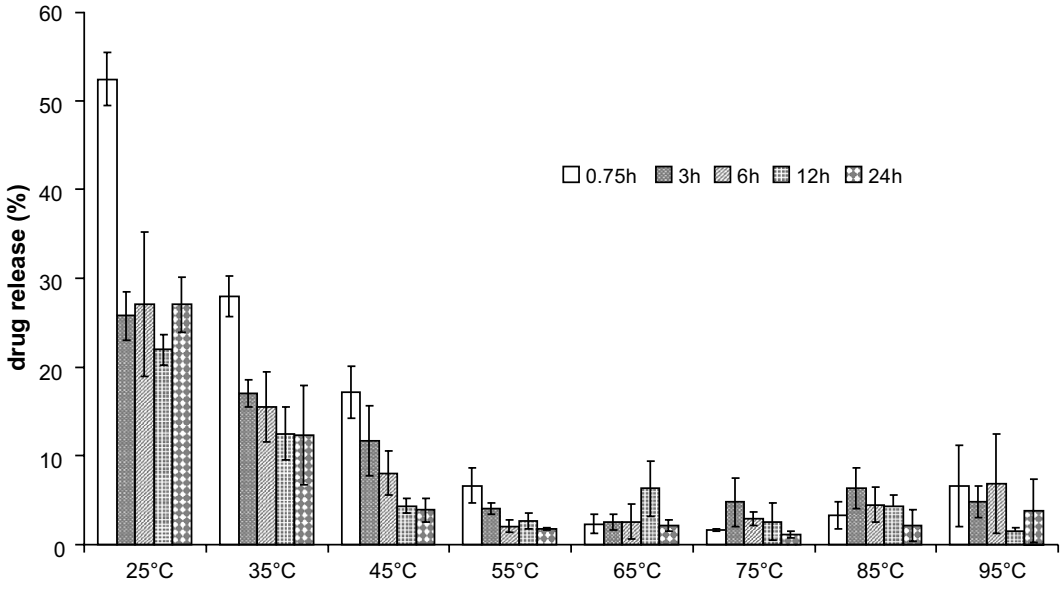

Fig. 3. Drug release in 750 ml of 0.1 N HCl (pH 1) of theophylline pellets after curing at 25, 35, 45, 55, 65 and 75 °C for 0.75, 3, 6, 12 and 24 h using 40 mg in each vessel, $n = 4$, mean ± STD.

formation is limited using SEM. Furthermore, it can be observed that film formation starts at the inner layers and continues to the outer ones (Fig. 4b–d). This might be caused by the higher plasticizer concentration on the substrate surface leading to an enhanced softening of the polymer particles of the inner layers with respect to the outer ones. Additionally, capillary forces emerging from the plasticizer prior to its uptake into the polymer particles may play a role as well. Furthermore, film formation of the inner part might be due to the higher residence time of the polymer particles of the inner layers in comparison to the outer ones. By curing at 35 °C film formation proceeds detected by a decrease of drug release to 27.9 ± 2.3%. A curing temperature of 45 °C results in a decreased drug release of 17.1 ± 2.9%. However, functional film formation is not obtained at these temperatures. At 55 °C, the outer layers still show a porous structure and the surface of the pellets is still rough. However film formation is already sufficiently good and film thickness already large enough to obtain enteric resistant pellets. At temperatures above 65 °C film formation is observed in the outer particle layers and the surface becomes increasingly smoother (Fig. 4e–h).

After pointing out that the needed curing temperature to achieve sufficient film formation is close to the T_g and after pointing out its importance regarding the theory of film formation, the influence of the curing time on drug release in 0.1 N HCl was determined. In addition to 0.75 h curing time at the above named temperatures the pellets were cured for 3, 6, 12, and 24 h (Fig. 3).

The drug release of pellets cured at 25 °C can be reduced to the half by increasing the curing time from 0.75 to 3 h. However, further prolongations of curing time do not show major changes of the drug release. Pellets cured at 35 °C also indicate a reduced drug release after 3 h curing in

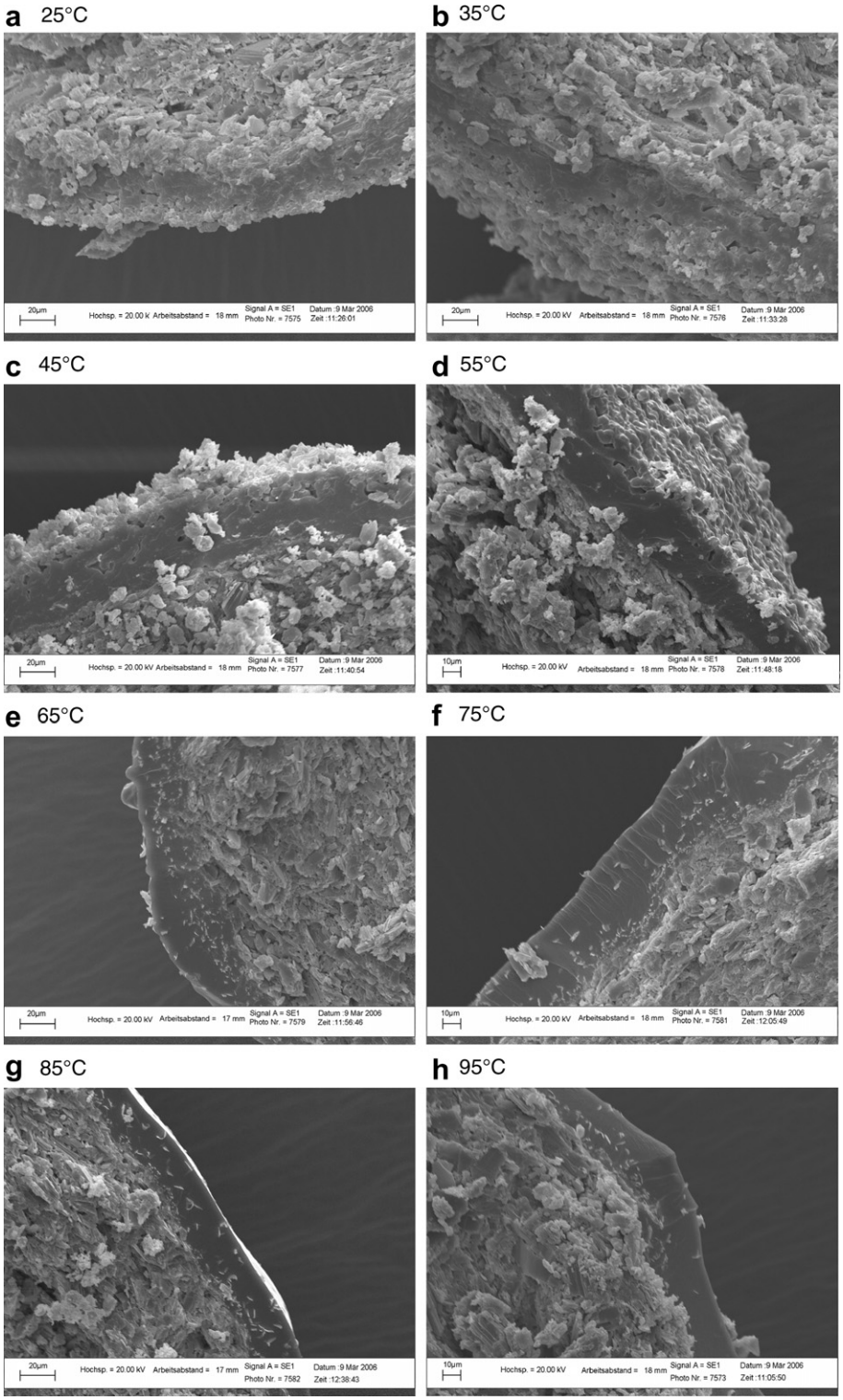

Fig. 4. Scanning electron micrographs of dry coated pellets cured at different temperatures for 0.75 h.

comparison to 0.75 h. After 6, 12, and 24 h no significant changes are observed. In both cases no enteric resistance according to the USP XXIX is obtained. This is in contrast to the pellets cured at 45 °C where enteric resistance can be achieved after 12 h curing determining a drug release of $4.36 \pm 0.8\%$. The higher plasticizer concentration on the substrate may be sufficiently high resulting in film formation slightly below the T_g. At 55 °C curing temperature enteric resistance was obtained already after 0.75 h. Nevertheless the drug release was even more reduced after 3 and 6 h. This is phenomenological for the film formation process because even above the T_g it takes a certain time for

film formation to complete. Pellets cured at higher temperatures do not show major changes when increasing the curing time. Obviously, film formation at this temperature has been accomplished already within 0.75 h. The irregular higher drug releases of the samples cured at 65 °C for 12 h, at 75 °C for 3 h as well as at 85 and 95 °C may be caused again by damages of the film caused by sample preparation prior to dissolution.

Considering the results, the efficiency of film formation is increased by higher curing temperature and longer curing time. At 55 °C and above 0.75 h curing time leads to an enteric resistance. Nevertheless by increasing the curing time up to 12 h enteric resistance can be achieved even slightly below the T_g at 45 °C (Fig. 3), which can be explained by looking again at the material application. Conducting the dry coating process the film formation starts at the inner parts of the layering caused by the higher concentration of plasticizer on the pellets' surface which leads to a decrease of T_g. As a function of time the plasticizer diffuses and migrates from the inner part of the film to the outer polymer layers according to the plasticizer gradient equilibrating the ratio between polymer and plasticizer in the film and, consequently, enabling further film formation. This results in an increase of the film's thickness, finally leading to enteric resistance, in the case of pellets cured at 45 °C after 12 h curing time.

Looking at the SEM micrographs again, it can be shown that between 25° and 35 °C, the porous structure of the polymer coating still remains, although the curing time is increased (Fig. 5a and b), and insufficient film formation is obtained in contrast to the pellets cured at 45 °C and above where the structure becomes more dense (Fig. 5c–e). Though, due to the dependency of film formation on both, curing temperature and time it is impossible to define a single value of temperature at which film formation occurs. Instead, the conditions necessary to obtain film formation

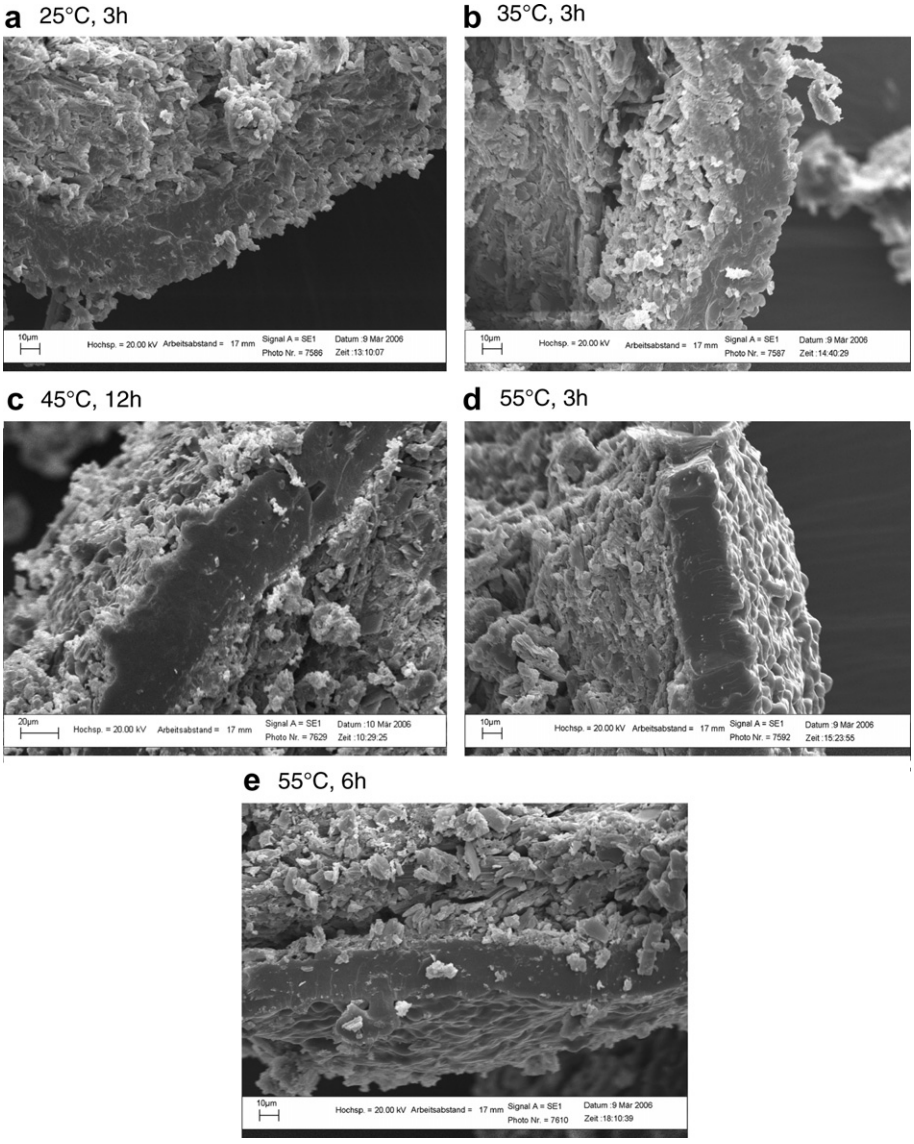

Fig. 5. Scanning electron micrographs of dry coated pellets cured at different temperatures and times.

Table 1
Curing temperature and curing time conditions which lead to film formation and enteric resistance, $n = 4$, mean ± SD

Curing temperature (°C)	Curing time (h)
25	−(>24)
35	−(>24)
45	>12
55	<0.75
65	<0.75
75	<0.75
85	<0.75
95	<0.75

consist always of a pair of curing temperature and time values (Table 1).

3.3. Glass transition temperature (T_g) of dry coated films

The T_g of the dry coated films was also determined using TMA in order to investigate whether it is similar to the one obtained from cast films using organic solutions. In contrast to aqueous dispersion based coatings isolated films cannot be cast using a MFT bench because of the missing dispersion media. In order to determine the T_g of films produced by the dry coating process the pellets cured at different temperatures were inserted in a specially designed sample holder (Fig. 6). By this exceptional setup the penetration of the sensor into the polymer layer can be determined in situ, namely on the pellet's surface.

The temperature range at which the sensor penetrates into the polymer layer was around 38.5 °C after curing at temperatures between 25 °C and 55 °C varying between 37.57 ± 1.27 °C (55 °C) and 39.37 ± 4.11 °C (45 °C) (Table 2). The temperature of penetration obtained from pellets cured at 65 °C was 43.65 ± 1.01 °C, lying in between pellets cured at lower temperatures and pellets cured at 75, 85 and 95 °C which exhibit temperatures in the range of 48.24 ± 1.77 °C and 50.9 ± 1.39 °C. Remembering the SEMs (Fig. 4a–d) a porous structure and only partly film formation especially of the outer layers was detected after curing at lower temperatures due to the described plasticizer gradient which promotes the film formation from the inner layers to the outer ones. This may cause a premature penetration of the sensor at temperatures below the glass transition temperature as the porous structure may collapse due to the rising temperature. Consequently the obtained T_g may be too low and therefore may be incorrect. Pellets cured at higher temperatures show higher T_gs meeting the expectations with regard to the SEMs where enhanced film formation and no porous structures are observed.

In order to measure the T_g of the films cured at lower temperatures correctly, the T_g of all films was redetermined after a second curing phase at 95 °C, 1 h expecting complete coalescence. All samples show T_gs between 47.41 ± 3.02 °C (75 °C curing temperature) and 55.72 ± 1.68 °C (35 °C curing temperature) (Table 2) indicating complete coalescence of the film. A similarity to the T_gs obtained from the pellets cured at 75 °C and above after the first curing phase is obvious. However, as TMA measurements are dependent on the film integrity and homogeneity and as still doubts about integrity and homogeneity of dry coated films might exist, organic solutions of polymer and plasticizer were cast and investigated by TMA. In comparison films consisting of 75% (w/w) HPMCAS and 25% (w/w) plasticizer obtained from a cast organic solution of the coating components exhibited a T_g of 51.7 ± 3.3 °C which confirms exactly the determined T_gs after the second curing.

Considering these results the glass transition temperature corresponds quite well with the temperature range of 45–55 °C in which satisfactory film formation and enteric resistance of the pellets were obtained. Thus, it can be assumed that in contrast to conventional coating processes using aqueous polymer dispersions a temporarily plasticizing effect does not exist confirming the hypothesis that the film's T_g must be close to the film formation temperature. Summarizing the results, the glass transition temperature of the plasticized polymer has to be considered as a key parameter for the adjusted curing temperature of the dry coating process.

Fig. 6. TMA sample holder designed to measure the film's glass transition temperature in situ.

Table 2
Glass transition temperature (T_g) after the first curing at different temperatures and after the second curing at 95 °C, $n = 3$, mean ± SD

Curing temperature (°C)	T_g (°C) 1. curing phase	T_g (°C) 2. curing phase
25	38.98 ± 2.79	52.86 ± 2.87
35	37.64 ± 1.25	55.72 ± 1.68
45	39.37 ± 4.11	51.49 ± 5.74
55	37.57 ± 1.27	46.05 ± 4.79
65	43.65 ± 1.01	49.31 ± 2.83
75	49.24 ± 1.77	47.41 ± 3.02
85	50.90 ± 1.39	47.93 ± 1.71
95	49.31 ± 2.38	47.92 ± 2.29

4. Conclusion

The key parameter of the dry coating process has been found to be the glass transition temperature of the film. This is in contrast to conventional coating processes where the minimum film formation temperature is the key parameter and is below the film's T_g. Enteric resistance using HPMCAS (75% (w/w)) and a mixture of TEC/Myvacet® (25% (w/w)) is obtained after curing at 55 °C for 0.75 h. Although, film formation is possible below the T_g, when applying highly extended curing times. Curing at 45 °C has to be performed for at least 12 h in order to achieve enteric resistance. Film formation slightly below the T_g is possible because of a plasticizer gradient along the coat. The gradient is caused by spraying the plasticizer 30 s before starting powder feeding during the coating phase. This results in a higher plasticizer concentration of the inner layers of the coat relatively to the outer ones. Therefore film formation of the inner layers is possible even slightly below the T_g. As the plasticizer diffuses to the outer layers during curing according to the plasticizer gradient, film formation proceeds as time goes by.

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