Drug Development and Industrial Pharmacy, 2011, 37(3): 320–328

ISSN 0363-9045 print/ISSN 1520-5762 online
DOI:10.3109/03639045.2010.512292

ORIGINAL ARTICLE

Influence of the inlet air temperature in a fluid bed coating process on drug release from shellac-coated pellets

Yassin Farag and Claudia Sabine Leopold

Department of Pharmaceutical Technology, Institute of Pharmacy, University of Hamburg, Hamburg, Germany

Abstract
Context: Since the introduction of aqueous ammoniacal solutions, shellac regained importance for pharmaceutical applications. However, as shellac is a material obtained from natural resources, its quality and thus its physicochemical properties may vary depending on its origin and the type of refining. *Objective*: In this study theophylline pellets were coated with aqueous solutions of three different commercially available shellac types. The inlet air temperature of the coating process was varied, and its influence on drug release from the coated pellet formulations was investigated. Film formation was correlated to the physicochemical and mechanical properties of the investigated shellac types. *Results*: Pellets coated at lower temperatures showed distinct cracks in the coating film resulting in a loss of the barrier function during dissolution testing. These cracks were nonreversible by additional curing. The physicochemical and mechanical properties of the investigated shellac types varied significantly and could hardly be related to the drug release performance of the investigated formulations. *Conclusion*: Obviously, with shellac a minimum inlet air temperature must be exceeded to achieve a coherent coating film. This temperature was dependent on the investigated shellac type.

Key words: Coating defects, curing, dissolution, film formation, fluid bed coating, inlet air temperature, pellet formulation, shellac

Introduction

Shellac is the purified product of the natural material lac, which is secreted by the small parasitic insect *Kerria lacca* on various host trees in India, Thailand, and Southeast Asia to protect the brood from extreme temperatures and predators. Shellac is the only commercially used resin of animal origin.

Shellac with an average molecular weight of about 1000 Da is a complex mixture mainly of polyesters of the main components aleuritic acid, butolic acid, shellolic acid, and jalaric acid with a small amount of free aliphatic acids[1–3]. However, its composition varies depending on the insect species as well as the host tree from which the raw material is gained.

Shellac is used in the dye industry as a component in lacquers and varnishes[4] because of its good film-forming properties, high gloss[5], and water resistance. Shellac is nontoxic, is physiologically harmless[6], and is therefore generally recognized as safe (GRAS) by the FDA. This allows its use as an additive in food products where the material already plays a major role as coating material for citrus fruits[7] or confectionaries.

Because of its acidic character shellac is often used as an enteric coating material for pharmaceutical products[8,9]. Moreover, its low permeability for water and gases[10] allows its use in other applications such as moisture protection and taste masking[11]. Also the use of shellac in sustained release[12] and colon-targeting formulations[13] as well as in coating material for microencapsulation[14] has been described.

Despite all these advantages, the use of this versatile material in pharmaceutical applications has greatly declined. Shellac coatings prepared from alcoholic solutions as well as shellac raw material consist of the acid form, which undergoes aging[15]. This aging leads to a hardening of the material resulting in changes in the release characteristics of shellac-containing dosage forms. However, since the introduction of aqueous ammoniacal solutions, shellac could regain importance

---

Address for correspondence: Prof. Claudia Sabine Leopold, Department of Pharmaceutical Technology, Institute of Pharmacy, University of Hamburg, Bundesstr 45, 20146 Hamburg, Germany. Tel: +49 40 42838 3479, Fax: +49 40 42838 6519. E-mail: claudia.leopold@uni-hamburg.de

(Received 1 Jun 2010; accepted 28 Jul 2010)

for pharmaceutical applications. It has been reported that shellac films prepared from aqueous ammoniacal solutions lack the instability problems of coatings prepared from organic shellac solutions[9]. Aqueous shellac solutions are translucent and show a low viscosity even at higher concentrations allowing for a fast increase of the film thickness during the coating process. In addition, the GRAS status of shellac allows its use in modified release formulations with the regulatory status of a food product or nutritional supplement such as vitamin formulations. This gives shellac an advantage over most other release-modifying film-coating materials, which lack this status. Moreover, the natural origin from renewable resources may be of interest for marketing purposes.

In fluid bed coating processes, agitation and drying of the product is caused by the inlet air[16]. The Wurster process is a variation of the fluid bed technology. The spraying nozzle is localized on the bottom of the product chamber in the so-called Wurster insert. During the process the product passes the spraying nozzle, which discharges the coating formulation. The product is moved upward, passes the Wurster insert, and drops back into the fluid bed.

Especially for the application of functional coatings, knowledge about the process and the materials used is essential to assure functionality and a reproducible quality of the coating film.

In many publications the influence of coating process parameters on the product quality of coated dosage forms is described. Christensen et al. provided a detailed description of the Wurster process[17]. Thermodynamic models[18], studies on the interactions between coating formulation and core material[19], as well as the influence of various process parameters on the quality of the product[20,21] helped to understand this complex manufacturing process. However, there is still need of further investigations.

It turned out that the inlet air temperature during the coating process is a key factor in the manufacture of coated dosage forms. Therefore, in this study the influence of the inlet air temperature on drug release from shellac-coated pellet formulations is investigated.

Materials and methods

Materials

The following types of shellac were investigated: Marcoat™ 125 (Marcoat), a ready-to-use shellac solution (25%, w/w) prepared from Bysakhi shellac of Indian origin (Emerson Resources, Norristown, PA, USA); SSB 55 Pharma (SSB 55), Kushmi shellac flakes of Indian origin (Stroever Schellack Bremen, Bremen, Germany); and Pearl N811F (Pearl), shellac flakes of Thai origin (Gifu Shellac, Gifu, Japan). All shellac types were refined by solvent extraction. Theophylline pellets were donated from Temmler (Killorglin, Ireland). Ammonium bicarbonate, potassium dihydrogen phosphate, sodium chloride, sodium hydroxide, and hydrochloric acid were purchased from Carl Roth, Karlsruhe, Germany.

Methods

Preparation of shellac-coating solutions

Ground shellac was dissolved in 1.5% (w/v) ammonium bicarbonate solution at 50°C to obtain a final concentration of 15% (w/w). As the presence of excess ammonium salt influences the dissolution properties of the final shellac films, the solutions were heated to 65°C to remove the excessive ammonium salt in the form of free ammonia and carbon dioxide. Evaporated water was replaced. The heating process was repeated until a constant pH was reached. The pH of the final solutions was between 7.4 and 7.8 (MP225 pH meter, Mettler Toledo, Columbus, OH, USA).

Preparation of theophylline pellets

Before coating, the theophylline pellets were cleaned from dust and characterized for their average weight and diameter. The weight of a single pellet corresponds to the average weight determined from a sample of 500 pellets. The pellet diameter was measured using a Wild M3 microscope (Wild, Völkermarkt, Austria) equipped with a AxioCam ICc and AxioVision software (both from Zeiss, Jena, Germany).

Coating of theophylline pellets

The required shellac mass was calculated from the overall pellet surface and the desired coating level for the respective batch.

Marcoat solution was diluted to a final concentration of 15% (w/w) with demineralized water. The other aqueous shellac solutions were used as prepared. Fifty grams of immediate-release theophylline pellets were cleaned from dust and coated with the aqueous shellac solutions in a Mini Glatt fluid bed coater (Glatt, Binzen, Germany) with Wurster insert (Ø30 mm, 10 mm gap), equipped with TEF 20 temperature sensors (LKM electronic, Geraberg, Germany) for the measurement of inlet air and product temperature (Software: Signasoft 6000, Peekel Instruments, Bochum, Germany). The coating solutions were applied using a 0.5-mm two-way nozzle at a spraying rate of 0.4 g/min to achieve a final coating level of 1 mg/cm^2. Atomizing air pressure was adjusted to 0.6–1.1 bar according to the weight gain of the pellets. For investigation of the temperature dependence of the process, theophylline pellets were coated at inlet air temperatures of 20°C, 40°C, or 60°C and an inlet air volume of 14 m^3/h.

The pellets were stored in a desiccator over silica gel at least for 24 hours before further processing.

Calculation of the coating level and coating yield

The average coating level was determined as mass of shellac per total pellet surface area as follows:

$$CL = \frac{m_{\text{shellac}}}{A} \tag{1}$$

CL	average coating level (mg/cm^2)
m_{shellac}	mass of shellac in the sample (mg)
A	pellet surface area of uncoated pellets in the sample (cm^2)

The *CL* was calculated from the difference in theophylline content between coated and uncoated pellets and the average diameter as well as the weight of the uncoated theophylline pellets as reported in a previous publication[22]. Briefly, 150 mg of shellac-coated pellets were dissolved in 250 mL of 0.1 M NaOH using an ultrasonic bath. After sufficient dilution the theophylline content of the sample was determined spectrophotometrically in 0.1 M NaOH at 275 nm (Lambda 25, PerkinElmer, Beaconsfield, UK).

A *CL* of 1 mg/cm^2 corresponds to a weight gain of 8% (w/w).

The *CY* was calculated from the shellac mass and the mass of pellet cores in the sample as determined from the CL data as well as from the batch size and the mass of shellac applied to the batch.

$$m_{\text{cores}} = m_{\text{sample}} - m_{\text{shellac}} \tag{2}$$

$$CY = \frac{m_{\text{shellac}} \cdot m_{\text{batch}} \cdot 100\%}{m_{\text{cores}} \cdot m_{\text{shellac-batch}}} \tag{3}$$

m_{cores}	mass of cores in the sample (mg)
m_{sample}	mass of sample (mg)
m_{shellac}	mass of shellac in the sample (mg)
CY	coating yield (%)
m_{batch}	batch size (mg)
$m_{\text{shellac-batch}}$	mass of shellac applied to the batch (%)

Dissolution experiments

Dissolution tests were performed according to the European Pharmacopoeia with approximately 100 mg pellets in 1000 mL dissolution medium. Gastric resistance was tested in simulated gastric fluid (pH 1.2) using the paddle apparatus (Sotax AT 7, Allschwil, Switzerland) at 100 rpm and 37°C for 2 hours. Drug release was measured in phosphate buffer (pH 7.4, 0.05 M) above the dissolution pH of shellac. The pellets remained at the bottom of the vessel throughout the dissolution test. Dissolution profiles were recorded spectrophotometrically at 271 nm using 1 mm flow through quartz cells.

Curing of shellac-coated pellets

Approximately 5 g of shellac-coated pellets was placed into Petri dishes. The samples were cured in a drying oven at 60°C for 2 hours and at 80°C for 12 hours.

Scanning electron microscopy

The surface of the coated pellets before and after dissolution testing was analyzed using scanning electron microscopy (SEM). The samples were coated with a thin carbon layer and analyzed using a LEO 1525 scanning electron microscope (LEO Elektronenmikroskopie, Oberkochen, Germany) and an accelerating voltage of 5 kV.

Preparation of free shellac films

Films were prepared using a casting and evaporation method. Twenty milliliter shellac solution was poured onto Teflon plates. The solvent was evaporated at 40°C for 4–5 hours. After complete drying the film was carefully peeled off the plates and cut into the desired shape for further investigation. The film samples were stored in a desiccator over silica gel at room temperature for at least 24 hours before use.

Glass transition temperatures

For determination of the glass transition temperature (T_g) the cast shellac films were cut into circles with a diameter of 6 mm with a circular punch. The samples were analyzed with DSC (DSC 7, TAC 7/DX, liquid nitrogen cooling system; PerkinElmer). Approximately 10 mg of film sample was accurately weighed into standard aluminum pans with a punctured cap and measured twice under nitrogen atmosphere over a temperature range of –40°C to 120°C. Between the heating runs at 20 K/min an isothermal step of 1 minute at 120°C was introduced to remove excessive water. The T_g was determined from the second heating run with the Perkin Elmer Pyris software.

Mechanical properties of free shellac films

For mechanical characterization shellac films were cut in a dumbbell shape with length of 25 mm and width of 4 mm. Film thickness was measured with a Digimatic Indicator (Mitutoyo, Kawasaki, Japan). The mechanical properties of free shellac films were investigated with a texture analyzer (Inspect mini, Hegewald and Peschke, Nossen, Germany) at a test speed of 10 mm/min. Tensile strength, elastic modulus, and elongation at break were determined with at least five samples and calculated as shown below[23]:

$$\text{Tensile strength} = \frac{F}{A}\ (\text{MPa}) \tag{4}$$

$$\text{Elastic modulus} = \frac{F \cdot l}{A \cdot \Delta l}\ (\text{MPa}) \tag{5}$$

$$\text{Elongation at break} = \frac{100 \cdot \Delta l}{A \cdot l}\ (\%/\text{mm}^2) \tag{6}$$

F Maximum force applied during the test (N)
A Initial cross-sectional area of the sample (mm^2)
l Initial length (mm)
Δl Change in length (mm)

Results and discussion

During the coating process the process parameters were kept constant with the exception of the atomizing pressure, which varied according to weight gain of the pellets to maintain an adequate product flow through the Wurster insert.

Pellets coated at lower inlet air temperatures were found to be less electrostatically charged. This was advantageous during discharge of the final product from the chamber of the coater. Whereas pellets coated at 60°C tended to stick to the Wurster insert and the coaters' wall, pellets coated at 20°C were easily removed from the product container. Because of the low temperature the moisture uptake of the inlet air was reduced, resulting in increased humidity of the product and thus less electrostatic charge. In addition, the *CY* was found to be higher at lower inlet air temperatures. Whereas the *CY* was about 88% for the batches coated with an inlet air temperature of 60°C, it increased to 95% and above for batches coated with an inlet air temperature of 20°C. This can be attributed to a reduced tendency of spray drying of the coating formulation at lower inlet air temperatures. Moreover, coating at lower inlet air temperatures has several advantages such as the processing of thermolabile drugs and a reduction of energy costs.

However, the dissolution profiles of the theophylline pellets coated at lower inlet air temperatures differed significantly from those coated at 60°C (Figure 1). With decreased inlet air temperature drug release was enhanced. All pellets coated at 20°C showed complete drug release at pH 7.4 within 10 minutes or less. However, there were distinct differences between the drug release profiles of the investigated shellac types. Whereas formulations coated with Pearl showed fast drug release almost independent at all three inlet air temperatures, with the other two shellac types a clear temperature dependence is observed. Fast drug release at high pH is desired for enteric-coated formulations. At first sight it seems that such release profiles may be obtained with shellac by reduction of the inlet air temperature.

However, drug release experiments at pH 1.2 showed that a reduction of the inlet air temperature resulted in a loss of gastric resistance of most of the pellet formulations (Figure 2). Whereas with pellets coated with Marcoat and Pearl gastric resistance was observed down to an inlet air temperature of 40°C, with SSB 55 only the formulation coated at an inlet air temperature of 60°C showed gastric resistance. All formulations coated at an inlet air temperature of 20°C showed pronounced drug release at pH 1.2.

SEM pictures (Figure 3) showed a smooth continuous coating layer of pellets coated at 60°C. In contrast, pellets coated at 20°C showed cracks all over the coating surface. These cracks represent defects in the barrier and are obviously the reason for the loss of gastric resistance. SEM pictures of pellets after dissolution testing proved this theory. Whereas the inner pellet core was completely dissolved, the empty shell of the coating layer remained undissolved.

Most likely, an interaction of several factors led to these coating defects. Dalton and Hancock[24] reported a higher moisture uptake for granule formulations during fluid bed granulation at lower temperatures. With regard to the product temperature another factor comes into focus. From the difference between the inlet air temperature and the product temperature the water removal efficiency can be estimated (Figure 4). Dry inlet air passes through the wet product and absorbs water. The resulting evaporative heat loss leads to a temperature decrease of both inlet air and product. The more water

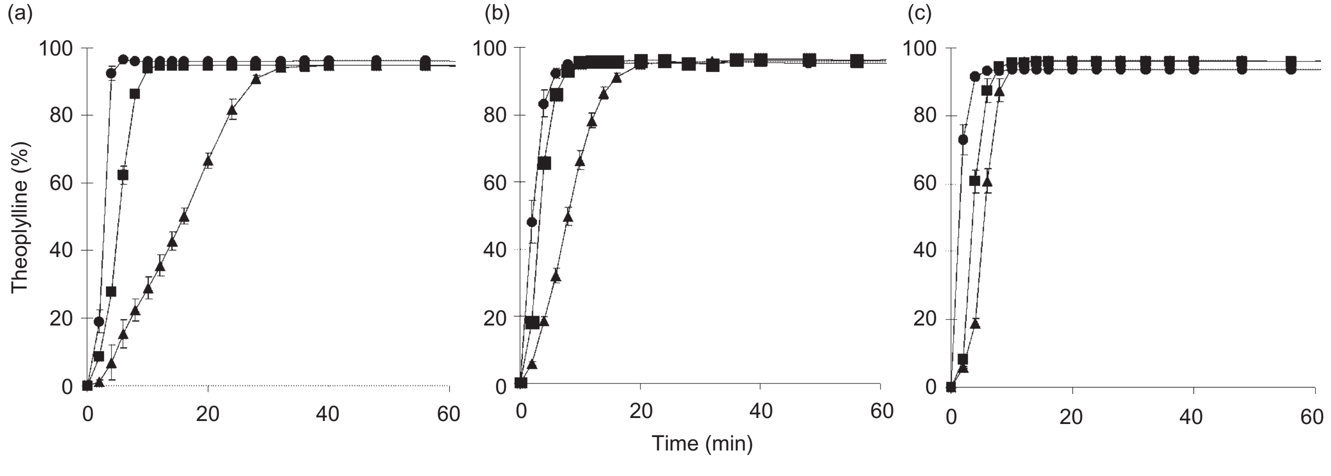

Figure 1. Influence of the inlet air temperature on drug release from shellac-coated pellets at pH 7.4 (means ± SD, $n = 3$). (a) Marcoat; (b) SSB 55; (c) Pearl. Inlet air temperature: ● 20°C ■ 40°C ▲ 60°C.

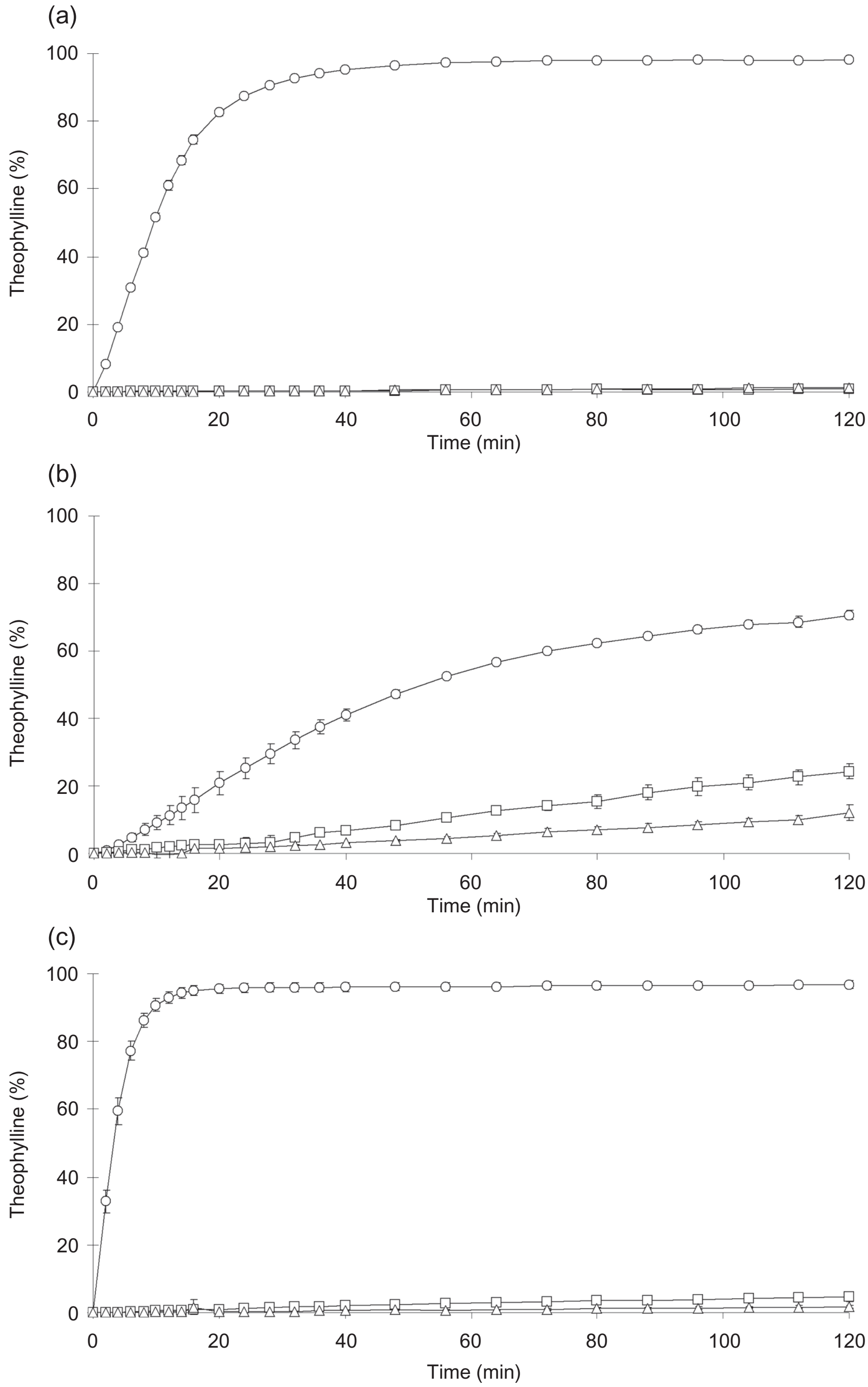

Figure 2. Influence of the inlet air temperature on drug release from shellac-coated pellets at pH 1.2 (means ± SD, $n = 3$). (a) Marcoat; (b) SSB 55; (c) Pearl. Inlet air temperature: ○ 20°C □ 40°C △ 60°C.

evaporates the lower the product temperature becomes. Whereas the difference between the inlet air temperature and the product temperature was 13°K at an inlet air temperature of 60°C, this difference was decreased to 6°K at 40°C and to less than 2°K at 20°C. Accordingly, water absorption and thus the drying capacity decreased at lower inlet air temperatures. Whereas about 4.8 g of water were absorbed per kilogram dry air at an inlet air temperature of 60°C, this absorption was decreased to about 2.4 g/kg at 40°C and 0.8 g/kg at 20°C. As the spraying rate was kept the same for all batches, it may be concluded that a major portion of the water remained in the

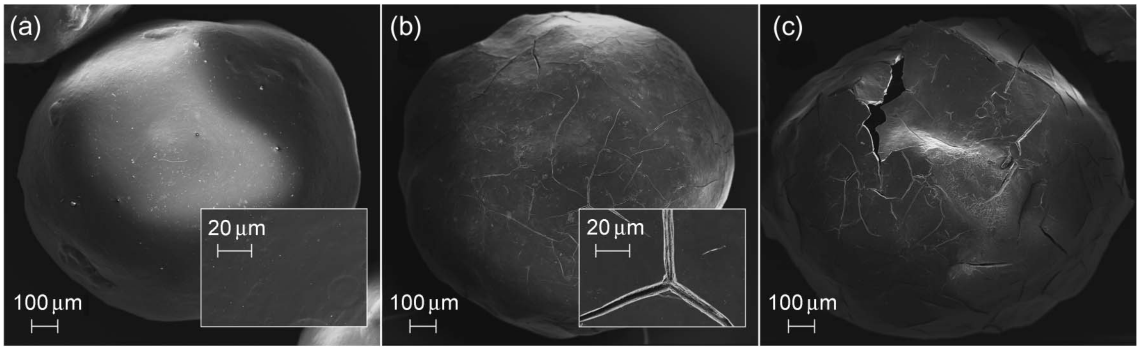

Figure 3. SEM pictures of pellets coated with Marcoat at different inlet air temperatures before and after dissolution testing at pH 1.2. (a) 60°C; (b) 20°C; (c) 20°C (after dissolution testing).

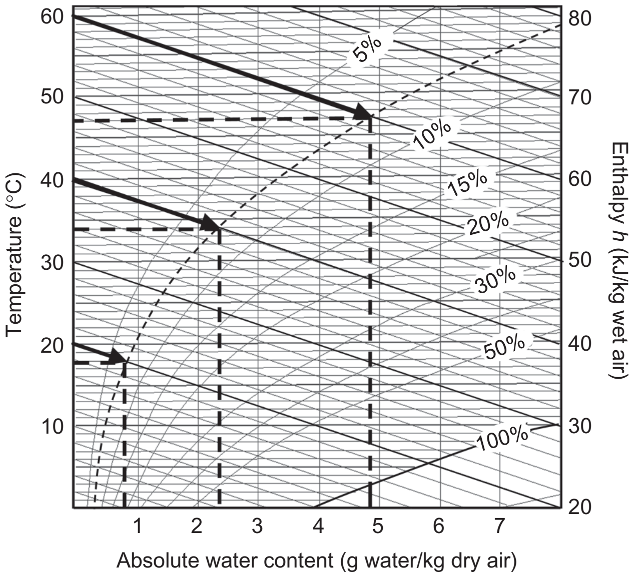

Figure 4. Modified Mollier h,x for the demonstration of the drying capacity at the used inlet air temperatures.

product at lower inlet air temperatures[25]. A combination of these factors—high humidity, low drying capacity, and high moisture uptake by the product—led to higher water content in both pellet core and film coating. The remaining water is partially incorporated into the coating film leading to a temporary increase of the film thickness. It has been reported that these conditions may cause an increased surface roughness of the films[21].

In addition to the process parameters during coating the storing conditions affect the properties of the final product. It has been described for tablets that they undergo significant dimensional changes during a coating process[26]. These changes were even more pronounced during storage and equilibration at ambient conditions. Aulton et al.[27] investigated the effect of storage conditions on the mechanical properties of hydroxypropyl methyl cellulose (HPMC) films. Storage at high humidity led to water uptake into the film samples and thus plasticization. In this study the samples were stored over silica gel. Under these conditions the opposite effect occurred. The water was removed from the film causing two effects, a loss of plasticization and a decrease in film thickness. Whereas the acid form of shellac has a comparatively low T_g[28], the T_g of the salt form is higher with values of about 65°C and above[15] depending on the shellac type. The removal of the residual water led to an increase of the T_g resulting in a loss of film flexibility. Together with the above-mentioned decrease of the film thickness and the dimensional changes of the pellet core, the resulting internal stress[29,30] most likely led to the cracks and the loss of gastric resistance.

Curing of pellets coated at low inlet air temperature

A loss of the barrier function as a result of low inlet air temperatures is a phenomenon well known from coatings applied as aqueous dispersions. If coating is performed below the minimum film-forming temperature, coalescence of the polymer particles and thus film formation does not take place[31]. However, with coatings prepared from aqueous dispersions film formation can be induced by a subsequent curing step with temperatures above the minimum film-forming temperature.

However, it has to be emphasized that the investigated pellets were coated with aqueous solutions and not aqueous dispersions of shellac. Nevertheless, an additional thermal treatment of the shellac-coated pellets was performed to clarify whether a final curing step removes the defects in the film.

The pellets were cured at two different temperatures: At 60°C, the temperature of the initial coating process, and at 80°C, a temperature above the T_g of the shellac salt form.

The results of the dissolution experiments are shown in Figure 5. Obviously, the cracks in the coating film were nonreversible. Drug release at pH 1.2 was decreased with pellets cured at higher temperatures and for longer curing periods. However, after 12 hours of curing at 80°C only 40% of the dose was released within 2 hours. Most likely, the curing process led to a decrease

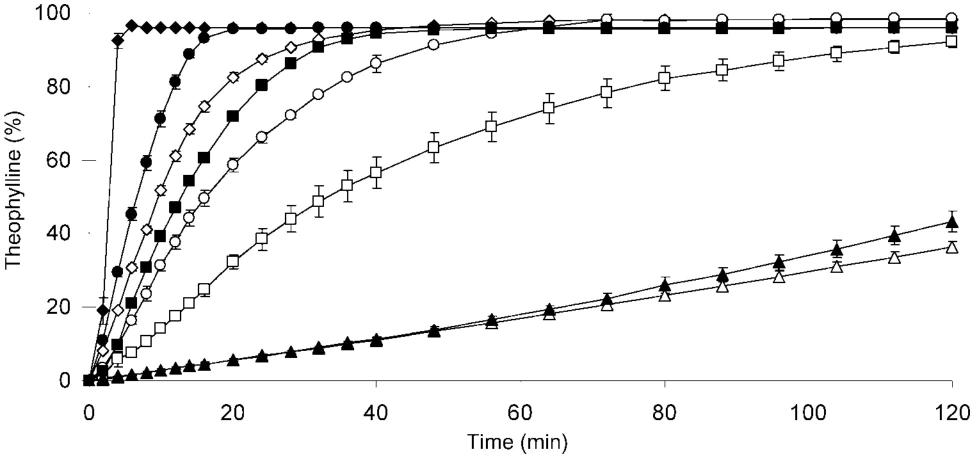

Figure 5. Influence of curing conditions on drug release profiles of pellets coated with Marcoat at 20°C (means ± SD, $n = 3$). pH 1.2: ◇ uncured; ○ 60°C, 2 hours; □ 80°C, 2 hours; △ 80°C, 12 hours. pH 7.4: ◆ uncured; ● 60°C, 2 hours; ■ 80°C, 2 hours; ▲ 80°C, 12 hours.

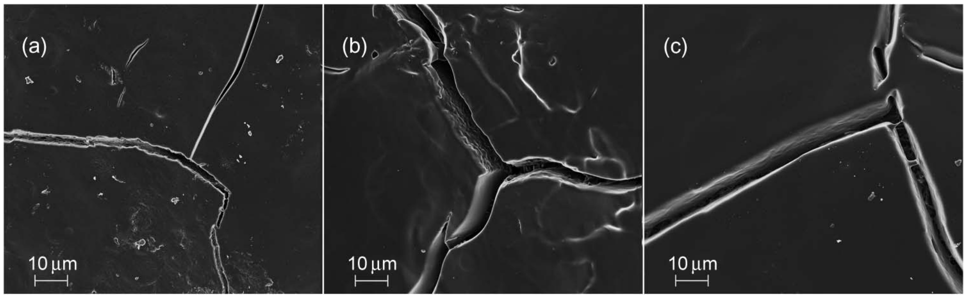

Figure 6. SEM pictures of pellets coated with Marcoat at 20°C treated under different curing conditions. (a) 60°C, 2 hours; (b) 80°C, 2 hours; (c) 80°C, 12 hours.

in number and the size of the cracks resulting in a decrease in drug release at pH 1.2. However, even after this long-term curing, a certain amount of cracks remained. SEM pictures of cured pellets support this hypothesis (Figure 6). It is obvious from these pictures that although the edges of the cracks became smoother with increasing temperature, the cracks themselves still remained.

In addition to the failure of the curing process regarding the film integrity, the thermal treatment led to changes in the material properties of the coating layer. This is apparent in the dissolution profiles at pH 7.4: Drug release was decreased even at this pH induced by artificial aging as a result of the thermal treatment. Prolonged thermal treatment of shellac led to polymerization and thus decreased solubility.

After 12 hours of curing at 80°C the dissolution profiles at pH 1.2 and 7.4 were almost superimposed. The coating layer was completely insoluble even at pH 7.4. Drug release took place only by diffusion through the cracks, independent of the pH.

Correlation of the dissolution profiles with the physicochemical properties of shellac

The T_g values of the investigated shellac types ranged from 66 to 82°C (Table 1). These values are high compared with the data found in the literature[28,32,33]. However, this discrepancy can easily be explained by the type of investigated shellac. In most publications the T_g of the acid form of shellac is determined. As described in a previous study[15], the T_g of shellac ammonium salt is significantly higher.

Ideally, coating films have a high tensile strength, a large elongation at break, and a high elastic modulus. Such films provide a good mechanical stability without being brittle[27]. The investigated shellac films show high values of tensile strength and elastic modulus. However, the low elongation at break proves the brittleness of the unplasticized material.

In Table 1 the physicochemical properties of the investigated shellac types are listed together with the film-forming properties. It is obvious that a prediction of the film formation is impossible on the basis of the physicochemical properties. The T_g could be related to the flexibility of the shellac coating and thus to the ability to resist internal stress and to form a continuous film even at low inlet air temperatures. However, a relationship between the T_g values of the shellac types and their film-forming properties could not be found. Even though the T_g of SSB 55 is 11°C lower than that of Pearl, its processing requires a higher temperature to obtain homogeneous films.

Table 1. Overview of the physicochemical and film-forming properties of the investigated shellac types (mean ± SD, T_g: $n = 3$; mechanical testing: $n = 5$).

Shellac type	Marcoat	SSB 55	Pearl
Mechanical properties			
T_g (°C)	67.7 ± 0.7	65.9 ± 0.8	77.5 ± 0.8
Tensile strength (MPa)	7.14 ± 0.64	5.43 ± 0.58	5.89 ± 0.55
Elastic modulus (MPa)	1820 ± 211	1107 ± 124	1344 ± 286
Elongation at break (%/mm^2)	0.308 ± 0.033	0.241 ± 0.051	0.266 ± 0.036
Continuous coating film (dependence on temperature)			
20°C	No	No	No
40°C	Yes	No	Yes
60°C	Yes	Yes	Yes

Generally, two possible measures to avoid cracking of film coatings are suggested: reduction of the stress buildup and increase of the cohesive strength of the film[34]. The latter has been shown for synthetic polymers by increasing their molecular weight. However, this modification is not possible for the natural material shellac. Hence, only the addition of a plasticizer can be used to reduce the internal stress buildup and thus to avoid cracking of the film coating. In this study with the modification of the inlet air temperature and the resulting increase of the drying capacity, a third option is provided to achieve a uniform coherent coating without addition of a plasticizer. However, it has to be considered that too high inlet air temperatures can lead to spray drying of the coating formulation and thus incomplete film formation[17]. Hence, for each formulation individual process parameters have to be established.

Conclusion

In this study the influence of the inlet air temperature on drug release from shellac-coated pellets was investigated. It was found that even though coating was performed with aqueous solutions, a minimum inlet air temperature had to be exceeded to obtain a continuous coating film. Below that temperature, cracks in the coating film appeared resulting in changes in the release profiles and especially loss of gastric resistance. It could be shown that the temperature dependence of the coating process was different for the investigated shellac types. This temperature dependence can hardly be predicted from the physicochemical and mechanical properties of the shellac types. In contrast to coatings from aqueous dispersions these coating defects were found to be non-reversible by a subsequent curing step.

Acknowledgments

The authors thank Temmler (Ireland) for the donation of theophylline pellets and Manfred Penning for providing free shellac samples.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

References

1. Chauhan VS, Sriram N, Subraman GB, Singh H. (1973). Chromatographic separation of alkaline hydrolysis products of shellac. J Chromatogr, 84:51–8.
2. Cockeram HS, Levine SA. (1961). The physical and chemical properties of shellac. J Soc Cosmet Chem, 12:316–23.
3. Wadia MS, Khurana RG, Mhaskar VV, Dev S. (1969). Chemistry of lac resin 1. Lac acids (Part 1): Butolic, jalaric and laksholic acids. Tetrahedron, 25:3841–54.
4. Ansari MF, Goswami DN. (2006). Shellac-acrylic emulsion paint for cementations surfaces. Pigm Resin Technol, 35:183–7.
5. Trezza TA, Krochta JM. (2001). Specular reflection, gloss, roughness and suface heterogeneity of biopolymer coatings. J Appl Polym Sci, 79:2221–9.
6. Okamoto MY, Ibanez PS. (1986). Final report on the safety assessment of shellac. J Am Coll Toxicol, 5:309–27.
7. McGuire RG, Hagenmaier RD. (2001). Shellac formulations to reduce epiphytic survival of coliform bacteria on citrus fruit postharvest. J Food Prot, 64:1756–60.
8. Pearnchob N, Dashevsky A, Siepmann J, Bodmeier R. (2003). Shellac used as coating material for solid pharmaceutical dosage forms: Understanding the effects of formulation and processing variables. STP Pharma Sci, 13:387–96.
9. Specht FM, Saugestad M, Waaler T, Müller BW. (1998). The application of shellac as an acidic polymer for enteric coating. Pharm Technol Eur, 10:20–8.
10. Hagenmaier RD, Shaw PE. (1991). Permeability of shellac coatings to gases and water vapor. J Agric Food Chem, 39:825–9.
11. Pearnchob N, Siepmann J, Bodmeier R. (2003). Pharmaceutical applications of shellac: Moisture protective and taste masking coatings and extended release matrix tablets. Drug Dev Ind Pharm, 29:925–38.
12. Kanokpongpaiboon A, Luangtana-Anan M, Nunthanid J, Limmatvapirat C, Puttipipatkhachorn S, Limmatvapirat S. (2005). Investigation of shellac as a material for sustained drug release. Proceedings of the 2nd AASP Symposium & 2nd ApEM Conference, Bangkok, Thailand, November 14–17.
13. Roda A, Simoni P, Magliulo M, Nanni P, Baraldini M, Roda G, et al. (2007). A new oral formulation for the release of sodium butyrate in the Ileo-cecal region and colon. World J Gastroenterol, 13:1079–84.
14. Sheorey DS, Kshirsagar MD, Dorle AK. (1991). Study of some improved shellac derivatives as microencapsulating materials. J Microencapsulation, 8:375–80.
15. Farag Y, Leopold CS. (2009). Physicochemical properties of various shellac types. Dissolut Technol, 16:33–9.

16. Dewettinck K, Huyghebaert A. (1999). Fluidized bed coating in food technology. Trends Food Sci Technol, 10:163–8.
17. Christensen FN, Bertelsen P. (1997). Qualitative description of the Wurster-based fluid bed coating process. Drug Dev Ind Pharm, 23:451–63.
18. Ende MTA, Berchielli A. (2005). A thermodynamic model for organic and aqueous tablet film coating. Pharm Dev Technol, 10:47–58.
19. Twitchell AM, Hogan JE, Aulton ME. (1995). The behavior of film coating droplets on their impingement onto uncoated and coated tablets. STP Pharma Sci, 5:190–5.
20. Ruotsalainen M, Heinamaki J, Guo HX, Laitinen N, Yliruusi J. (2003). A novel technique for imaging film coating defects in the film-core interface and surface of coated tablets. Eur J Pharm Biopharm, 56:381–8.
21. Ruotsalainen M, Heinamaki J, Taipale K, Yliruusi J. (2003). Influence of the aqueous film coating process on the properties and stability of tablets containing a moisture-labile drug. Pharm Dev Technol, 8:443–51.
22. Farag Y, Leopold CS. (2010). Investigation of drug release from pellets coated with different shellac types. Drug Dev Ind Pharm, in press, doi: 10.3109/03639045.2010.504210.
23. Macleod GS, Fell JT, Collett JH. (1997). Studies on the physical properties of mixed pectin/ethylcellulose films intended for colonic drug delivery. Int J Pharm, 157:53–60.
24. Dalton CR, Hancock BC. (1997). Processing and storage effects on water vapor sorption by some model pharmaceutical solid dosage formulations. Int J Pharm, 156:143–51.
25. Pourkavoos N, Peck GE. (1994). Effect of aqueous film coating conditions on water removal efficiency and physical properties of coated tablet cores containing superdisintegrants. Drug Dev Ind Pharm, 20:1535–54.
26. Okutgen E, Hogan JE, Aulton ME. (1991). Effects of tablet core dimensional instability on the generation of internal-stresses within film coats 3. Exposure to temperatures and relative humidities which mimic the film coating process. Drug Dev Ind Pharm, 17:2005–16.
27. Aulton ME, Abdulrazzak MH, Hogan JE. (1981). The mechanical properties of hydroxypropylmethylcellulose films derived from aqueous systems 1. The influence of plasticizers. Drug Dev Ind Pharm, 7:649–68.
28. Buch K, Penning M, Wächterbach E, Maskos M, Langguth P. (2009). Investigation of various shellac grades: Additional analysis for identity. Drug Dev Ind Pharm, 35:694–703.
29. Croll SG. (1979). Origin of residual internal stress in solvent cast thermoplastic coatings. J Appl Polym Sci, 23:847–58.
30. Rowe RC. (1983). A reappraisal of the equations used to predict the internal stresses in film coatings applied to tablet substrates. J Pharm Pharmacol, 35:112–3.
31. Brown GL. (1956). Formation of films from polymer dispersions. J Polymer Sci, 22:423–34.
32. Limmatvapirat S, Limmatvapirat C, Puttipipatkhachorn S, Nuntanid J, Luandana-Anan M. (2007). Enhanced enteric properties and stability of shellac films through composite salts formation. Eur J Pharm Biopharm, 67:690–8.
33. Pearnchob N, Dashevsky A, Bodmeier R. (2004). Improvement in the disintegration of shellac coated soft gelatin capsules in simulated intestinal fluid. J Controlled Release, 94:313–21.
34. Rowe RC. (1985). Film-Coating—the ideal process for the production of modified-release oral dosage forms. Pharm Int, 6:14–7.