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Investigation of drug release from pellets coated with different shellac types

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Abstract

Context: Even though most commercially available shellac types meet the specifications of the pharmacopoeias, their physicochemical properties and thus drug release may vary considerably. So far a comparison of drug release from dosage forms coated with different shellac types has not been made. *Objective*: Drug release from pellets coated with different shellac types was investigated and the data correlated to the physicochemical properties of shellac. *Methods*: Theophylline pellets were coated with three different commercially available shellac types of Indian and Thai origin. The minimum coating level (CL) to achieve gastric resistance was determined for each shellac type. The drug release characteristics from the different formulations were correlated with the physicochemical properties of the shellac types such as pK_a, acid value, and intrinsic dissolution rate. *Results*: Gastric resistance was achieved at comparatively low CLs for all investigated shellac types. At pH 7.4 all investigated formulations showed complete drug release within 45 minutes. Drug release at pH 6.8 was prolonged and occurred by swelling and drug diffusion through the coating layer. However, the required minimum CL and drug release profiles especially at pH 6.8 varied considerably. Of the investigated shellac types, the Thai shellac stands out providing both gastric resistance at low CLs and fast drug release at high pH 6.8. *Conclusion*: Although a prediction of the release characteristic could not be made from the pK_a, the intrinsic dissolution rate turned out to be a good indicator for the drug release behavior.

Key words: Coating, coating level, dissolution, drug diffusion, drug release, enteric coating, natural material, physicochemical properties, shellac, swelling

Introduction

Shellac is the purified product of the resin lac. The small parasitic insect *Kerria lacca* secretes lac on various host trees in India, Thailand, and Southeast Asia to protect the brood from extreme temperatures and predators. The resin lac forms thick encrustations around the twigs. After harvesting, the obtained sticklac is chopped and cleaned from wood and insect residues. A washing step with water, which dissolves soluble ingredients (e.g., laccaic acid), leads to the intermediate product seedlac.

There are three different ways of refining shellac, resulting in different shellac qualities. Wax-containing shellac is obtained by the traditional melting filtration process where molten seedlac is pressed through a filter and cast to a film. After cooling the film breaks into typical flakes. The color of this type of shellac corresponds to that of the seedlac used.

Bleached shellac is gained by dissolution of seedlac in aqueous alkali solutions and followed by treatment with sodium hypochlorite. Shellac is precipitated after addition of sulfuric acid. Solutions of bleached shellac are almost colorless, which can be advantageous in many applications. However, the bleaching process leads to changes in the molecular structure such as chlorination resulting in a higher reactivity and thus reduced stability.

Shellac obtained by melting or bleaching processes is usually intended for technical use. Shellac for pharmaceutical applications is usually refined by solvent extraction: seedlac is dissolved in ethanol. The obtained solution is filtered and decolorized by addition of activated carbon. After a second filtration step, the solvent is evaporated and the resulting film breaks into flakes. Solvent extraction

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is a gentle process that does not affect the molecular structure. It allows the production of shellac with narrow specifications[1].

Shellac with a molecular weight of about 1000 Da mainly consists of polyesters of aleuritic acid and shellolic acid as well as a small amount of free aliphatic acids[2,3]. The composition varies depending on the insect species as well as the host tree from which the raw material is gained.

Shellac is widely used in the dye industry as a component in lacquers and varnishes[4] because of its good film-forming properties and water resistance. It is nontoxic, physiologically harmless[5], and is therefore generally recognized as safe by the FDA allowing its use as an additive in food products where shellac already plays a major role as coating material for citrus fruits[6] or confectionaries. The generally-recognized-as-safe status opens the field also for modified release applications with the regulatory status of a food product or nutritional supplement such as vitamin formulations. In addition, its natural origin from renewable resources may be of certain ideological interest at least for marketing purposes.

In addition to the excellent film-forming properties of the material, shellac films provide a high gloss and a low permeability for water and gases[7]. This low permeability allows the use of shellac as protective coating or in taste-masking applications[8–10].

Because of its acidic character, shellac is often used as an enteric coating[11,12]. Other applications are sustained release[13], microencapsulation[14], and colon targeting[15].

Despite all these advantages, the use of shellac as a pharmaceutical excipient has declined. As the properties of this natural material are strongly dependent on the raw material used, a consistent shellac quality requires a careful selection of the seedlac. Otherwise, there is a risk of batch-to-batch variations. In addition, shellac coatings prepared from alcoholic solutions as well as shellac raw material consists of shellac in its acid form which undergoes aging. This aging process is a result of polymerization and is manifesting itself in hardening of the material[16,17]. Aging of shellac is accompanied by a loss of gastric resistance and a decrease of solubility in the intestinal fluids. This is a major disadvantage in comparison to synthetic and partially synthetic polymers such as polymethacrylates and cellulose derivates.

Since the introduction of aqueous solutions, shellac could regain importance. Although shellac is water insoluble, aqueous solutions can be obtained by addition of volatile alkali such as ammonium carbonate. These solutions are translucent and show a low viscosity even at higher shellac concentrations allowing for a quick mass increase of the coating film during the coating process. In addition to the technical advantages of aqueous compared to organic coating solutions, shellac films prepared from aqueous ammoniacal solutions show a good long-term stability[12]. It has been reported that chemical stability may be even further improved by salt formation with other counter ions such as 2-amino-2-methyl-1-propanol[18].

Many publications are available on shellac and its use in pharmaceutical applications. However, in most publications the shellac-containing drug formulations are discussed without further specification of the type and origin of the shellac used. Because of its natural character and different origin, the physicochemical properties and thus drug release may vary. Nevertheless, a comparison of different shellac types and their effect on drug formulations has not yet been done.

The pharmacopoeias classify different shellac types only by the way of refining. A chemical characterization is done only by the determination of the acid value (AV). As shown in previous studies, the physicochemical properties of shellac may differ widely even if the pharmacopoeias' specification for the AV is met[17]. This requirement may be fulfilled even with aged shellac, which is completely unacceptable for pharmaceutical applications.

In this study, theophylline pellets were coated with different shellac types. The minimum coating level (CL) to achieve gastric resistance was determined. Drug release below and above the dissolution pH of shellac was investigated. The drug release characteristics were correlated with the physicochemical properties of the investigated shellac types.

Materials and methods

Materials

The following types of shellac were investigated: Marcoat™ 125 (Marcoat), 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, Stroever Schellack Bremen, Bremen, Germany); Kushmi shellac flakes of Indian origin, Pearl N811F (Pearl Gifu Shellac, Gifu, Japan), shellac flakes of Thai origin. All shellac types were refined by solvent extraction. The used theophylline pellets were immediate release matrix core pellets obtained by extrusion and spheronization containing 96.5% theophylline (donation from Temmler, Ireland). Ammonium bicarbonate, potassium dihydrogen phosphate, sodium chloride, sodium hydroxide, and hydrochloric acid were of analytical grade and purchased from Carl Roth, Karlsruhe, Germany.

Methods

Processing of shellac raw material

Ground shellac was prepared by milling shellac flakes in a Waring Blender fly cutter (Waring, Torrington, CT, USA) and sieving it through a sieve (400 μm mesh). Ground shellac was used for preparation of shellac solutions and for determination of the AV.

For determination of the pK_a values and the intrinsic dissolution (ID) rate, micronized shellac was used.

Approximately 10 g of ground shellac were micronized at 400 rpm for 3 minutes in a Fritsch Pulverisette 6 planetary mono mill (Fritsch, Idar-Oberstein, Germany) equipped with a 250 mL zirconium oxide grinding bowl prefilled with 30 zirconium oxide grinding balls (Ø 10 mm). The mean particle size (x_{50}) was 120 µm (x_{16} = 60 µm; x_{84} = 200 µm) determined from a 2 g sample with a HELOS laser diffraction spectrometer equipped with a RODOS dry dispersion system (all from Sympatec, Clausthal-Zellerfeld, Germany).

Acid value

The acid value (AV) was determined by an acid–base titration method adapted from the European Pharmacopoeia (Ph. Eur.). Briefly, 0.4 g of ground shellac was dissolved in a mixture of diethylether and ethanol (1:1) and titrated with 0.1 M potassium hydroxide solution. Because of the dark color of the shellac solutions, the endpoint was determined potentiometrically (Mettler Toledo DL70ES Titrator, Greifensee, Switzerland). The AV is expressed as milligrams of potassium hydroxide per gram of shellac. The mean of five measurements was determined.

Preparation of aqueous shellac 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 shellac films, the solutions were heated to 65°C to remove the excessive ammonium salt by evaporation of the resulting free ammonia and carbon dioxide. Evaporated water was replaced. This process was repeated until a constant pH was reached. The pH of the final solutions was between 7.4 and 7.8 (Mettler Toledo MP 225 pH-meter).

Coating of theophylline pellets

Before the coating experiments, the theophylline pellets were characterized with regard to their size and weight. The pellet diameter was determined using a Wild M3 microscope (Wild, Völkermarkt, Austria) equipped with a Zeiss AxioCam ICc and AxioVision software (Jena, Germany) by calculating the mean diameter of 500 pellets. The required shellac mass was calculated from the overall pellet surface and the desired CL for the respective batch.

The 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 removed from dust and coated with the aqueous shellac solutions in a Mini Glatt fluid bed coater (Glatt, Binzen, Germany) with Wurster insert (Ø 30 mm, 10 mm gap). The coating solutions were applied using a 0.5 mm two-way nozzle at a spraying rate of 0.4 g/min to achieve final CLs of 0.5, 1, and 2 mg/cm^2, respectively. Atomizing air pressure was adjusted to 0.6–1.1 bar according to the weight gain of the pellets and the inlet air temperature was set to 60°C at 14 m^3/h.

To avoid the effect of residual water, the pellets were stored in a desiccator over silica gel at least for 24 hours before further processing.

Calculation of the coating level

The average CL was determined as mass of shellac (m_{shellac}) applied to the pellet surface (A):

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

Before coating, the theophylline pellets were characterized with regard to their average mass ($m_{\text{uncoated pellet}}$) and radius ($r$). The theophylline content ($c_{\text{uncoated pellet}}$) was determined spectrophotometrically at 275 nm after dissolution of approximately 150 mg of the uncoated pellets in 0.1 M NaOH (Lambda 25, Perkin Elmer, Waltham, MA, USA).

After coating, a sample of approximately 150 mg shellac-coated pellets (m_{sample}) was withdrawn and dissolved in 0.1 M NaOH using an ultrasonic bath. The theophylline content of this sample ($m_{\text{theo sample}}$) was determined as described above.

The mass of shellac in the sample may be calculated from the difference between the mass of the sample and the mass of the cores (m_{cores}) in the sample:

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

where m_{shellac} is the mass of shellac in the sample (mg); m_{cores} the mass of pellet cores in the sample (mg); and m_{sample} the mass of the sample (mg).

Because of the applied coating film, the relative mass of theophylline in the sample (=coated pellets) is decreased compared to the uncoated pellets. The mass of pellet cores in the sample can be calculated as follows:

$$m_{\text{cores}} = 100 \frac{m_{\text{theo sample}}}{c_{\text{uncoated pellets}}}, \tag{3}$$

where $m_{\text{theo sample}}$ is theophylline mass in the sample (mg) and $c_{\text{uncoated pellets}}$ the theophylline content of uncoated pellets (%).

The surface area of the sample was calculated from the average radius and the number of pellets (n) which is determined from the mass of one uncoated pellet and the mass of cores in the sample:

$$n = \frac{m_{\text{cores}}}{m_{\text{uncoated pellet}}}, \tag{4}$$

where n is the number of pellets in the sample and $m_{\text{uncoated pellet}}$ the average mass of one uncoated pellet (mg):

$$A = 4\pi r^2 n, \quad (5)$$

where r is the average radius of uncoated pellets (in cm).

A CL of 1 mg/cm^2 corresponds to a weight gain of 8% (w/w) corresponding to a coating thickness of 10 μm determined microscopically from the average diameter increase of at least 500 pellets.

Dissolution experiments

Dissolution tests were performed according to the Ph. Eur. with approximately 150 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 buffers (0.05 M) below (pH 6.8) and above (pH 7.4) 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.

pK_a *values*

For determination of the pK_a values acid–base backtitrations were performed based on a method adapted from Parke and Davis[19]. Briefly, 0.2 g of micronized shellac, accurately weighed, was dissolved in 8.0 mL of 0.1 M NaOH solution. Longer dissolution time periods led to hydrolysis of shellac by this alkali treatment, manifesting itself in a darkening of the solutions. It is described in the literature that the effect of hydrolysis on the pK_a values is nonsignificant[20]. Our experiments confirmed this assumption. However, the samples were titrated immediately after complete dissolution and dissolution time periods were kept the same for all samples. Titrations were done in 50 μL steps with 0.1 M hydrochloric acid and the titration profile was recorded potentiometrically. A blank curve was recorded by titration of 8.0 mL of 0.1 M NaOH solution without shellac. The shellac titration curves were subtracted from the blank curve and standardized referring to the sample weight. The pK_a was determined from the pH value at a titration grade of 0.5.

Intrinsic dissolution rate

As the coating with shellac was applied from aqueous ammoniacal solutions, the intrinsic dissolution (ID) rate was also determined with the salt form for a better comparability. Therefore, 20 mL of shellac solution was poured onto Teflon plates and dried at 40°C for 4–5 hours. The resulting film was carefully peeled off the plate and stored in a desiccator over silica gel at room temperature for at least 24 hours. Afterward, the film was micronized as was done with the samples for the pK_a value determination.

Eighty milligrams of micronized sample was weighed into the die (9 mm diameter) of a paddle over disk ID apparatus and compressed for 2 minutes at a compression force of 200 kg. Dissolution is performed in ID vessels at 37°C and 100 rpm in 1000 mL phosphate buffer (pH 7.4). The dissolution profiles were recorded spectrophotometrically at 223 nm in triplicate using 1 cm flow through Quartz cells. The ID rate was determined from the slope of the dissolution profile and expressed as milligrams shellac dissolved per square centimeter and minute.

Results and discussion

Acid value

As described earlier, the solvent extraction process provides shellac raw material in its acid form, which is less stable and subject to aging. Except for Marcoat, which is already an ammoniacal aqueous solution, the AV was determined and compared to the manufacturer's certificate of analysis to confirm the shellac quality (Table 1). For SSB 55 and Pearl shellac flakes, the AV complied with the certificate of analysis. Thus, these raw materials were suitable for further processing.

Preparation of aqueous shellac solutions

Shellac is generally classified by the Lovibond color index, which is determined from a 20% ethanolic solution of the material[21]. However, the color difference of the investigated shellac types was also apparent with the

Table 1. Overview of the physicochemical properties and the drug release performance of the investigated shellac types; means ± SD; $n = 3$.

Shellac type			Marcoat	SSB 55	Pearl
Acid value: measured/certificate of analysis			—	73.1 ± 0.2/73	71.5 ± 0.1/71.2
pK_a			—	5.89 ± 0.06	6.02 ± 0.04
ID rate [mg/(cm^2·min)]			0.088 ± 0.008	0.151 ± 0.006	0.335 ± 0.004
Gastric resistance: Yes/no (dependent on the CL)	CL	0.5 mg/cm^2	Yes	No	Yes
		1 mg/cm^2	Yes	No	Yes
		2 mg/cm^2	Yes	Yes	Yes
Time for complete drug release at pH 7.4 (dependent on the CL)		0.5 mg/cm^2	20 minutes	10 minutes	10 minutes
		1 mg/cm^2	30 minutes	20 minutes	10 minutes
		2 mg/cm^2	45 minutes	35 minutes	15 minutes

prepared aqueous solutions. The bright yellow color of the SSB 55 solution was much lighter than the darker Marcoat or the deep orange Pearl solution. This difference in the color may be a result of the different origins of the investigated materials but most likely because of the discoloration treatment with activated carbon during the refining process.

Coating experiments

Process times varied between 45 minutes for the 0.5 mg/cm^2 batches and 200 minutes for the 2 mg/cm^2 batches. Coating yields were at least 95% and above for a CL of 0.5 mg/cm^2 and decreased with increasing CL to about 80%. This decrease may be explained by the initially good adhesion of the coating solution to the pellet core. Later, once a continuous film is formed on the pellet surface, the adhesion of droplets to this smooth surface is reduced.

Dissolution experiments

The acidic character of shellac allows its use as an enteric coating. In Figure 1 drug release profiles at pH 1.2 are shown. As expected, drug release was reduced with increasing CL with all shellac types. The minimum CL to achieve gastric resistance (<10% drug release within 2 hours) was low compared to other coating polymers used for enteric coating. With Marcoat and Pearl, gastric resistance could be achieved even at a CL of only 0.5 mg/cm^2. Pellets with a CL of 1 mg/cm^2 of SSB 55 exceeded the drug release limit only after 110 minutes.

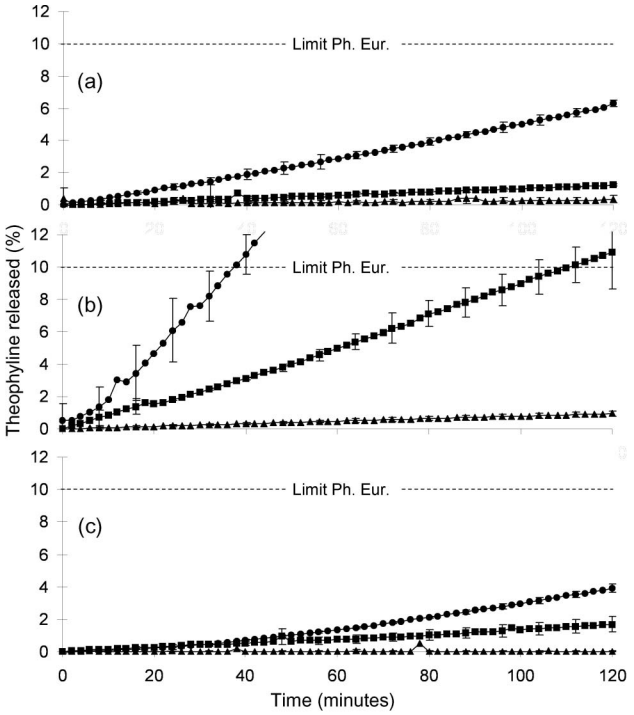

Figure 1. Influence of the coating level on gastric resistance; means ± SD (n = 3). Coating level: ● 0.5 mg/cm^2; ■ 1 mg/cm^2; ▲ 2 mg/cm^2. (a) Marcoat; (b) SSB 55; (c) Pearl.

At a CL of 2 mg/cm^2, the amount of drug released within 2 hours was negligible with all shellac types.

Shellac has a comparatively high dissolution pH of about 7.3[18]. This is disadvantageous if a fast release in the proximal small intestine is desired. Various attempts have been made to improve drug release from shellac-coated formulations at lower pH. One approach was the addition of pore formers or swelling agents such as hydrophilic polymers, water-soluble plasticizers, or aliphatic acids to the coating solution[22]. Another approach was the modification of shellac itself by partial hydrolysis[20]. Although the dissolution pH could be reduced, hydrolyzed shellac was found to be less stable than the unmodified material[23].

Because of the high dissolution pH, drug release was measured not only at the standard pH of 6.8 for testing of enteric coated dosage forms (Ph. Eur.) but also at pH 7.4, which is above the dissolution pH of the material.

The results of the dissolution tests at pH 7.4 are shown in Figure 2. With all formulations complete, drug release was observed within 40 minutes. Fastest drug release was monitored with Pearl-coated pellets. Interestingly, drug release from pellets coated with this shellac type was almost independent of the CL. All formulations coated with the Thai shellac released the complete dose within a time period of 10–15 minutes.

In contrast, drug release from pellets coated with Marcoat and SSB 55 was much slower and clearly dependent on the CL.

Formulations with the lowest CL of SSB 55 showed drug release as fast as pellets coated with the highest CL of Pearl. A higher CL further delayed drug release. Formulations with 1 mg/cm^2 of SSB 55 released the complete dose within 20 minutes, those with 2 mg/cm^2 within 35 minutes.

For formulations coated with Marcoat, drug release was even slower and the dependence on the CL was more pronounced. However, all formulations released the complete dose within 45 minutes.

At pH 6.8, pronounced differences in the drug release profiles between the investigated shellac types were apparent (Figure 3). This pH is below the dissolution pH of shellac. Therefore, drug release was not the result of shellac dissolution and subsequent liberation of the drug but of swelling of the shellac coating film followed by drug diffusion through the coating layer. As film integrity was proven in the dissolution studies at pH 1.2, the drug flux through the coating film may be described by Fick's first law of diffusion[24]:

$$J = \frac{P_m}{d}(c_p - c_d), \tag{6}$$

where J is the flux [g/(m^2 s)], P_m the permeability coefficient [m^2/s], d the film thickness [m], c_p the concentration of dissolved drug in the pellet [g/m^3], c_d the concentration in the dissolution medium [g/m^3].

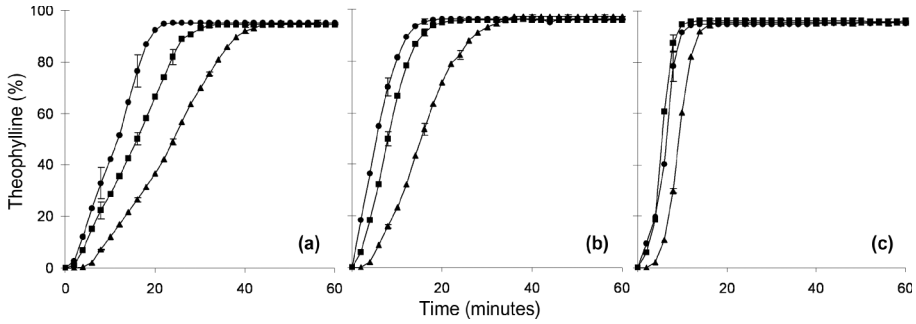

Figure 2. Influence of the coating level on drug release at pH 7.4; means ± SD (n = 3). Coating level: ● 0.5 mg/cm^2; ■1 mg/cm^2; ▲ 2 mg/cm^2. (a) Marcoat; (b) SSB 55; (c) Pearl.

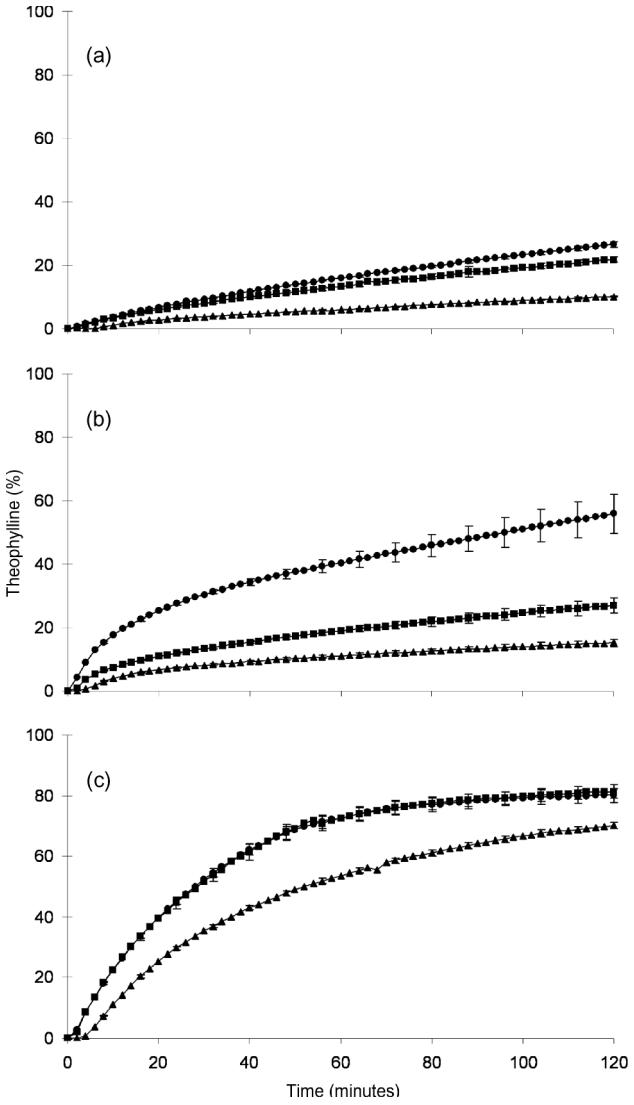

Figure 3. Influence of the coating level on drug release at pH 6.8; means ± SD (n = 3). Coating level: ● 0.5 mg/cm^2; ■ 1 mg/cm^2; ▲ 2 mg/cm^2. (a) Marcoat; (b) SSB 55; (c) Pearl.

After an initial lag phase where the coating layer swells, drug release can be described by a zero-order kinetic as long as undissolved drug is present in the pellet and sink conditions are maintained in the dissolution medium. This release kinetic was observed with pellets coated with Marcoat and SSB 55. After an initial lag phase, all drug release profiles showed an almost linear shape. The flux can be determined from the slope of the drug release profiles divided by the total pellet surface area of the sample. As the flux is inversely proportional to the coating thickness the drug release rate decreases with increasing CL.

Drug release from formulations with SSB 55 is fast in the initial phase. However, the slope of the linear part of the dissolution profile does not differ significantly from that of Marcoat at the same CL. This indicates that the permeability and thus the swelling characteristic of the coating layer are almost similar with both shellac types.

In contrast, drug release from Pearl-coated pellets differed significantly from pellets coated with the other shellac types. A linear shape of the drug release profile could not be observed with any of these formulations. In addition, the amount of released drug within the 2-hour test period was about twice that of the formulations with the other shellac types. For this shellac type, drug release profiles of pellets with a CL of 0.5 and 1 mg/cm^2 were superimposed, whereas with a CL of 2 mg/cm^2, drug release from the formulation was found to be marginally slower. It is hypothesized that swelling of the Pearl coating layer is much more pronounced than that of the coating layers of the other shellac types resulting in a reduced barrier function especially with the lower CLs. This leads to a higher permeability and thus increased drug release. In contrast, the thicker coating layer at a CL of 2 mg/cm^2 represents a stronger diffusion barrier.

However, pellets of all formulations remained intact during dissolution testing at pH 6.8, confirming drug diffusion through the coating layer as release mechanism.

Even though the high dissolution pH of shellac is too high for the application as an enteric coating, it allows for an application in sustained release or colon targeting formulations. The coating layer remains intact during the passage of the upper GI tract. Drug release is prolonged and results from diffusion through the coating film. Once the drug formulation reaches the distal colon, the higher luminal pH[25] causes dissolution of the coating and thus a fast release of the drug.

Correlation of the dissolution profiles with the physicochemical properties

The pK_a values determined in this study differ from those described in the literature. pK_a values found in publications from Thailand are about one unit higher[20,26]. A possible explanation for this discrepancy is the different refining method of the investigated shellac types. Large differences in the pK_a between differently refined shellac types have recently been reported[27]. The pK_a values determined in that study with shellac types refined by solvent extraction correspond to those presented in this study.

In Table 1, the physicochemical properties of the investigated shellac types are listed together with the data from drug dissolution studies. Interestingly, the pK_a value seems to be an unsuitable parameter for the prediction of the drug release profile. For instance, SSB 55 showed the lowest pK_a value implying a higher degree of dissociation and thus a faster drug release than formulations coated with Pearl with its higher pK_a. However, this theory could not be confirmed. The ID rate seems to be a more suitable indicator for the prediction of drug release characteristics from shellac-coated dosage forms. From pellets coated with Marcoat, which showed the lowest ID rate, drug release was slowest. Accordingly, with pellets coated with Pearl, which showed the highest ID rate, the fastest drug release at pH 7.4 and 6.8 was observed. This high ID rate also explains the independency of drug release from the CL of formulations coated with Pearl shellac at pH 7.4. The shellac coating dissolved rapidly resulting in a very fast drug release and thus only minor differences between the different CLs. In comparison to Pearl, the ID rate of the other shellac types was much lower. Hence, dissolution of the coating layer was much slower and the drug release profiles were more dependent on the CL.

Conclusion

From the data presented in this study, it may be concluded that coating with shellac allows a reduction of the process time for the production of enteric-coated dosage forms as gastric resistance can be achieved at comparatively low CLs. At pH 6.8, drug release occurred by swelling and drug diffusion through the coating layer offering potential for the application in sustained release or colon targeting formulations rather than enteric coating formulations.

It has to be considered that different shellac types may differ significantly in their drug release profiles. For the prediction of drug release from shellac-coated pellets, the ID rate of the material turned out to be a more suitable indicator than the pK_a value.

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Declaration of interest

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

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