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RESEARCH PAPER

Pharmaceutical Applications of Shellac: Moisture-Protective and Taste-Masking Coatings and Extended-Release Matrix Tablets

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ABSTRACT

Shellac is a natural polymer, which is used as enteric coating material in pharmaceutical applications. The major objective of the present study was to investigate the potential of shellac for other purposes, namely to provide moisture-protective and taste-masking coatings as well as extended-release matrix tablets. The efficiency of shellac to achieve moisture protection and taste masking was compared with that of hydroxypropyl methylcellulose (HPMC), which is most frequently used for these purposes. Shellac-coated tablets showed lower water uptake rates than HPMC-coated systems at the same coating level. The stability of acetylsalicylic acid was higher in tablets coated with shellac compared with HPMC-coated systems, irrespective of the storage humidity. Therefore, lower shellac coating levels were required to achieve the same degree of drug protection. Shellac coatings effectively masked the unpleasant taste of acetaminophen tablets. Compared to HPMC, again lower coating levels were required to achieve similar effects. The resulting drug release in simulated gastric fluid was not significantly altered by the thin shellac coatings, which rapidly ruptured due to the swelling of the coated tablet core. In addition, shellac was found to be a suitable matrix former for extended-release tablets. The latter could be prepared by direct compression or via wet granulation using ethanolic or ammoniated aqueous shellac binder solutions. The resulting drug-release patterns could effectively be altered by varying different formulation and processing parameters.

Key Words: Shellac; Moisture protection; Taste-masking; Coating; Extended release; Matrix tablets.

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INTRODUCTION

Shellac is a natural polymer that is obtained from the resinous secretion of the insect Kerria lacca. Being water-insoluble at low pH and water-soluble at high pH, it is commonly used as an enteric coating material.[1–5] The major aims of the present study were to investigate the potential of shellac for other pharmaceutical applications.

Various drugs are sensitive to moisture and degrade during storage. To limit these reactions, the drug-containing dosage forms can be coated with protective polymeric films.[6–8] Commonly, hydroxypropyl methylcellulose (HPMC) is used for this purpose.[9,10] But also acrylic polymers, e.g., Eudragit L, show good moisture-protective properties.[11] Irrespective of the type of coating polymer, care has to be taken that the resulting drug-release kinetics within the stomach remains unaltered. Thus, the moisture-protective coatings must rapidly dissolve and/or rupture upon contact with the release medium.

Other drugs exhibit a bitter taste and/or unpleasant odor, leading to reduced patient compliance.[12,13] Again, HPMC is the most commonly used polymer for taste-masking purposes.[14,15] To improve taste-masking properties, ethyl cellulose can be added to HPMC-based coatings.[16] Also, thin acrylic polymer films can be applied.[16–18]

The use of enteric polymers, such as cellulose acetate phthalate, cellulose acetate trimellitate, hydroxypropyl methylcellulose phthalate, and acrylic polymers, as matrix formers in controlled drug-delivery systems has been studied by Palmieri et al.[19] Tablets were prepared by direct compression of drug and polymer powders or by tabletting microparticles based on these substances. In addition, blends of ibuprofen/starch granules and ibuprofen/Eudragit RS microsphere granules were compressed into tablets, and the drug-release behavior was studied in vitro.[20] Hilton and Deasy[21] investigated the use of hydroxypropyl methylcellulose acetate succinate (HPMCAS) as a matrix former in amoxicillin trihydrate-containing tablets. Compared to compacts of pure drug, the resulting release rate could significantly be reduced at low pH and increased at high pH. Although the release of tablets containing amoxicillin, HPMCAS, lactose, and lubricants (prepared via an ethanolic wet granulation process) showed promising sustained-release behavior in vitro, the relative bioavailability of the drug in vivo was found to be only 64.4% (studies in humans). Yamakita et al.[22] investigated the release of an antihistaminergic drug from HPMCAS-based matrix tablets in vitro and in vivo. In fasted dogs, the maintenance of approximately constant plasma drug levels could be achieved, whereas in fed dogs the absorption of the drug was markedly diminished, indicating the importance of food effects.

The major objectives of the present study were: (i) to evaluate the ability of shellac coatings to protect moisture-sensitive drugs from degradation during storage; (ii) to study the potential of shellac to provide taste masking; and (iii) to use shellac as a matrix-forming polymer in controlled drug-delivery systems.

MATERIALS AND METHODS

Materials

The following chemicals were obtained from commercial suppliers and used as received: acetaminophen, acetylsalicylic acid, theophylline, verapamil hydrochloride (Abbott, Ludwigshafen, Germany); hydroxypropyl methylcellulose (HPMC; Methocel E5, Colorcon, Orpington, UK); shellac (SSB 55 Pharma, dewaxed shellac, Stroever Schellack Bremen, Bremen, Germany); polyethylene glycol 4000 (PEG 4000; BASF, Ludwigshafen, Germany); triethyl citrate (TEC; Morflex, Greensboro, NC); colloidal silicone dioxide (Aerosil 200; Degussa, Hanau, Germany); cross-linked carboxymethylcellulose sodium (Ac-Di-Sol), microcrystalline cellulose (Avicel PH-200) (FMC c/o Lehmann and Voss, Hamburg, Germany); magnesium stearate (Caelo, Caesar and Loretz, Hilden, Germany); spray-dried lactose (Flowlac; Meggle, Wasserburg, Germany); talc (Merck, Darmstadt, Germany), and ethanol (96% v/v).

Tablet Preparation

Tablets were prepared by direct compression (core tablets for film coating and extended-release matrix tablets) or via wet granulation and subsequent compression (extended-release matrix tablets).

Direct compression: The core tablets for film coating consisted of drug, microcrystalline cellulose, and cross-linked carboxymethylcellulose (18:80:1, w:w:w). The respective powders were sieved (800 μm) and blended in a tumble mixer (Turbula, W.A. Bachhofen Maschinenfabrik, Basel,

Switzerland) for 15 min, followed by the addition of 1% (w/w) of a 1:1 magnesium stearate:colloidal silicone dioxide mixture and further blending for 5 min. In acetylsalicylic acid-containing tablets, magnesium stearate was replaced by the same amount of talc to avoid base-induced drug hydrolysis.[23,24] The extended-release matrix tablets consisted of drug, shellac, and lactose (different ratios were studied: 1:1:0, 1:2:0, 1:2:1, and 2:1:1, w:w:w). The respective powders were sieved (800 μm) and blended in a tumble mixer (Turbula) for 15 min, followed by the addition of 1% (w/w) of a 1:1 magnesium stearate:colloidal silicone dioxide mixture and further blending for 5 min. The tablets (core tablets for film coating: diameter: 8 mm, hardness: 100–150 N, weight: 300 mg; extended release matrix tablets: diameter: 10 mm, hardness: 40–80 N, weight: 350 mg) were prepared with a single-punch press (EK-0, Korsch, Berlin, Germany).

Wet granulation: Ethanolic or ammoniated aqueous shellac binder solutions were used (30% w/w). The granules consisted of drug, shellac, and lactose (8:1:2, w:w:w). The drug and lactose powders were sieved (800 μm) and mixed in a tumble mixer (Turbula) for 15 min. This powder blend was moistened with the respective shellac solution in a mortar and subsequently passed through a 1000-μm sieve. The obtained granules were dried for 24 h at 40°C and blended with shellac powder that had been milled in a ball mill (Retsch Schwingmühle, Type MM 2000, Retsch, Haan, Germany) (0%, 5.5%, or 16.8% w/w shellac, based on the total tablet mass), magnesium stearate (0.5% w/w, based on the total tablet mass), and Aerosil (0.5% w/w, based on the total tablet mass) for 5 min in a tumble mixer (Turbula). The tablets [diameter: 10 mm, hardness: 160–180 N (ethanolic solution) and 45–50 N (aqueous solution); weight: 350 mg] were prepared with a single-punch press (EK-0).

Tablet Coating

Tablets were coated in a pan coater (Glatt GC-300, Glatt, Binzen, Germany) using an ethanolic solution of shellac (10% w/v, based on total solution) and TEC (5% w/w, based on the polymer mass), or an aqueous solution of HPMC (7% w/w, based on total solution) and PEG 4000 (20% w/w, based on the polymer mass). Talc was added to the shellac solution as an antitacking agent (30% w/w, based on the polymer mass). The coating conditions were as follows: inlet air temperature: 20–25°C (shellac solution) and 60–65°C (HPMC solution); product temperature: 21–23°C (shellac solution) and 42–46°C (HPMC solution); pneumatic spraying pressure: 1.2 bar; spraying rate: 6–7 g/min; air flow rate: 130 m^3/h; pan rotation speed: 15 rpm. The indicated coating levels (% w/w) are based on the mass of the tablet cores.

Evaluation of the Taste-Masking Ability

The taste-masking ability was determined by healthy volunteers in a double-blind study ($n = 3$). Taste evaluation began immediately after administration and continued for up to 60 sec. The taste-masking period was defined as the difference between the administration time and the onset time of bitter taste.

Moisture-Uptake and Drug-Stability Studies

Acetylsalicylic acid-containing tablets were stored under controlled temperature and relative humidity in a desiccator containing a saturated aqueous NaCl solution (75% relative humidity) or distilled water (100% relative humidity), respectively. At predetermined time intervals, samples were withdrawn. The water uptake was measured gravimetrically ($n = 3$); the amounts of intact acetylsalicylic acid and of the degradation product salicylic acid were determined spectrophotometrically as follows: Ten tablets were ground in a mortar. One gram of the obtained powder was suspended in ethanol (which was adjusted to pH 1 with HCl, 37% w/w).[25] After stirring for 1 h, the suspension was centrifuged (3000 rpm, 15 min). The clear supernatant was filtrated and spectrophotometrically assayed at 277 nm (acetylsalicylic acid) and 305 nm (salicylic acid), respectively (UV-210PC, Shimadzu, Duisburg, Germany). The salicylic acid content of the tablets before storage (at time $t = 0$) was determined to be 1.2% (w/w).

In Vitro Release Studies

In vitro drug release was determined using the United States Pharmacopeia (USP) 25 rotating paddle method [900 mL 0.1 N HCl or phosphate buffer pH 7.4 (USP 25), 100 rpm, 37°C] (Vankel 700, Vankel Industries, Edison, NJ). At predetermined

time intervals, samples were withdrawn (3 mL, not replaced) and assayed spectrophotometrically at the following wavelengths: 244 nm (acetaminophen), 267 nm (acetylsalicylic acid), 270 nm (theophylline), and 278 nm (verapamil hydrochloride) in 0.1 N HCl; 271 nm (theophylline) and 278 nm (verapamil hydrochloride) in phosphate buffer pH 7.4, respectively (UV-210PC). Each experiment was conducted in triplicate.

RESULTS AND DISCUSSION

Moisture-Protective Polymer Coatings

The water uptake behavior of coated tablets exposed to different relative humidities can be used as a measure for the ability of a film coating to protect the dosage form against moisture. Figure 1 shows the effects of the type of coating polymer, relative humidity, and coating level on the resulting moisture uptake of coated tablets consisting of acetylsalicylic acid, microcrystalline cellulose, and cross-linked carboxymethylcellulose (18:80:1, w:w:w). Figures 1A and 1B illustrate shellac-coated tablets exposed to 75% and 100% relative humidity; Figs. 1C and 1D show HPMC-coated systems exposed to 75% and 100% relative humidity, respectively. The coating level was varied from 0% to 5.0% w/w for shellac and from 0% to 4.9% w/w for HPMC. Clearly, the moisture uptake curves leveled off within the observation period when the tablets were exposed to 75% relative humidity (irrespective of the type of coating polymer and coating level), whereas no plateau values were attained upon exposure to 100% relative humidity within 30 days. Uncoated tablets showed the highest water uptake rates in all cases. With increasing coating level the moisture uptake rate generally decreased. Interestingly, shellac-coated tablets showed significantly lower water uptake rates compared with the HPMC-coated systems at 100% relative humidity (Fig. 1B vs. 1D), whereas these differences were less pronounced at 75% relative humidity (Fig. 1A vs. 1C).

The effects of the coating level of shellac- and HPMC-coated tablets on the relative moisture uptake after 30-day storage at 75% and 100% relative humidity are shown in Figs. 2A and 2B, respectively. The moisture uptake decreased with increasing coating level due to the increasing thickness of the moisture barrier. At similar coating levels, the water uptake of shellac-coated tablets was lower than that of HPMC-coated systems. This might indicate that shellac has a higher potential for moisture protection than HPMC, especially at high relative humidities. However, caution has to be paid because the total amount of water within the coated tablets is not the crucial factor for drug degradation, but the amount of water that comes into contact with the drug and that is available for chemical reactions (''free'' or ''active'' water). Hydroxypropyl methylecellulose is known to have the ability to effectively and permanently bind water within film coatings. This ''trapped'' moisture is not available for drug degradation and, thus, does not affect drug stability.[26]

To evaluate the ability of a film coating to protect an incorporated drug against 'active' water, the chemical integrity of a moisture-sensitive drug can be monitored as a function of the exposure time to different relative humidities. Figures 3A and 3B show the effects of the type of coating polymer and coating level on the stability of the model drug acetylsalicylic acid within microcrystalline cellulose-based tablets exposed to 75% and 100% relative humidity, respectively. Acetylsalicylic acid is hydrolytically labile, being degraded into salicylic acid and acetic acid. The salicylic acid level after 30-day storage is plotted as a function of the coating level. The observed stability behavior did not completely correlate with the measured moisture uptake patterns (Fig. 2). For example, the water uptake was much higher at 100 % relative humidity compared with 75% relative humidity for all formulations (12.2–19.2% vs. 3.0–4.2%), whereas the differences in drug stability were not as pronounced (3.1–4.4% vs. 3.2–4.2% salicylic acid contents after 30-day storage) (Figs. 2 vs. 3). This was true even for the uncoated tablets. These phenomena might be attributable to the location and availability of the water within the respective formulations. As discussed above, only water that is not strongly bound to any excipient and that comes into contact with the acetylsalicylic acid in the tablet core can lead to hydrolytical drug degradation. For example, microcrystalline cellulose within the tablet core has the ability to swell and bind water.[27] However, the qualitative tendency, ''increasing water uptake leads to decreased drug stability,'' was observed in all cases. Interestingly, much lower shellac-coating levels were required to achieve similar moisture protection compared with HPMC (Fig. 3).

Moisture-protective polymer coatings should effectively protect the pharmaceutical dosage form against water during storage, but should rapidly

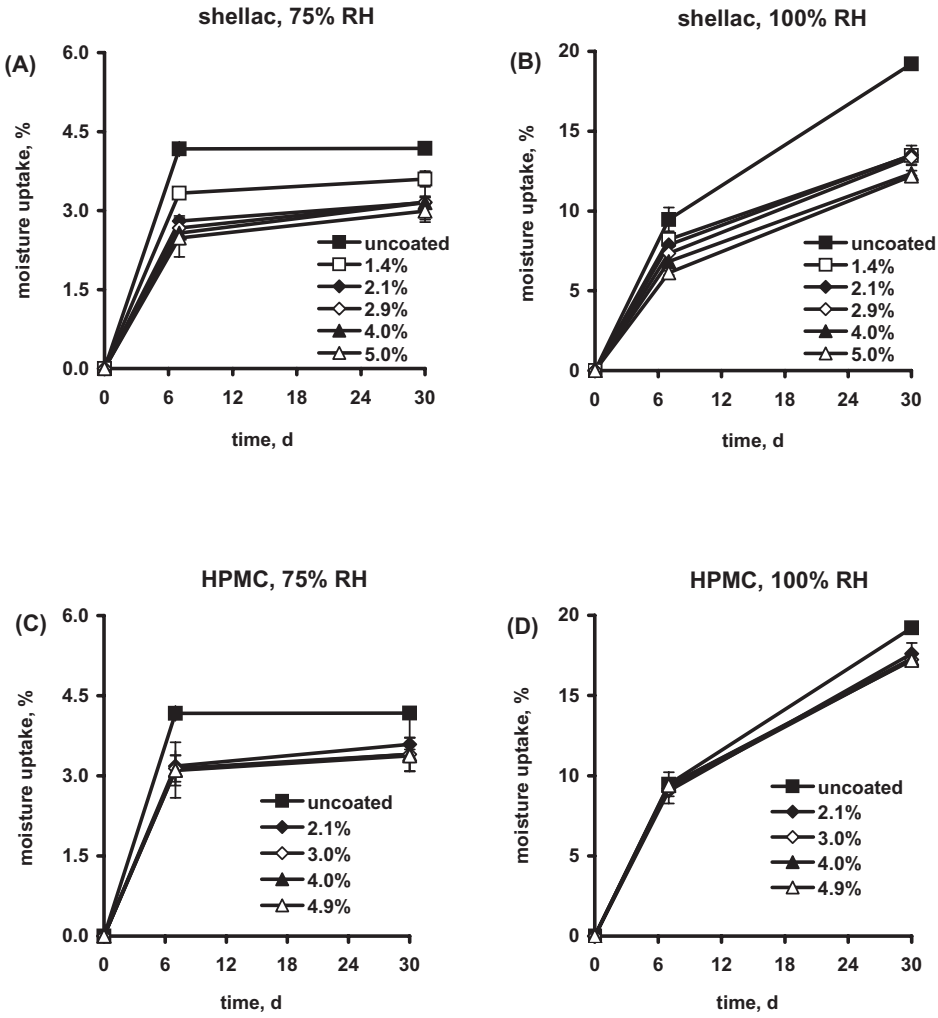

Figure 1. Moisture uptake of coated tablets containing acetylsalicylic acid: Effect of the type of coating polymer, relative humidity, and coating level: (A) shellac-based coatings, 75% relative humidity; (B) shellac-based coatings, 100% relative humidity; (C) HPMC-based coatings, 75% relative humidity; (D) HPMC-based coatings, 100% relative humidity.

rupture, disintegrate, or dissolve upon contact with gastric fluid to assure unaltered drug-release kinetics. Low molecular weight HPMC rapidly dissolves in water. Thus, drug release was not affected by the HPMC coatings (Fig. 4A). The release rate of acetylsalicylic acid in 0.1 N HCl from microcrystalline cellulose-based tablets coated with HPMC and its independence on the coating level (ranging from 0% to 4.9% w/w) are shown. In contrast, shellac being an enteric polymer is water-insoluble at low pH. To provide unaltered drug release within the stomach, sufficient amounts of disintegrants need to be incorporated within the tablet cores, causing the rapid rupture of the coatings upon contact with gastric fluid. Figure 4B shows the effect of the shellac-coating level on the in vitro release kinetics of acetylsalicylic acid from microcrystalline cellulose-based tablets (containing small amounts of carboxymethylcellulose) in 0.1 N HCl. Clearly, thin shellac coatings did not significantly slow down the resulting drug-release rates. However, higher coating levels led to sustained acetylsalicylic acid release from the tablets, indicating that the incorporated disintegrant was not able to provide rapid and complete rupture of the shellac coatings. Importantly, only low shellac coating levels (1–2% w/w) were sufficient to achieve effective moisture protection (Figs. 2 and 3). Thus, unaltered drug-release patterns can be combined with effective moisture protection at low shellac-coating levels.

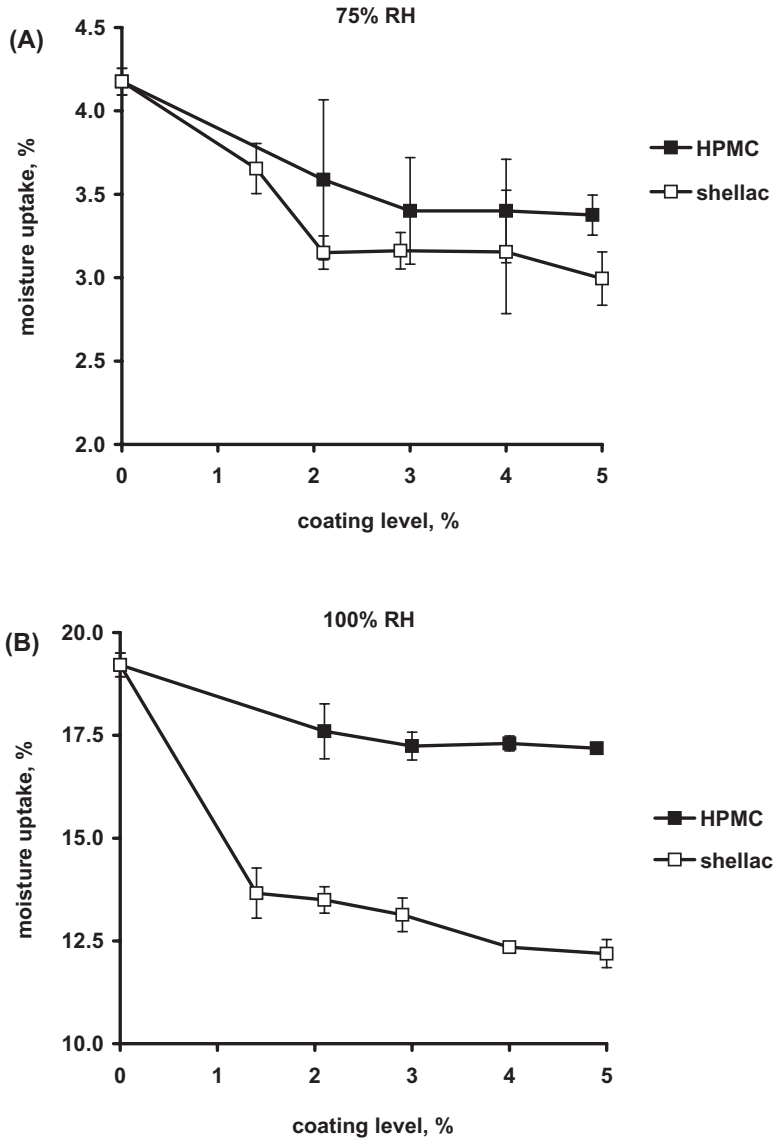

Figure 2. Effect of the type of coating polymer (indicated in the figure legends), relative humidity, and coating level on the moisture uptake of coated tablets containing acetylsalicylic acid after storage for 30 days at: (A) 75% relative humidity; (B) 100% relative humidity.

Taste-Masking Polymer Coatings

The ability of a polymeric coating to mask the unpleasant taste and/or odor of a drug depends on various factors, such as its permeability for the drug and water, mechanical stability, water-solubility, and coating thickness. Figure 5 shows the taste-masking periods that were observed in vivo with microcrystalline cellulose-based, acetaminophen-loaded tablets (healthy volunteers, $n = 3$). Shellac- and HPMC-based coatings were investigated, and the effect of the coating thickness was studied for each type of polymer. The taste-masking efficiency increased with increasing coating thickness in both cases. This can be attributed to the increasing diffusion pathways for water and drug with increasing coating levels. Once the dosage form comes into contact with the saliva in the oral cavity, water imbibes into the system (due to concentration gradients), leading to the swelling and/or dissolution of the coating polymer. Water reaching the tablet core dissolves the drug, which subsequently diffuses out of the dosage form (due

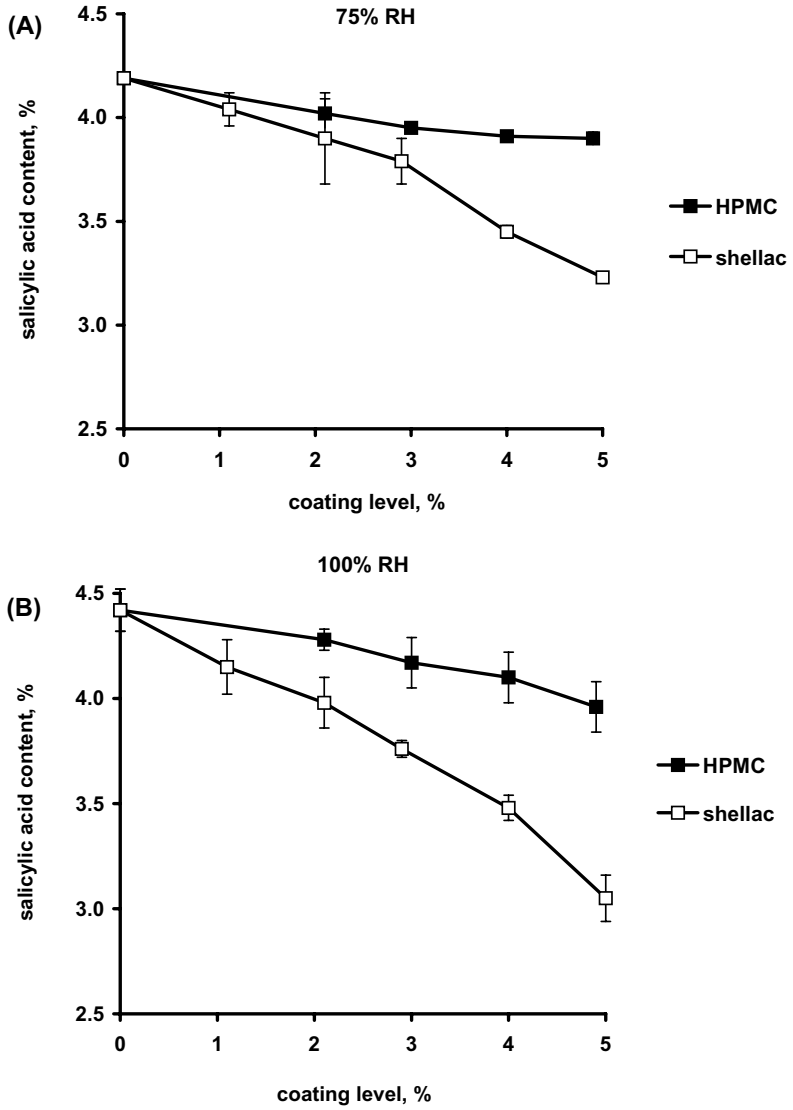

Figure 3. Stability of acetylsalicylic acid in coated tablets after storage for 30 days: Effect of the type of coating polymer (indicated in the figure legends), relative humidity, and coating level on the contents of the degradation product salicylic acid: (A) storage at 75% relative humidity; (B) storage at 100% relative humidity.

to concentration gradients) and causes the bitter taste.

Much lower coating levels were required with shellac-based coatings compared with HPMC-based systems to achieve the same taste-masking effect. For example, a period of 20 sec was provided at a coating level of 2% shellac and 5% HPMC, respectively. Also, the slopes of the taste-masking period vs. coating level curves were significantly different. With increasing relative coating level, the taste-masking ability of shellac increased more than that of HPMC. These observations can be explained by the different physicochemical properties of the two polymers. In contrast to shellac, HPMC rapidly dissolves within the saliva in the mouth cavity. Thus, the thickness of the protective barrier decreases in the case of HPMC and remains about constant in the case of shellac. Consequently, much lower shellac-coating levels (approximately 2%) were sufficient to provide effective taste-masking compared with HPMC.

Once the coated dosage forms reach the stomach, the taste-masking coatings should rapidly dissolve or rupture to assure unaltered drug-release kinetics. Figure 6 shows the in vitro drug release rates of acetaminophen from HPMC- and shellac-coated

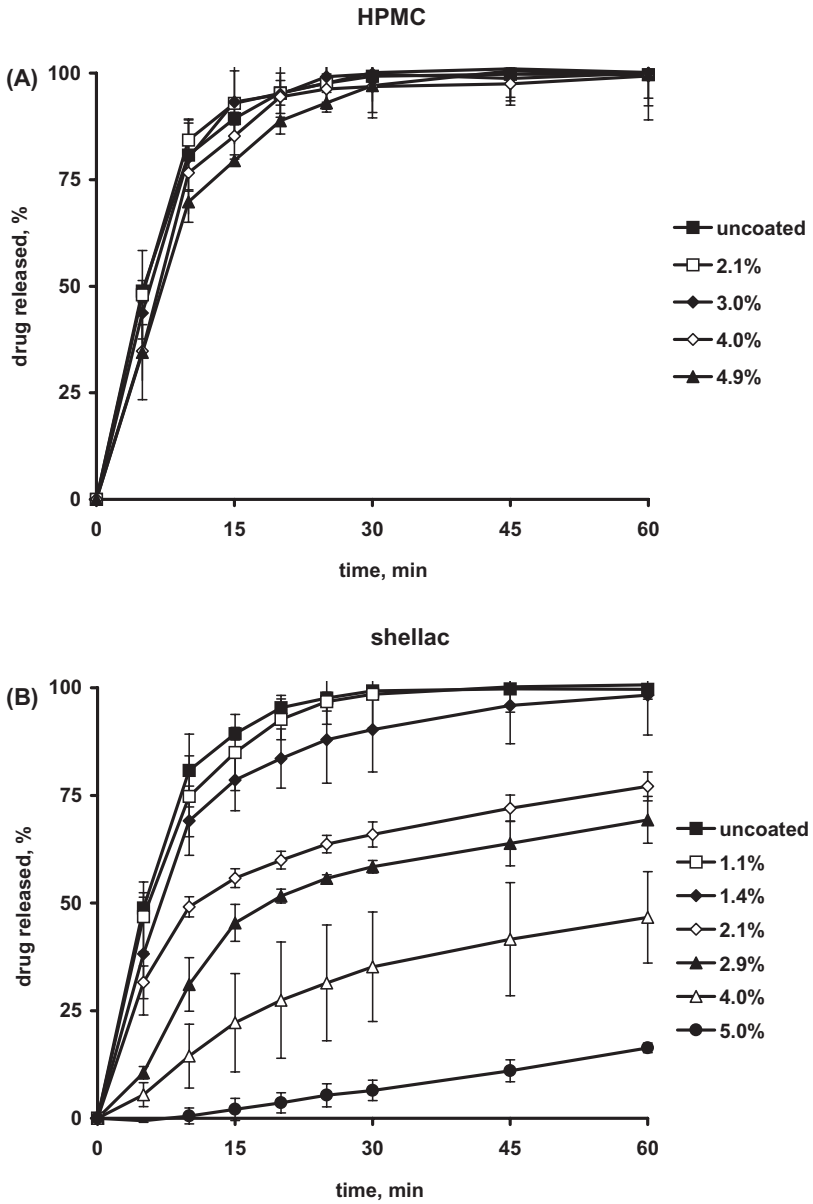

Figure 4. Effect of the type of coating polymer and coating level (indicated in the figure legends) on the in vitro drug release behavior of acetylsalicylic acid in 0.1 N HCl from tablets coated with: (A) HPMC; (B) shellac.

microcrystalline cellulose-based tablets in 0.1 N HCl as a function of the coating level. Drug release from uncoated tablets is plotted as a reference. Clearly, the HPMC coatings did not significantly alter the resulting acetaminophen-release patterns, irrespective of the coating level (1.3% to 5.8%). This is due to the rapid polymer dissolution upon contact with the release medium. In contrast, high shellac-coating levels lead to a significant reduction of the resulting drug-release rate. However, at low coating levels (up to 2%) acetaminophen release was still rather fast (more than 90% was released within the first 30 min). Thus, good taste-masking properties can be combined with unaltered drug-release kinetics at low shellac-coating levels.

Extended Release Matrix Tablets

The ability of shellac to act as a matrix former in controlled drug-delivery systems is illustrated in Fig. 7. The in vitro release rates of theophylline

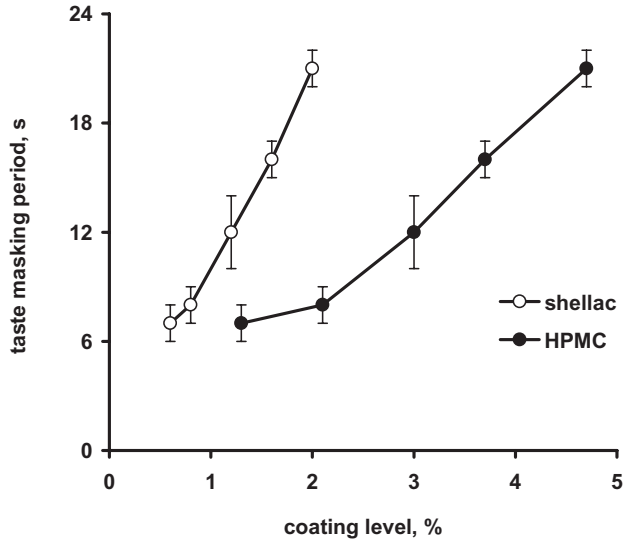

Figure 5. Effect of the type of coating polymer (indicated in the figure legends) and coating level on the taste-masking period observed with acetaminophen-containing tablets (healthy volunteers, $n = 3$).

in 0.1 N HCl (Fig. 7A) and in 0.1 N HCl/phosphate buffer pH 7.4 (medium change after 2 h) (Fig. 7B) from tablets prepared by direct compression are illustrated. Four different tablet compositions were investigated: two binary drug:shellac and two tertiary drug:shellac:lactose mixtures. The relative masses of the components were varied as follows: drug:shellac 1:1 and 1:2, drug:shellac:lactose 2:1:1 and 1:2:1. The resulting release rates were controlled in all cases, independent of the type of release medium. With increasing shellac content the resulting release rate decreased in the case of the binary blends (1:2 vs. 1:1) as well as in the case of the tertiary mixtures (1:2:1 vs. 2:1:1). This indicates the release rate controlling role of the matrix former shellac. In contrast, the addition of lactose accelerated drug release (1:2:1 vs. 1:2 blends), probably because lactose acts as a pore former, leading to increased tablet porosities and, thus, increased apparent drug diffusion coefficients, and because the relative shellac content consequently decreased (from 67% to 50% w/w).

Interestingly, the release rate of theophylline from the extended-release matrix tablets did not significantly increase after medium change (Fig. 7B: 0.1 N HCl was replaced by phosphate buffer pH 7.4 after 2 h; vs. Fig. 7A). This indicates that the dissolution of shellac and its leaching from the tablets at high pH was effectively hindered under these conditions (shellac significantly swelled upon contact with phosphate buffer pH 7.4, visual observation). The lower solubility of theophylline in phosphate buffer pH 7.4 (12 mg/mL) compared with 0.1 N HCl (15 mg/mL) at 37°C[28] might also contribute to this effect, leading to reduced drug concentration gradients, the driving forces for diffusion.

In both media, the limited solubility of the drug probably played a major role for the overall control of drug release. When the poorly soluble theophylline was replaced by verapamil HCl (being highly soluble in 0.1 N HCl: >150 mg/mL),[29] drug release from matrix tablets prepared by direct compression (drug:-shellac 1:1) drastically increased (Figs. 7 vs. 8). In contrast to the theophylline-loaded tablets, verapamil HCl-containing systems rapidly disintegrated upon contact with the release medium (visual observation). Thus, under these conditions shellac was not able to control the release of the drug.

To overcome this restriction and to be able to use shellac as a matrix former also for highly water-soluble drugs, the tablet structure was altered. Drug:shellac:lactose granules (8:1:2) were prepared by wet granulation using ethanolic shellac binder solutions. The granules were subsequently compressed into tablets with or without adding further shellac powder. The effects of the preparation method (direct compression vs. wet granulation) and tablet composition (indicated in the figure legends) on the resulting drug-release rate of verapamil HCl are shown in Fig. 8: (A) in 0.1 N HCl; and (B) in 0.1 N HCl/phosphate buffer pH 7.4 (medium change after 2 h), respectively. Clearly, the wet granulation step led to a significant decrease in

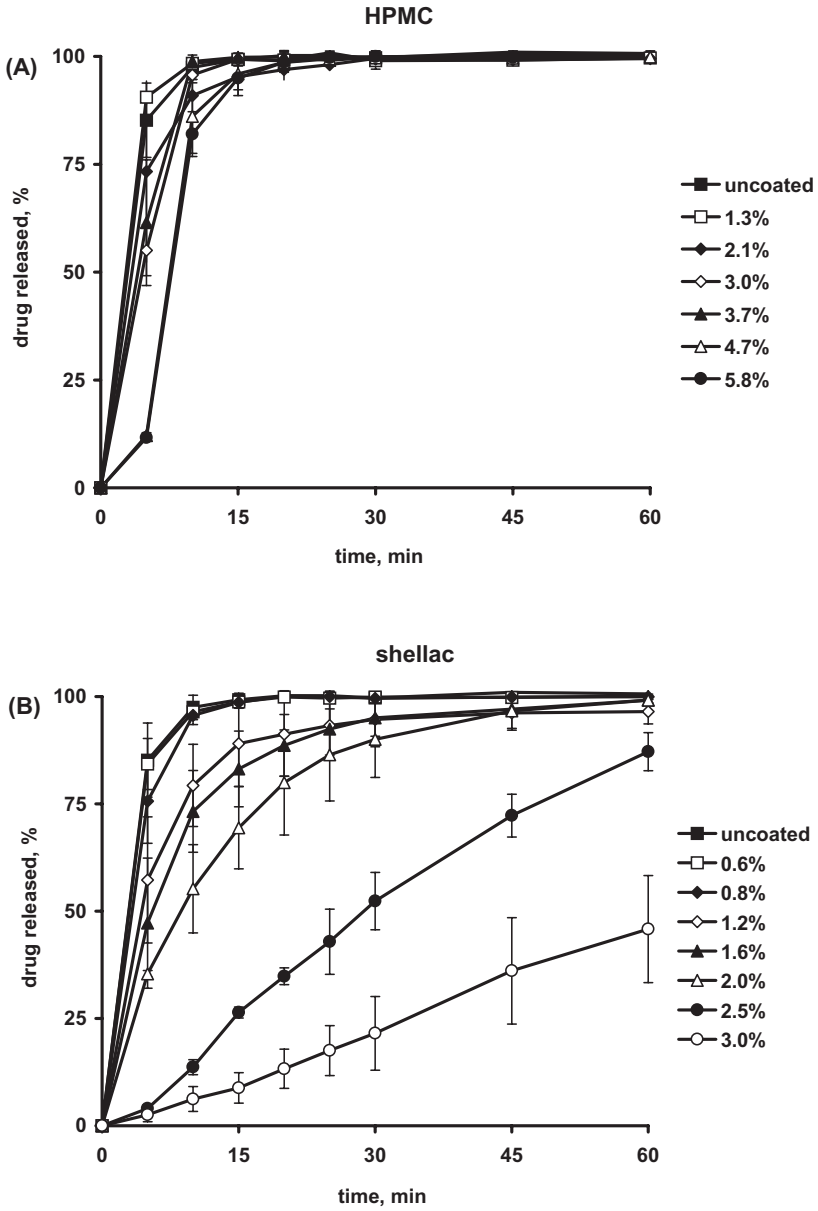

Figure 6. In vitro release of acetaminophen from coated tablets in 0.1 N HCl: Effect of the type of coating polymer and coating level (indicated in the figure legends): (A) HPMC-based coatings; (B) shellac-based coatings.

the resulting drug-release rate (even though the relative amount of shellac in the tablets decreased). This can be explained by the different localization of shellac within the tablets. In systems prepared by direct compression, most of the drug particles have direct acccess to the release medium, resulting in fast drug release. In contrast, the drug particles are (at least partially) covered by shellac films within tablets prepared via wet granulation. This leads to a significant reduction in the portion of the drug that has direct access to the release medium and, thus, to decreased drug-release rates.

Furthermore, the effect of adding different amounts of shellac powder (5.5% and 16.8% w/w, referred to the total tablet mass) to the drug:shellac :lactose granules (8:1:2) prior to compression on the resulting drug-release rate was studied (Fig. 8). As can be seen, the addition of 5.5% shellac did not significantly alter the verapamil HCl release patterns, whereas drug release was slowed down with 16.8%

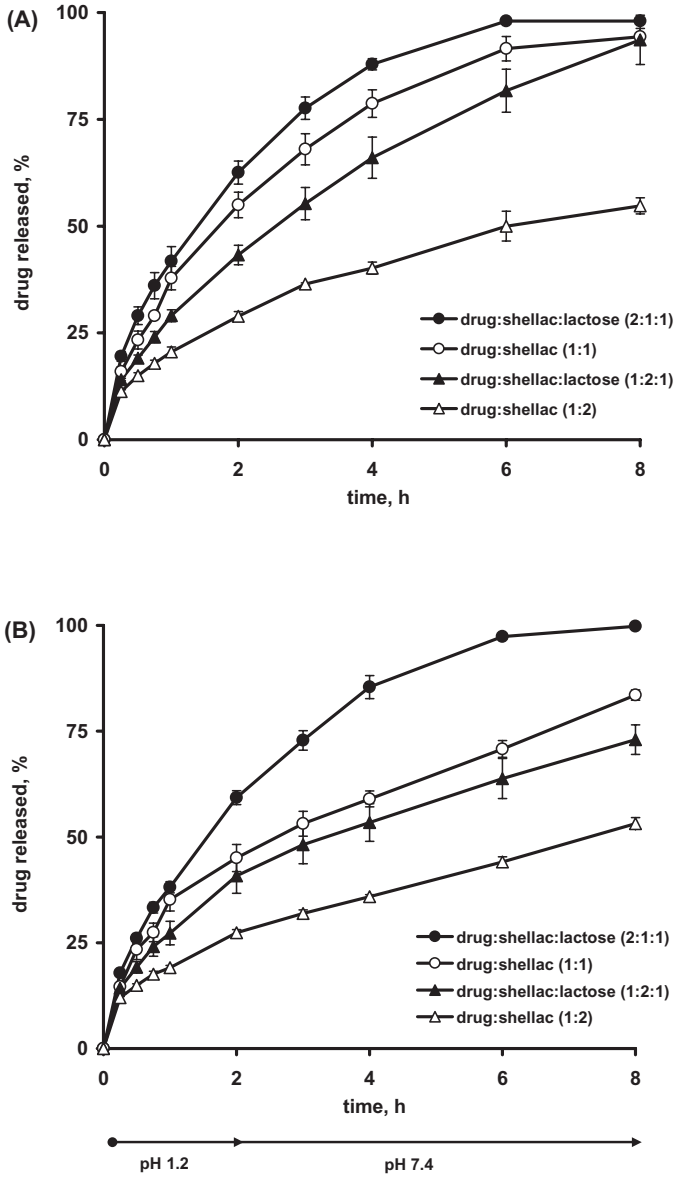

Figure 7. Effect of the tablet composition (indicated in the figure legends) on the in vitro release of theophylline in: (A) 0.1 N HCl; (B) 0.1 N HCl and phosphate buffer pH 7.4 (medium change after 2 h), from shellac-based matrix tablets prepared by direct compression.

additional shellac powder. This further reduction in the release rate can be attributed to the increased hindrance of drug and water diffusion within the tablets upon contact with the release medium due to the increased shellac content. However, this effect became only significant at higher additional shellac amounts. Similar to the investigated theophylline-containing tablets, the medium change from 0.1 N HCl to phosphate buffer pH 7.4 did not accelerate drug release. Thus, also in the tablets prepared via wet granulation, the dissolution and leaching of the enteric polymer from the systems at high pH was significantly hindered.

Instead of ethanolic also ammoniated aqueous shellac binder solutions can be used for the preparation of the drug:shellac:lactose granules (8:1:2). The resulting verapamil HCl release kinetics from tablets prepared by compression of these granules with or without adding further shellac powder is illustrated in Fig. 9 (with medium change after 2 h: 0.1 N HCl

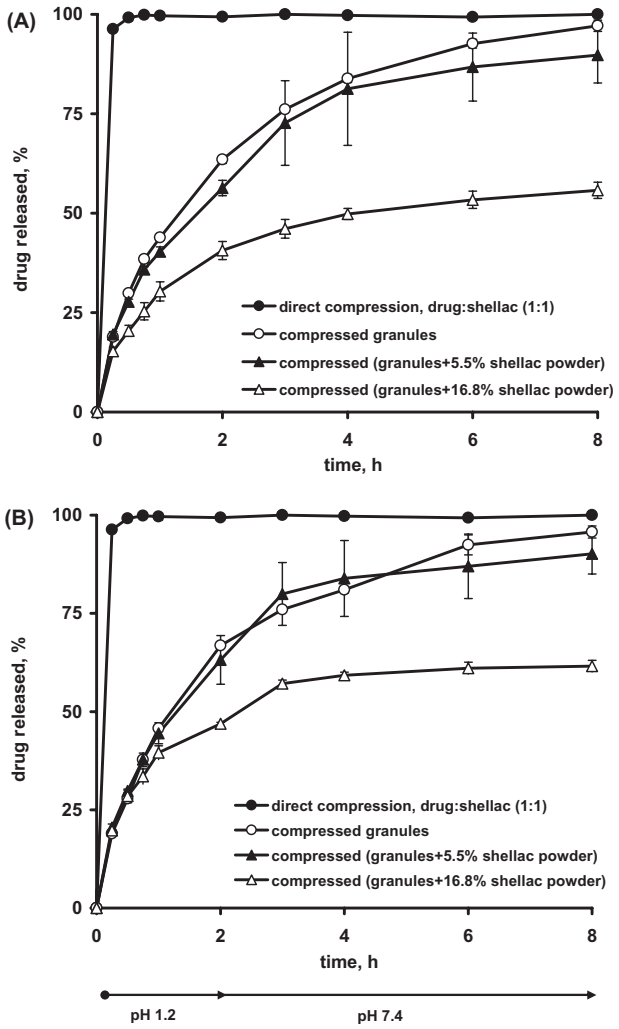

Figure 8. Effect of the preparation method and tablet composition on the in vitro release of verapamil HCl from matrix tablets in: (A) 0.1 N HCl; (B) 0.1 N HCl and phosphate buffer pH 7.4 (medium change after 2 h) (preparation method and tablet composition indicated in the figure legends). Ethanolic shellac binder solutions were used for wet granulation. The granules consisted of verapamil HCl, shellac, and lactose (8:1:2).

was replaced by phosphate buffer pH 7.4). For reasons of comparison, also drug release from tablets prepared by direct compression of verapamil HCl:shellac 1:1 mixtures is illustrated. Interestingly, drug release from tablets prepared via wet granulation using ammoniated aqueous shellac binder solutions was much faster than from tablets prepared via wet granulation using ethanolic shellac binder solutions (Figs. 8B vs. 9). This can be explained by the formation of ammonium salts of shellac when using aqueous binder solutions. These salts are more water-soluble than the respective free acids.[30–32] The higher water-solubility leads to a higher dissolution and leaching rate of shellac out of the tablets and, thus, less hindrance for water and drug diffusion, resulting in higher drug-release rates.

CONCLUSIONS

In addition to its enteric applications, shellac has a high potential as a coating material for moisture protection and taste masking. In contrast to commonly used cellulose derivatives, much lower coating levels are required to achieve similar effects while keeping drug release unaltered. Furthermore, shellac can be used as a matrix former in extended-release tablets. A large spectrum of drug-

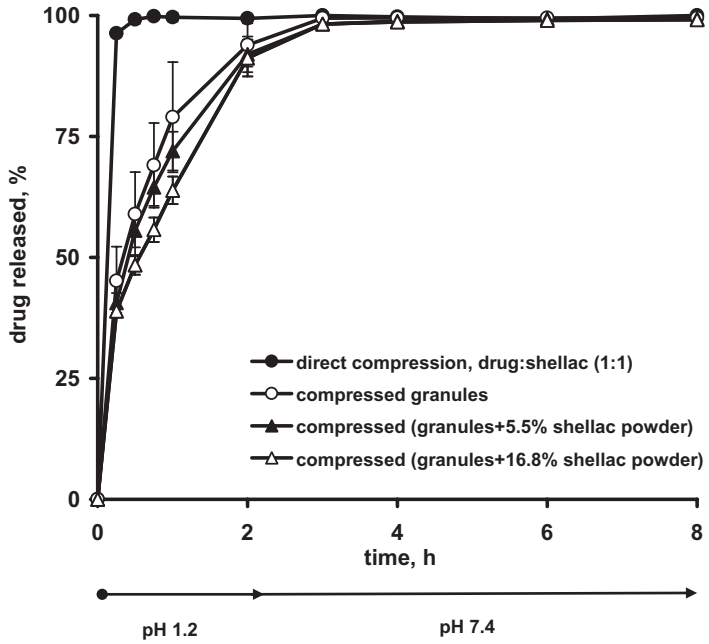

Figure 9. In vitro release of verapamil HCl from matrix tablets prepared by direct compression or via wet granulation using ammoniated aqueous shellac binder solutions (preparation method and tablet composition indicated in the figure legends). The granules consisted of verapamil HCl, shellac, and lactose (8:1:2). After 2 h the release medium was changed: 0.1 N HCl was replaced by phosphate buffer pH 7.4.

release patterns can be provided by varying the tablet composition and/or preparation method.

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