Drug Development and Industrial Pharmacy, 1:99–108, 2005

ISSN: 0363-9045 print / 1520-5762 online
DOI: 10.1081/DDC-200044226

Taylor & Francis
Taylor & Francis Group

Investigation of the Effect of Various Shellac Coating Compositions Containing Different Water-Soluble Polymers on In Vitro Drug Release

Basel Qussi and Wolfgang G. Suess
Department of Pharmaceutical Technology, Institute of Pharmacy, University of Leipzig, Leipzig, Germany

ABSTRACT In this study drug pellets were coated with aqueous shellac coating formulations containing different amounts of polyvinyl alcohol (PVA), hydroxypropyl methylcellulose (HPMC), and carbomer 940. The coating level needed for enteric coating was determined. The influence of different amounts of PVA, HPMC, and carbomer on drug release and mechanism; the porosity, and the stability of shellac coatings was investigated. The results show that the incorporation of different concentrations of HPMC into shellac coatings, due to the increasing of pores, could considerably increase the drug release from the pellets in purified water. Moreover, the swelling effect of carbomer 940 leads to much more diffusivity through shellac coatings in water. In addition, PVA results in small cracking in the films and much more diffusion of drug in water. Furthermore, all coating systems containing different hydrophilic polymers that were used in the present work could prevent the dissolution of drug in simulated gastric juice for 2 hours. On the other hand, a rapid and complete release of drug within 45 minutes was observed in simulated intestinal fluid. Drug release from shellac coated pellets and ones containing different amounts of carbomer was affected between 3–6 months, whereas shellac coatings containing different amounts of PVA or HPMC show the same dissolution profiles with small deviation after 12 months.

KEYWORDS Shellac, Hydroxypropyl methylcellulose, Polyvinyl alcohol, Carbomer, Enteric coating, Water-soluble polymers, Dissolution, Stability, Pellets

Address correspondence to Wolfgang G. Suess, Department of Pharmaceutical Technology, Institute of Pharmacy University of Leipzig, Schönauer Str. 160, Leipzig 04207, Germany; Fax: 0049341-4123007; E-mail: suess@rz.uni-leipzig.de

INTRODUCTION

Generally, enteric coating of pharmaceutical preparations has been carried out for the purposes of the protection of the active ingredient susceptible to acid attack from the gastric juice and the drug-release controlled system. In the enteric-coated pharmaceutical preparations, the intended purpose has been previously achieved by covering tablet surfaces with coating. In recent years, however, the reports were published that the enteric-coated pellets, when compared with the enteric-coated tablets from a biopharmaceutical point of view, do not produce individual variation in gastric emptying rate and absorption and are almost free from influence by meals (Lorck et al., 1997; Munday, 2003; Ozturk et al., 1990; Vetchy & Rabiskova, 2002).

Nevertheless, the conventional enteric films themselves show deteriorated strength, and when pellets being provided with the enteric coating are for example pharmaceutically processed into tablets or capsules, such enteric coating films in many instances are destroyed due to mechanical shock during processing and consequently fail to perform the function of the enteric coating. For the prevention of such problems, plasticizers are required to be added, but the addition of plasticizers often results in lowered effect of the enteric coating (Zhu et al., 2002). For example, it is known that addition of polyethylene glycols to hydroxypropyl methylcellulose phthalate brings deterioration in enteric coating performance (Enteric Film and Preparation Thereof, 1989).

One of the most important problems in the pharmaceutical industry has been the preparation of dosage forms that are safe and do not disintegrate or change during shelf-life, and which disintegrate as planned in the stomach or intestines when taken by the patient.

Shellac is a thermosetting resin secreted by the lac insect "karria lacca." Shellac has been used as a coating material in pharmaceuticals due to its various unique properties, such as thermoplasticity, cohesiveness, and insulating ability, along with its nontoxic nature. Over the years shellac has been used for a variety of applications, which include: a modified release coating, an enteric coating, and a seal for tablet cores prior to sugar coating.

For these applications shellac suffers from the general drawback that it is a material of natural origin and consequently suffers from occasional supply problems and quality variation. There also are stability problems associated with increased disintegration and dissolution time at storage (Cole et al., 1995; Maiti & Rahman, 1986; Wang et al., 1999).

Moreover, the provision of enteric coating on solid pharmaceutical dosage forms, such as tablets, pellets, capsules, and the like has been carried out by a method comprising coating the dosage forms with various enteric-coating materials dissolved in an organic solvent with the addition, if necessary, of plasticizers and coloring agents. This method is disadvantageous from both economical and safety viewpoints due to the use of a large amount of expensive solvents for the preparation of the coating solutions and the risk of fires or explosions during the coating operation. A further disadvantage of the method is that air pollution caused by the vapors of the organic solvent, which are discharged during the coating operation, most of which is released into the atmosphere (Kamakura et al., 1977).

It is therefore the objectives of this study to provide an improved method for providing enteric coatings from shellac on pellets that is free of the above-described disadvantages and difficulties and, for the purpose, characterized by the absence of organic solvents in the formulations of the coating solutions. Another objective is to provide a method or coating formulation that optimizes the stability of shellac enteric coating, and also the drug dissolution from shellac-coated pellets.

In order to attain the objectives of this study, different formulations of aqueous shellac coating solutions containing different amounts of hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), and carbomer 940 were prepared. Parameters of coating processes were determined, and the influence of these polymers and concentrations on the drug release and the porosity of coated pellets were studied. Comparative stability studies were performed over a period of 12 months.

EXPERIMENTAL METHODS

Materials

Shellac, 2011, Muster SM 1766, Marchand & Cie, Germany.

Polyethylene glycol, Polyethylenglycol 1500 Pract, Ferak (LABORAT GmbH BERLIN WEST, Germany).

Hydroxypropyl methylcellulose, HPMC-Metholose 65 SH 4000. ShinEtsu, Japan.

Polyvinyl alcohol, POLYVIOL G 28/10, AB-NR. 4391113 POS.: 2, LOT-NR.: 1, Wacker-Chemie GmbH, München, Germany.

Carbomer, Carbopol 940, Ch.-b.: 53458076. Caesar & Loretz GmbH, 40721 Hilden, Germany.

Theophylline, anhydrous, Arzneimittelwerk Dresden GmbH, Germany.

Methods

Preparation of Aqueous Shellac Coating Solutions

Shellac, like other polymers with carboxyl groups, is not soluble in water. However, it is possible to prepare aqueous shellac solutions of alkali salts. The selection of the base and the method for dissolving will influence the properties of the film (Specht et al., 1999). A volatile alkali is preferable. Therefore, ammonium hydrogen carbonate was chosen as the base.

The aqueous solutions were prepared by dissolving shellac in purified water with ammonium hydrogen carbonate under stirring and heating. At temperatures between 55–60°C the forming of CO_2 and NH_3 occurred; both compounds are volatile. Therefore, excessive ammonium hydrogen carbonate that was not used for the ammonium salt formation of shellac evaporated from the solution. The pH of the clear shellac solution was 7.5–8. After cooling to room temperature, polyethylene glycol (PEG) 1500 10% w/w relative to shellac as plasticizer was added.

For preparing PVA solutions, water was heated to 80°C and PVA was added gradually under stirring of the solution for 2–3 hours. After cooling the solution, PVA was added slowly to the alkaline aqueous shellac/plasticizer solution under stirring for 8 hours.

The HPMC solutions were prepared at room temperature by adding very slowly to the water under stirring. Then the HPMC solution was mixed with shellac/plasticizer solution under stirring for 4 hours.

Carbomer solutions were prepared at room temperature with water and then were mixed with shellac/plasticizer solution under stirring for 6 hours.

Preparation of Shellac-Coated Pellets

Pellets from microcrystalline cellulose (MCC) and theophylline as a model drug were prepared using the rotor-granulation technique (Glatt, GmbH, GPCG1, Germany) and coated with alkaline shellac solutions (against the gastric juice) containing 10% w/w PEG 1500 as a plasticizer and varying amounts of different water soluble polymers (HPMC, PVA, carbomer 940), using a fluid bed coating apparatus (Wurster, bottom-spray, Glatt, GmbH, GPCG1, Germany). The formulations and the process parameters for the coating are stated in Table 1. The pellets were examined by determining the particle size and surface characterization using imagine analyzer (IA-3001 Image Analysis System, LECO, Kirchheim, Germany) and by the analysis of contents and dissolution tests.

Dissolution Test

The most obvious way to evaluate coated pellets physically is to conduct a dissolution test. To date, this is the best physical test available to correlate with in vivo performance (McGinity, 1989). The U.S. Pharmacopeia (USP) paddle method was used to measure the dissolution rate of theophylline from shellac coated pellets at 37°C ± 0.5. The dissolution of drug was conducted in a medium of changing pH by starting with 750 mL 0.1 M HCl of pH 1.2 for 2 hours. Then, 250 mL of phosphate buffer was added and the pH was adjusted to 7.4±0.1 with a solution of 1 M NaOH (the p*K*a value of shellac ranges between 6.9–7.5.

TABLE 1 Processing Conditions of Film Coating Using Aqueous Alkaline Shellac Solutions Containing Different Additives

	Carbomer 940	HPMC or PVA
Batch size [g]	250	250
Shellac [g]	100	100
Ammonium hydrogen carbonate [g]	10	10
Polymer additive [g]	0.5–2.5	10–25
PEG 1500 [g]	10	10
Talcum (micron.) [g]	10	10
Purified water [g]	600–750	650–850
Inlet temperature [°C]	40	40
Atomizing air pressure [bar]	1.5	1.5
Air volume [m^3]	80–90	90–110
Spray rate [g/min]	3.1–9.3	3.1–7.2

Therefore, slow release was found at pH 6.8). The stirring speed was set at 50 rpm. At a predetermined time interval, a 5 mL sample was withdrawn and replaced with fresh dissolution medium. A dissolution test was also performed in purified water for all batches up to 6 hours.

The theophylline concentrations were determined by UV/VIS spectrophotometer (Perkin Elmer, Lambda 11) at a wavelength of 271 nm. Comparative dissolution studies between all batches were performed and cumulative percentage of drug release was calculated.

Measurement of Coating Levels

The levels of the coating were calculated from the surface area of the pellets and the difference in the theophylline content in 100 mg pellets before and after coating. The obtained values for the surface area were calculated from the average of 200 samples. The following example illustrates the calculation of coating level:

Drug content of uncoated pellets:	900 μg/100 mg
Drug content of coated pellets:	790 μg/100 mg
Solid film material/100 mg	990 μg/(100 mg+Y) =790 μg/100 mg
⟹	Y=25.3 mg
The surface area of uncoated pellets	
	$A=\pi \cdot r^2=\pi \cdot 1\ mm^2$ $=3.14\ mm^2$/pellet
The weight of pellet (uncoated)	1 mg (n=200)
The surface area of 100 mg pellets	$3.14\ cm^2$
Solid film material	$25.3/3.14\ cm^2$ $=8.06\ mg/cm^2$
Shellac coating level	$=6.2\ mg/cm^2$ pellet

Measurement of the Porosity

The weight of coated pellets was exactly measured and the density and the specific volume were determined using a helium pycnometer (Multi Volume Pycnometer 1305, Micromeritics GmbH, Neuss, Germany).

Porosity and the pore size distribution in the coated pellets were measured by mercury intrusion porosimetry, employing a mercury porosimeter (Quanta chrome Corp, PoreMaster 60, Fairfield, NJ).

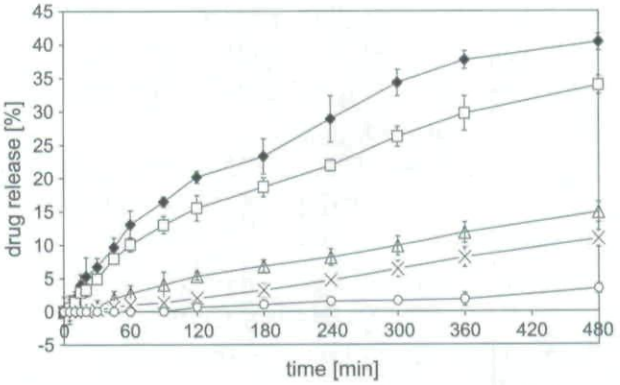

FIGURE 1 **The Influence of Coating Level on the Drug Release in Water. (◆) 3 mg/cm², (□) 4 mg/cm², (△) 5 mg/cm², (X) 6 mg/cm², (○) 9 mg/cm². Mean±SD, n=12.**

Porosity is defined as the percentage of void space in a solid. Total porosity (ε) is often evaluated from mercury density (ρ_{Hg}) and helium density (P_{He}) values (Mattsson & Nyström, 2001).

Laser Scanning Microscopy (LSM)

The surfaces of the coated pellets were examined prior to and after the dissolution test using confocal laser scanning microscope (CLSM), LSM 510 META, Carl Zeiss, Jena Ltd., Germany.

Stability Study

A stability test was conducted by storing the pellets at room temperature (22–25°C) and relative humidity 40–45%. All the batches were examined by dissolution test and drug contents at time intervals between 3–12 months.

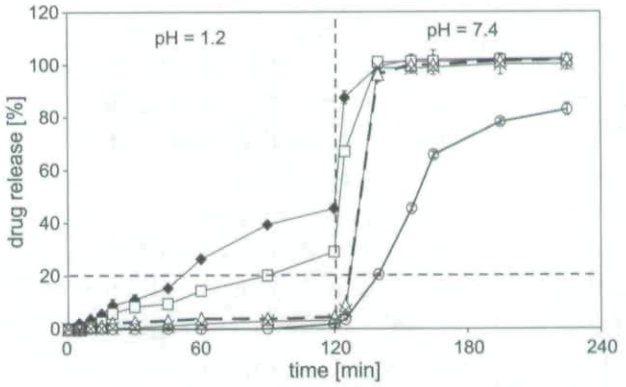

FIGURE 2 **Determination of the Coating Level Needed for Enteric Coating. (◆) 3 mg/cm², (□) 4 mg/cm², (△) 5 mg/cm², (X) 6 mg/cm², (○) 9 mg/cm². Mean±SD, n=12.**

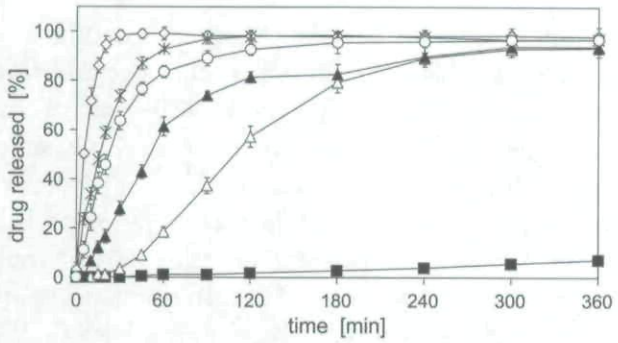

FIGURE 3 The Influence of HPMC on the Drug Release of Shellac/Plasticizer Coated Pellets (Shellac Coating Level was About 6 mg/cm^2) in Water, (■) HPMC 0%, (△) HPMC 10%, (▲) HPMC 15%, (○) HPMC 20%, (x) HPMC 25%, (◇) Without Coating. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

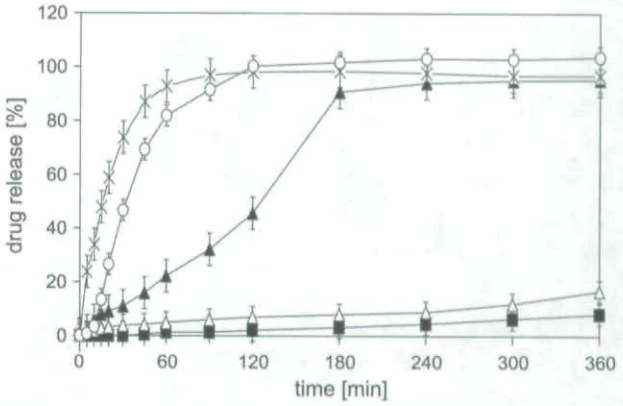

FIGURE 5 The Influence of Carbomer 940 on the Drug Release of Shellac/Plasticizer Coated Pellets (Shellac Coating Level was About 6 mg/cm^2) in Water, (■) Carbomer 0%, (△) Carbomer 0.5%, (▲) Carbomer 1%, (○) Carbomer 2%, (x) Carbomer 2.5%. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

RESULTS AND DISCUSSION

Pellets were successfully coated with different aqueous shellac coating formulations. The particle size and the drug content were analyzed.

The Influence of Coating Level

The drug release rate is inversely proportional to the amount of coating applied to the drug pellets. Thus the thicker the film coat is, the slower the release rate (Ueda et al., 1994). The mechanism obeys the theory of diffusion applicable to reservoir-type systems. Several release rates may be obtained with the same formulation by adjusting the level of coating and hence altering the diffusional path length.

The release of theophylline from coated pellets was investigated with different coating levels ranging from 3 to 9 mg polymer/cm^2 pellet. As shown in Fig. 1, the initiation of the drug release in water was delayed with the increase in coating level, and a coating level no less than 5 mg/cm^2 is necessary in order to sustain drug release in an apparent zero-order function in water. Moreover, coated pellets with coating levels under 5 mg/cm^2 pellet could not prevent the dissolution of theophylline in simulated gastric juice of pH 1.2 for 2 hours, whereas shellac-coated pellets with coating levels between 5–6 mg/cm^2 pellet could prevent the dissolution of theophylline in simulated gastric juice. On the other hand, a rapid and complete drug release was found in simulated intestinal fluid of pH 7.4. Shellac-coated pellets with a coating level of 9 mg/cm^2 show slower drug release in simulated intestinal fluid as shown in Fig. 2.

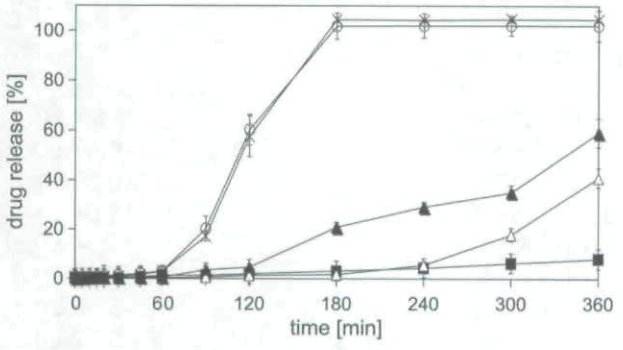

FIGURE 4 The Influence of PVA on the Drug Release of Shellac/Plasticizer Coated Pellets (Shellac Coating Level was About 6 mg/cm^2) in Water, (■) PVA 0%, (△) PVA 10%, (▲) PVA 15%, (○) PVA 20%, (x) PVA 25%. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

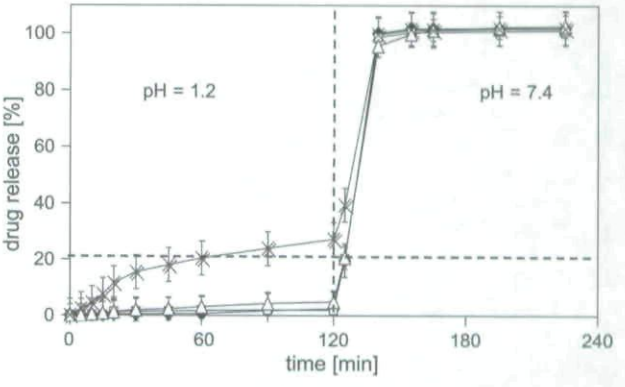

FIGURE 6 Dissolution Profiles of Coated Pellets with Shellac/Plasticizer Solutions Containing Different Amounts of HPMC (Shellac Coating Level was About 6 mg/cm^2), (◆) HPMC 10%, (□) HPMC 15%, (△) HPMC 20%, (x) HPMC 25%. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

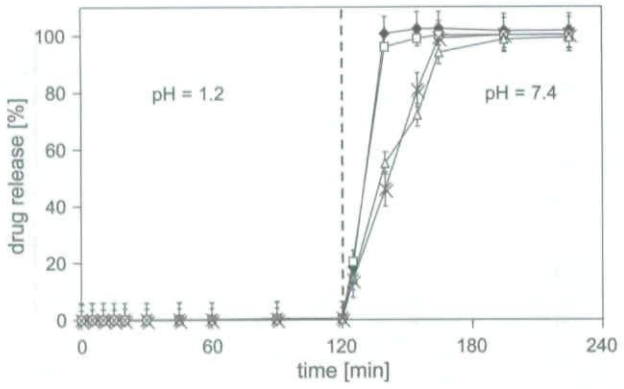

FIGURE 7 Dissolution Profiles of Coated Pellets with Shellac/Plasticizer Solutions Containing Different Amounts of PVA (Shellac Coating Level was About 6 mg/cm^2), (◆) PVA 10%, (□) PVA 15%, (△) PVA 20%, (x) PVA 25%. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

Effect of Water-Soluble Polymers and Different Concentrations on Drug Release

In some cases, after a plasticizer has been chosen and its optimum level established, a water-soluble polymer may be added to the system to aid in controlling the release characteristics. Since shellac is completely insoluble in water, a film formed from shellac may not be permeable enough to provide the target release profile. Therefore, water-soluble additives may be added to provide a channel in membrane for permeation in an aqueous environment.

Water-soluble polymers such as hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), and carbomer were used for this application. The amounts are determined at a certain coating level (about 6 mg shellac/cm^2) to achieve the targeted release rate. Figures 3, 4, and 5 show how release patterns can be modified by addition of different concentrations of HPMC, PVA, and carbomer in addition of plasticizer. Figures 6, 7, and 8 show that the incorporation of these polymers into shellac/plasticizer coating systems could also prevent the dissolution of drug in simulated gastric juice (except shellac coating containing HPMC 25% w/w), and a complete and rapid drug release in simulated intestinal fluid was observed.

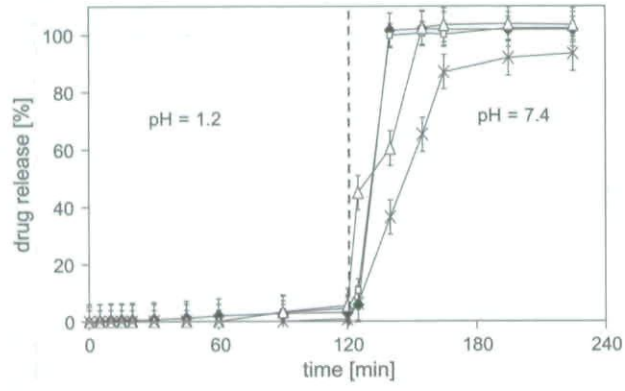

FIGURE 8 Dissolution Profiles of Coated Pellets with Shellac/Plasticizer Solutions Containing Different Amounts of Carbomer 940 (Shellac Coating Level was About 6 mg/cm^2), (◆) Carbomer 0.5%, (□). Carbomer 1%, (△) Carbomer 2%, (x) Carbomer 2.5%. (Polymer Additive w/w Relative to Shellac). Mean±SD, n=18.

The Influence of Water-Soluble Polymers on the Porosity of Shellac/Plasticizer Coating

Porous diffusion may play a minor role in the drug transport mechanism. The results show that the use of water-soluble polymers can affect the drug release from shellac/plasticizer-coated pellets. In order to support and clarify the mechanism of drug release from the pellets, porosity tests for shellac/plasticizer-coated pellets with different amounts of polymers were performed (Table 2).

The results show that HPMC has a large effect on the porosity of shellac/plasticizer coating. Thus, the porosity of coated pellets with shellac solution containing 25% w/w HPMC increased to 14.34% (the porosity of shellac coating was 4.7%) (Figs. 9 and

TABLE 2 The Influence of Polymers on the Porosity of Shellac Coated Pellets, Mean±SD, n=4

Polymer additive (w/w relative to shellac)	Porosity of the pellets [%]
Shellac+10% w/w PEG 1500 (A)	4.7±0.5
A+10% HPMC	6.7±0.7
A+15% HPMC	8.67±0.5
A+20% HPMC	10.23±1.2
A+25% HPMC	14.34±1
A+10% PVA	5.34±0.3
A+15% PVA	5.61±0.4
A+20% PVA	5.59±0.1
A+25% PVA	5.82±0.2
A+0.5% carbomer 940	4.68±1
A+1% carbomer 940	5.5±0.6
A+2% carbomer 940	6.72±0.3
A+2.5% carbomer 940	7.11±0.3

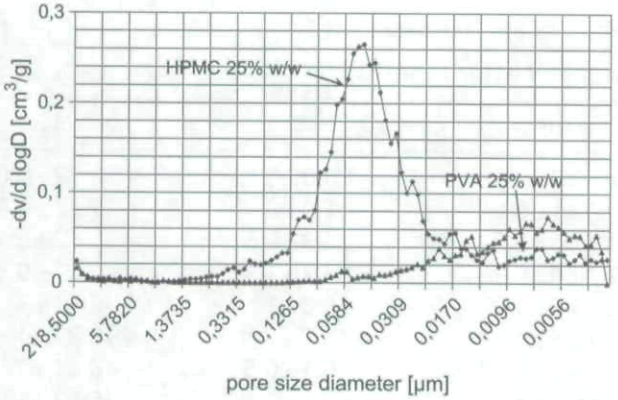

FIGURE 9 The Influence of PVA and HPMC on the Porosity of Shellac/Plasticizer Coated Pellets.

10). On the other hand, both carbomer and polyvinyl alcohol have no marked effect on the porosity of shellac coatings.

Investigation of Drug Release Mechanisms

During coating, each pellet is sprayed in a random fashion with a very small fraction of the formulation each time it traverses the spray path. The intermittent layering of the coating formulation on the substrate eventually produces a coating material containing channels. In addition, the porosity of shellac coatings can be increased through the incorporation of hydrophilic additives dissolved in hydrophobic coating (incorporation of HPMC into shellac coatings), thereby creating a microporous membrane resulting in higher drug release (Fig. 10).

The swelling of shellac coating was rising with the increase of the concentration of carbomer 940

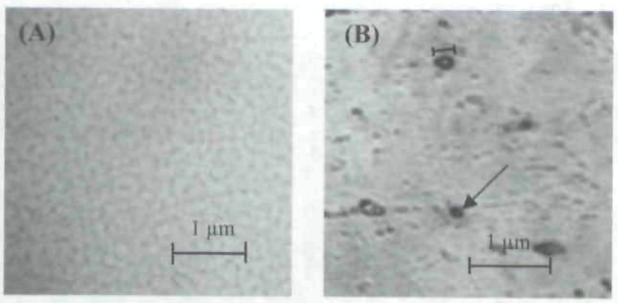

FIGURE 10 (A) Confocal Laser Scanning Micrograph Showing the Surface of a Pellet Coated with Shellac/Plasticizer Formulation. (B) Confocal Laser Scanning Micrograph Showing the Surface of a Pellet Coated with Shellac/Plasticizer Formulation Containing HPMC 25% w/w.

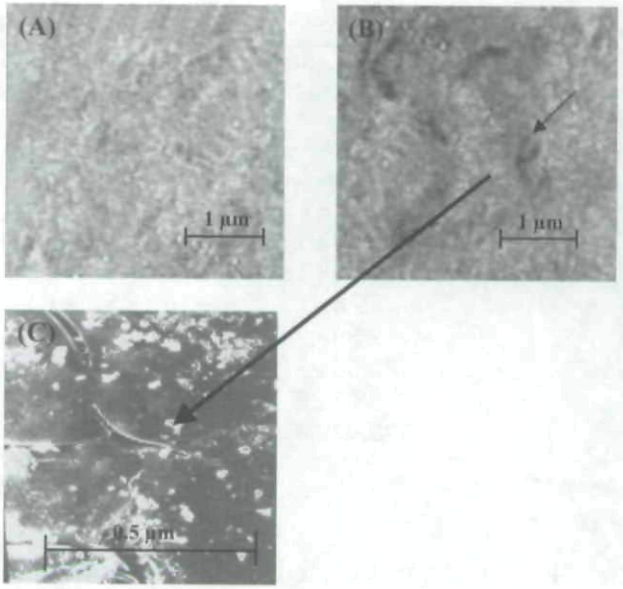

FIGURE 11 (A) Confocal Laser Scanning Micrograph Showing the Surface of a Pellet Coated with Shellac/Plasticizer Formulation Containing PVA 25% w/w Prior to the Dissolution Test. (B) and (C) Confocal Laser Scanning Micrographs Showing the Surface of a Pellet Coated with Shellac/Plasticizer Formulation Containing PVA 25% w/w After the Dissolution Test in Water.

[carbomer increases the viscosity of alkaline solutions due to hydration of the carboxyl groups in its structure, resulting in increasing the swelling of coating material (Muramatsu et al., 2000)]. Thus, much higher diffusivity can be expected in these coatings.

Moreover, the observed increase of drug release from shellac/plasticizer coatings containing different amounts of PVA could be explained based on the physicochemical properties of the film coatings (molecular interaction between shellac and PVA) (Qussi & Suess, 2004). Polyvinyl alcohol increases the softening temperature and decreases the elasticity of shellac-coated films, resulting in small cracking in

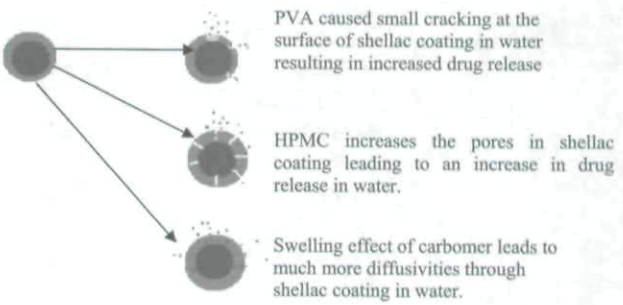

FIGURE 12 Drug Release Mechanisms of Coated Pellets with Shellac/Plasticizer Containing Different Polymers (PVA, HPMC, Carbomer).

TABLE 3 Stability Study of Shellac/Plasticizer Coated Pellets Containing 10% w/w PVA Relative to Shellac

	Drug release [%] after months				
Time [hr]	0	3	6	9	12
0	0.0±0	0.0±0.1	0.0±0	0.0±0	0.52±0.01
1	0.31±0.1	0.22±0.2	0.11±0.01	1.0±0.2	1.22±0.02
2	1.35±1	1.8±1	1.55±0.5	2.33±0.6	2.2±0.1
3	1.75±1	2.1±0.5	1.84±0.1	3.52±1	3.1±0.5
4	5.6±1	5.1±1	4.8±1	5.8±1	5.47±3
5	17.89±2	16.32±2	16.5±1	18.7±3	18.22±1
6	40.96±3	37.81±2	38.9±3	40.1±0.5	40.41±2
7	58.1±2	55.44±3	55.0±1	57.5±3	58.3±1
8	78.42±4	76.2±3	79.12±3	80.8±2	80.3±4

Mean±SD, n=12.

the films in aqueous mediums and much more diffusion of drug (Fig. 11).

Shellac coating and shellac coating containing varying amounts of different polymers showed prevention of drug dissolution at pH 1.2 (with the exception of.shellac coating containing HPMC 25% w/w, probably due to the high porosity), but due to the polymers' dissolving of coatings at high pH values (resulting in increased drug diffusivity), drug was completely and rapidly released at pH 7.4. Figure 12 clarifies the drug release mechanisms of shellac-coated pellets.

Stability of Shellac-Coated Pellets

Although shellac coatings have been used as enteric coatings against gastric juice and provide sustained-release products, there has been concern that film hardening could occur as a function of time and lead to a reduction in drug release rate. Reproducible release rates were obtained when shellac/plasticizer coated pellets were stored at room temperature up to 3 months, or when the pellets coated with shellac/plasticizer solution containing different amounts of carbomer were stored at room temperature up to 6 months. In addition, pellets coated with shellac/plasticizer formulations tend to stick to one another at higher temperatures and usually form soft lumps. Although these lumps are broken up easily at lower temperatures, they appear to have an effect on the dissolution behavior of the pellets. Stability data on theophylline pellets collected over a period of 12 months, however, indicated that shellac/plasticizer coatings containing different amounts of PVA or HPMC are stable during storage at room temperature (22–25°C) and did not show large.deviations in dissolution profiles. Tables 3, 4, and 5 show the results of the stability study of

TABLE 4 Stability Study of Shellac/Plasticizer Coated Pellets Containing 10% w/w HPMC Relative to Shellac

	Drug release [%] after months				
Time [hr]	0	3	6	9	12
0	0.0±0	0.0±0.1	0.2±0.1	0.0±0	0.32±0.01
1	18.5±2	19.1±0.5	19.4±0.2	19.0±1	20.2±1.2
2	37.3±4	35.3±1	37.6±2	37.42±1.3	37.51±1
3	79.34±4	80.4±2	81.12±2	80.5±1	81.4±4
4	89.2±2.4	90.2±1	90.7±1	91.2±2	91.46±3
5	92.9±3	94.32±1	94.4±1	94.71±1	95.1±0.5
6	93.5±1.5	95.13±2	94.6±2.1	95.3±2	95.9±3
7	94.1±2	95.21±1	95.0±3	95.5±1.3	96.4±2
8	95.3±1	96.2±2	95.33±2	95.4±1.7	96.55±3

Mean±SD, n=12.

TABLE 5 Stability Study of Shellac/Plasticizer Coated Pellets Containing 0.5% w/w Carbomer Relative to Shellac

	Drug release [%] after months				
Time [hr]	0	3	6	9	12
0	0.9±0.01	0.0±0	0.2±0.1	0.5±0	1.1±0.01
1	4.8±0.5	5.1±0.6	7.33±1	11.9±0.5	12.1±0.2
2	6.85±1	6.3±0.6	8.3±1	15.33±1	16.3±1
3	7.9±0.5	8.11±1	11.13±1	18.6±1	19.8±1
4	8.8±0.4	8.7±1	14.5±2	25.12±1.5	26.7±1.3
5	11.9±1	10.32±1	17.4±1	29.11±2	29±2
6	16.7±1.5	15.23±2	22.33±2	35.66±1	37.8±1
7	20.22±2	19.21±1	27.0±2	38.22±3	40.29±1.2
8	25.3±1	25.5±1.2	30.66±1	42.1±2	44.3±1

Mean±SD, n=12.

shellac/plasticizer coating containing PVA, HPMC, and carbomer.

CONCLUSIONS

The results presented in this discussion indicate the suitability of incorporation of some water-soluble polymers into a shellac/plasticizer coating system for preparing modified-release dosage forms. Moreover, some water-soluble polymers (in this study, PVA and HPMC) showed a positive effect on the stability of shellac-coating systems.

While shellac can be applied to various types of pharmaceutical products, in order to obtain optimal results in each, careful consideration should be given to the process conditions, the exact coating formulation that is to be used (especially incorporation of water-soluble polymers and plasticizers), and the quantity of shellac coating that should be applied not only to obtain the correct release profiles but also to facilitate uniform application throughout the entire batch of product to be coated. The results show that the coating level is an important parameter of the formulation of shellac enteric coating. Too little coating can result in release failure in the acidic environment of the stomach. Too much coating, on the other hand, may lengthen the intestinal disintegration time such that drug dissolution and absorption are inadequate to reach a therapeutic range.

REFERENCES

Cole, G., Hogan, J., & Aulton, M. (1995). Film-coating materials and their properties. In G. Cole (Ed.), *Pharmaceutical Coating Technology*. London, United Kingdom: Taylor & Francis Ltd., pp. 6–52.

Enteric Film and Preparation Thereof. European Patent Application, 0361 873 A2, (1989 September). Takeda Chemical Industries, Ltd.

Kamakura, S. O., Higashikurune, N. H., & Yono, F. S. Method for Providing Enteric Coating on solid Dosage Forms. US Patent 4,017,647, April 12, 1977.

Lorck, C. A., Grunenberg, P. C., Jünger, H., & Laicher, A. (1997). Influence of process parameters on sustained-release theophylline pellets coated with aqueous polymer dispersions and organic solvent-based polymer solution. *European Journal of Pharmaceutics and Biopharmaceutics, 43*, 149–157.

Maiti, S., & Rahman, M. S. (1986). Application of shellac in polymers. *Macromolecular Chemistry Physics, C 26*(3), 441–481.

Mattsson, S., & Nyström, C. (2001). The use of mercury porosimetry in assessing the effect of different binders on the pore structure and bonding properties of tablets. *European Journal of Pharmaceutics and Biopharmaceutics, 52*, 237–247.

McGinity, J. W. (1989). Aqueous polymeric coating for modified-release pellets. In J. W. McGinity (Ed.), *Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms*. New York: Marcel Dekker, pp. 63–79.

Munday, D. L. (2003). Film coated pellets containing verapamil hydrochloride: enhanced dissolution into neutral medium. *Drug Development and Industrial Pharmacy, 29*, 575–583.

Muramatsu, M., Kanada, K., Nishida, A., Ouchi, K., Saito, N., Yoshida, M., Shimoaka, A., Ozeki, T., Yuasa, H., & Kanaya, Y. (2000). Application of Carbopol® to controlled release preparation I. Carbopol® as a novel coating material. *International Journal of Pharmaceutics, 199*, 77–83.

Ozturk, A. G., Ozturk, S. S., Palsson, B. O., Wheatley, T. A., & Dressman, J. B. (1990). Mechanism of release from pellets coated with an ethylcellulose-based film. *Journal of Controlled Release, 14*, 203–213.

Qussi, B., & Suess, W. (2004). The influence of polyvinyl alcohol (PVA) on the mechanical and thermal properties of free shellac films and drug release from shellac coated pelletsControlled Release and Drug Delivery, Proceedings of the International Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Nuremberg, Germany, March 15–18; Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik (APV); 567, 65.

Specht, F., Saugestad, M., Waaler, T., & Müller, B. W. (1999). The application of shellac as an acidic polymer for enteric coating. *Pharmmaceutic Technology, 10*, 146–154.

Ueda, S., Yamaguchi, H., Kotani, M., Kimura, S., Tokunaga, Y., Kagayama, A., & Hata, T. (1994). Development of a novel drug release system, time-controlled explosion system (TES). II. Design

of multiparticulate TES and in vitro drug release properties. *Chemical and Pharmaceutical Bulletin*, *42*, 359–363.

Vetchy, D., & Rabiskova, M. (2002). High drug loaded pellets produced by rotoagglomeration technology. Solid Dosage Forms, Proceedings of the 4th World Meeting, Florence, Italy, April 8–11, 2002; Florence, Italy: ADRITELF/APGI/APV, 29, p. 95.

Wang, L., Ishida, Y., Ohtani, H., & Tsuge, S. (1999). Characterization of natural resin shellac by reactive pyrolysis-gas chromatography in the presence of organic alkali. *Analytical Chemistry*, *71*(7), 1316–1322.

Zhu, Y., Shah, N. H., Malick, A. W., Infeld, M. H., & McGinity, J. W. (2002). Solid-state plasticization of acrylic polymer with chlorpheniramine maleate and triethyl citrate. *International Journal of Pharmaceutics*, *241*, 301–310.