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Note

Preparation and evaluation of shellac pseudolatex as an aqueous enteric coating system for pellets

Rong-Kun Chang [1], Gonzalo Iturrioz [2] and Ching-Wang Luo [1]

[1] *Schering Research, Schering-Plough Corp., 999 NW 159 Drive, Miami, FL 33169 (U.S.A.) and* [2] *Ivax Pharmaceuticals, Miami, FL 33178 (U.S.A.)*

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Summary

A soap-free shellac pseudolatex was prepared using a changing solvent technique. In the present study, theophylline sustained release pellets were used as model cores for the shellac coatings. The enteric quality of the film produced from the aqueous dispersion is comparable to that applied from the organic solution.

Because of the explosion hazard, toxicity, and expense associated with organic solvent systems, attempts have been made to eliminate these solvents from coating formulations. The most commonly used methods employ mixed organic-aqueous solvent system (Osterwald, 1985), coating emulsion (Bauer and Osterwald, 1979), neutralization with a base to prepare a water solution of film former (Stafford, 1982) and latex or pseudolatex coatings (Banker and Peck, 1981; Chang et al., 1987, 1989; Chang and Hsiao, 1989). Mixed organic-aqueous solvent systems and coating emulsions still contain considerable amounts of undesirable solvents. The neutralization technique, commonly used for enteric materials, requires substantial quantities of alkaline compound which may have an adverse effect on film properties. Latex or pseudolatex appears to be a practical and feasible means to end the use of solvent-based coating in the pharmaceutical industry.

This report concerns a changing solvent technique for preparing shellac pseudolatex and an evaluation of enteric performance of this shellac pseudolatex using theophylline sustained release pellets as coating substrates.

The experimental methods are described as follows. Shellac (18 g, Food Grade refined wax free Vac dry bleached shellac, William Zinsser, Somerset, NJ) was dissolved in 450 ml of a mixed water-miscible organic solvent system, i.e., acetone : methanol (2 : 1 by volume) by stirring with a three-blade stainless-steel impeller (2.5 cm diameter) at 500 rpm. The time required to dissolve the shellac in the solvent system was 60 min. The resin solution was then directly dispersed in 900 ml deionized water by stirring with the aforementioned impeller at 1500 rpm. The organic solvents and part of the water were subsequently eliminated

Correspondence: R.-K. Chang, Schering Research, Schering-Plough Corp., 999 NW 159 Drive, Miami, FL 33169, U.S.A.

in a hood under mild agitation (500 rpm) to leave a stable shellac pseudolatex with 3% w/w solids content. The evaporation process took 48 h to strip the polymer solvent completely.

Batches of 500 g of theophylline sustained release pellets were coated by using a fluidized bed coating technique (Uni-Glatt, Glatt Air Technique, Ramsey, NJ). The inlet air temperature was 55–60 °C. Coating dispersions or solutions were pumped to the atomizer at a rate of 8–10 ml/min, operating at a spray pressure of 0.8 Bar with a spray nozzle orifice of 0.8 mm. Enteric coats were applied to achieve a theoretical 2% weight increase with respect to initial pellet weight. After the coating process, the pellets were dried in the coating chamber for another 15 min at the same temperature and rate of air flow.

Theophylline release characteristics were determined by dissolution testing using a modified rotating paddle dissolution apparatus designed by Schering's Method Development Laboratory in Miami (Chang et al., 1989). A stationary, stainless-steel, 40-mesh basket was suspended in an appropriate dissolution medium, positioned in close proximity to the paddle, and the pellets containing a total of 450 mg theophylline were inside the basket. The paddle constantly stirred the dissolution fluid at 100 rpm. Serial sampling of the fluid at appropriate times, with subsequent HPLC analysis for theophylline content, was performed to generate a cumulative percent released-time profile.

Shellac is a water-insoluble, natural polymer. However, it is very soluble in most alcohols and can be dispersed in water to give a pseudolatex. Negative charge on the latex spheres, determined by a flocculation technique using cationic drugs and positively charged pseudolatices as flocculating agents, stabilizes the shellac pseudolatex. The shellac pseudolatex particles were in the range 0.05–0.2 μm with the average particle size at 0.15 μm (determined by scanning electron microscopy). As a consequence, the shellac pseudolatex exhibited very little precipitation with time. However, shellac pseudolatex supported mold growth and proliferation. The use of freshly prepared shellac pseudolatex or preservative(s) in latex preparations is recommended to prevent this potential problem. The shellac pseudolatex did not require plasticizer, probably because of its low glass transition temperature or self-plasticizing effect due to a mixture of lower molecular weight fatty acid esters in the interstices of the shellac structure (Cockeram and Levine, 1961). In addition to shellac, polyvinyl acetate phthalate and methacrylic acid copolymers can also be dispersed in water to form pseudolatices. However, completely aqueous enteric coating dispersions based

TABLE 1

Theophylline release from sustained release pellets and 2% shellac coated sustained release pellets in simulated gastric fluid and simulated intestinal fluid

Time (h)	Cumulative % dissolved per h					
	Sustained release pellets (cores for the enteric coatings)		Solvent-based shellac coating [a]		Shellac pseudolatex coating [b]	
	SGF [c]	SIF [d]	SGF	SIF	SGF	SIF
1	9.6 ± 1.2	10.8 ± 0.3	1.7 ± 0.1	20.1 ± 1.3	2.3 ± 0.1	12.1 ± 0.6
2	22.9 ± 2.0	25.2 ± 0.9	3.1 ± 0.2	42.7 ± 1.8	3.8 ± 0.3	28.0 ± 0.7
4	51.2 ± 3.6	56.7 ± 2.0	6.8 ± 0.3	79.4 ± 2.0	7.3 ± 0.4	60.1 ± 0.6
6	75.7 ± 3.6	81.5 ± 1.6	11.6 ± 0.5	95.4 ± 0.9	11.2 ± 0.8	83.4 ± 0.5
8	91.3 ± 2.2	94.9 ± 0.6	18.5 ± 0.6	100.3 ± 0.5	14.8 ± 0.9	95.1 ± 0.7
10	99.2 ± 1.0	100.4 ± 0.3	26.3 ± 0.7		18.3 ± 1.0	100.0 ± 0.6

[a] 3% w/w shellac in ethanol as a coating solution.
[b] 3% w/w shellac aqueous dispersion as a coating system.
[c] Simulated gastric fluid without enzyme.
[d] Simulated intestinal fluid without enzyme.
NB: Data represent means ±S.D. of six determinations of two batches.

TABLE 2

Theophylline release from 2% coateric and aquateric coated sustained release pellets in simulated gastric fluid and simulated intestinal fluid

Time (h)	Cumulative % dissolved per h			
	Coateric coating [b]		Aquateric coating [a]	
	SGF [c]	SIF [d]	SGF	SIF
1	6.5±0.8	11.3±1.1	10.4±1.8	10.1±2.7
2	16.2±1.2	26.1±1.7	25.7±2.8	26.3±3.7
4	36.9±2.7	58.1±2.8	57.8±3.6	60.7±3.6
6	56.5±2.5	83.4±1.9	82.5±3.3	85.0±1.4
8	73.0±2.9	96.7±1.2	95.1±1.1	96.0±0.8
10	85.3±2.0	100.2±0.2	100.2±0.8	100.0±0.3

[a] 10% w/w Aquateric aqueous dispersion containing 15% diethyl phthalate (based on Aquateric amount) as a coating system.

[b] 10% w/w Coateric aqueous dispersion containing 30% ammonium hydroxide (4 ml/100 g Coateric) as a coating system.

[c] Simulated gastric fluid without enzyme.

[d] Simulated intestinal fluid without enzyme.

NB: Data represent means ±S.D. of six determinations of two batches.

on these polymers have been commercially available for years.

Theophylline sustained release pellets (model cores for the enteric coatings) were prepared using a fluidized bed coating technique which allows the active drug to be coated onto sucrose crystals. The ethyl cellulose coating which controls the release of theophylline is sprayed on after the active drug layer has been applied. Table 1 shows the cumulative percent of theophylline release from core pellets in simulated gastric fluid and simulated intestinal fluid. The product released theophylline pH-independently with apparent zero-order kinetics. Table 1 also lists the dissolution data for a shellac pseudolatex and a shellac solution coated theophylline sustained release pellets. Dissolution profiles revealed that both products resisted dissolution in the simulated gastric fluid; however, the shellac solution coated theophylline sustained release pellets gave faster release than the original sustained release pellets in simulated intestinal fluid. This may be due to the partial destruction of the ethyl cellulose film during the solvent-based shellac coating process. On the other hand, the shellac dispersion coating did not alter the dissolution profile in simulated intestinal fluid significantly. To provide enteric release without destroying the previous sustained release coating is a significant advantage for the shellac pseudolatex.

Two commercially available aqueous enteric coating systems based upon cellulose acetate phthalate (Aquateric, FMC, Princeton, NJ) and polyvinyl acetate phthalate (Coateric, Colorcon, West Point, PA) have also been used to coat the theophylline sustained release pellets at 2% polymer coating level under the present coating conditions (Table 2). Neither system gave a good gastric fluid resistant film which was comparable to the film formed from solutions or shellac pseudolatex. These redispersible coating systems contain considerable amounts of additives which may change the enteric film properties.

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