

Electrostatic Dry-Powder Functional and Active Coating Using Conventional Pan Coaters

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ABSTRACT

Purpose: To develop formulations and methods for functional and active film coating in a conventional pan coater.

Methods: Functional and non-functional coating materials including pharmaceutical coating mixtures, plasticizers, colorants and flow aids were considered for formulation development and studied by differential scanning calorimetry. Up to 1 kg per batch of model tablets containing ibuprofen were coated using an electrostatic powder coating method. The tablet cores were heated in a non-perforated pan. Then the coating formulation and additional plasticizer were applied together, followed by curing for up to two hours at approximately 50 °C. The tablet appearance was examined visually and by scanning electron microscopy (Hitachi Model S-2600N). The function of the film coat was evaluated immediately and on stability by dissolution testing. The coating uniformity of both the powder coated and solvent coated tablets (purchased commercially) was compared using Laser Induced Breakdown Spectroscopy (LIBS) in a PharmaLIBSTM 250 instrument.

Results: The coating compositions were chosen based on the glass transition temperature of the film coat formulations. After studying the process under different conditions, acceptable appearance was observed from dry powder coated tablets containing Eudragit L, Eudragit EPO, Acryl-eze or Opadry II 85. Powder coating with formulation containing Opadry AMB needs to be improved. Tablets containing Eudragit L or Eudragit EPO passed the USP enteric function test performed after coating and storage at 40°C/75%RH for up to 3 months. Tablets coated with Eudragit EPO containing formulation also showed satisfactory dissolution at pH = 1.0. However, a slight reduction of dissolution rate was observed after 3 months storage at 40°C/75%RH because of potential interaction between ibuprofen and the film coat polymer system. LIBS analysis of titanium and magnesium showed the coating uniformity of powder coated tablets was superior to that of solvent coated tablets.

Conclusion: The results suggest that tablets of various release profiles and satisfactory appearance have been produced by dry powder film coating in conventional equipment. This process may also be useful for active drug coating because the film coat uniformity is shown to be better than that obtained by traditional film coating process.

INTRODUCTION

Pharmaceutical coating is generally performed using either an aqueous or solvent process in a rotary pan or fluidized bed, which utilizes a large amount of energy and expensive HVAC systems. Solvent coating also introduces explosivity risks and pollutes the environment. Therefore a dry powder coating process has been investigated with the following objectives:

- Acceptable functional and cosmetic coating
- Less energy consumption
- Environmentally friendly
- Low capital and maintenance cost
- Robust GMP coating process
- Acceptable by regulatory bodies, common excipient

Early studies demonstrated electrostatic dry powder coating could produce coated tablets and pellets with acceptable appearance.^{1,2} In this study, ibuprofen tablets were used as a model to evaluate the coating process, the coating performance before and after storage under accelerated stability condition, and the coat uniformity.

METHODOLOGY

Electrostatic Dry Powder Coating

Tablets consisting of ibuprofen, starch and magnesium stearate were prepared by direct compression. The components of the coating formulations were mixed and processed using powder fluidization additives (US Patent 6,833,185).

Up to 1 kg per batch of tablets were heated in a non-perforated (coating) pan. Then the coating formulation was accurately metered into electrostatic spray gun using a powder feeder. The charged powder was applied to the tablets in the rotating coating pan. A suitable plasticizer may also be sprayed on the tablet before or during coating. The coated tablets were cured for up to two hours at approximately 50 °C. A typical process diagram is presented in Figure 1. Pharmaceutical grade polymers, coating compositions, excipients, and plasticizers were used.

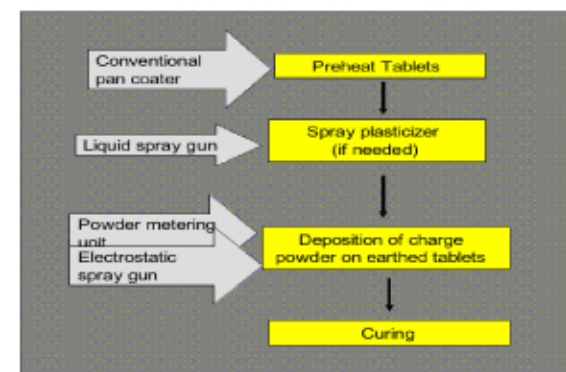


Fig 1—Electrostatic dry powder coating process in conventional coating pan

Coating Surface Analysis

The tablet appearance was examined visually by optical microscopy (Opti-Tech) and by scanning electron microscopy (Hitachi Model S-2600N).

Dissolution Testing

The performance of the tablet film coat was evaluated after coating and at stability pull points by USP dissolution testing (paddle method at 100 rpm; 37.0°C; n = 6) in 0.1N HCl solution or tribasic sodium phosphate solution (pH 6.8). The dissolution samples were assayed by UV spectroscopy at 222 nm.

Differential Scanning Calorimetry

The glass transition temperature (T_g) of coating formulations alone and in the presence of plasticizers were examined using a Mettler differential scanning calorimeter at a scanning rate of 5°C/min using nitrogen as the purge gas.

Laser Induced Breakdown Spectroscopy (LIBS)

The coating uniformity of the powder coated tablets and that of solvent coated tablets (purchased commercially) was compared using Laser Induced Breakdown Spectroscopy (LIBS) in a PharmaLIBSTM 250 instrument. Both horizontal and vertical surface were examined (Figure 2)

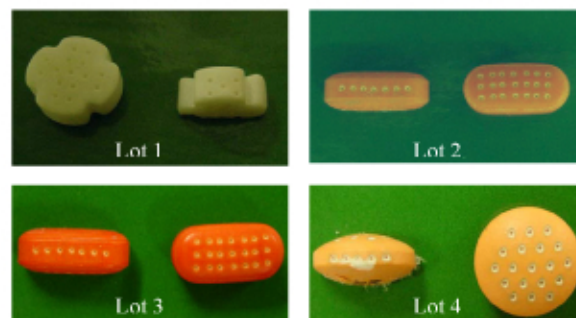


Figure 2—Dry powder (Lots 1-3) and conventional (Lot 4) film coated ibuprofen tablets evaluated using LIBS

RESULTS AND DISCUSSION

Good powder film coating quality (Fig 3) has been observed visually, by optical microscopy, and by scanning electron microscopy. The results suggest that a suitable film forming process occurred as a result of the molecular movement of polymers and excipients in a rubbery state during the electrostatic deposition and curing. The hypothesis is supported by a decrease of the glass transition (T_g) when several coating formulations were examined in the presence of suitable plasticizers by DSC (Table 1). An earlier onset of T_g was also observed. This early onset indicates that some of the polymer molecules become more mobile at a lower temperature for film forming. The film formation continues during curing and the quality and the function of the film coat are found to be related to the curing temperature and time. An example of this relation is presented in Figure 4.



Figure 3—Dry powder ibuprofen tablets film coated using formulations containing (a) Acryl-eze MP or (b) Eudragit EPO.

Table 1. T_g of coating powders with and without plasticizer determined using differential scanning calorimetry

Polymer/coating composition in coating material	T _g without plasticizer, °C	T _g with plasticizer, °C
Eudragit EPO	58	50
Eudragit L	85	55
Opadry AMB (PVA)	100	65
Acryl-EZE MP	65	55

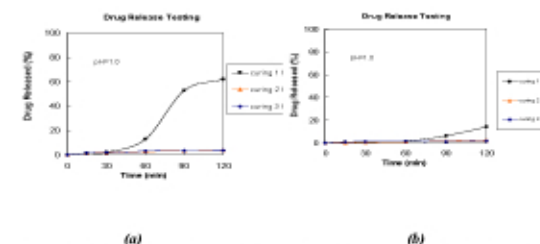


Figure 4—Effect of curing time on the enteric coating properties of ibuprofen tablets film coating with materials containing Eudragit L and cured at (a) 50°C and (b) 60°C.

Both immediate release (e.g. for coating containing Eudragit EPO) and enteric coating behaviors were confirmed by dissolution testing. The enteric coating properties of the film coat were maintained after accelerated stability storage in HDPE containers at 40°C/75%RH for up to 3 months (Fig 5). For Eudragit EPO coated tablets, a reduction of dissolution rate was observed upon storage at 40°C/75%RH. There may be an interaction between ibuprofen and the film coat polymer (Fig 5). Ibuprofen is known to form eutectic mixtures with pharmaceutical excipients. Further studies will be required to understand the material interactions.

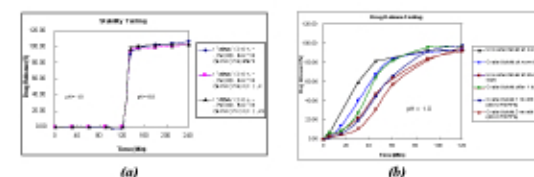


Figure 5—Dissolution profiles of (a) enteric coated and (b) immediate release dry powder film coated tablets collected after coating and storage at 40°C/75%RH in HDPE containers for up to 3 months. The coating formulations contain Eudragit L and Eudragit EPO, respectively.

The distribution of titanium and magnesium in powder film coated and conventional film coated tablets were compared using LIBS. The results suggested that the dry powder process gives more uniform distribution of titanium in the film coat. Therefore electrostatic dry powder coating may be desirable for active drug coating. As expected magnesium was not found in the non-powder coated tablet because it is generally not used for the manufacture of ibuprofen tablets. Ibuprofen forms a eutectic mixture with magnesium stearate. The data also show that some magnesium stearate may migrate to the film coat of the powder coated tablets.

Table 2—Determination of titanium and magnesium content in electrostatic powder film coated tablets (Lots 1-3) and conventional film coated ibuprofen tablets using LIBS

Lot #	Ti			Mg		
	Intensity	RSD (%) Inter-tablet	Average RSD Inter-site (%)	Intensity	RSD (%) Inter-tablet	Average RSD Inter-site (%)
1	30	3.6	14	2023	7.1	25
2	241	2.7	20	1922	5.1	20
3	26	6.2	18	2144	8.4	23
4	2074	14	13	ND	N/A	N/A

ND = Not detected

CONCLUSIONS

It is possible to use electrostatic powder film coating in conventional pans with common pharmaceutical excipients for cosmetic and functional applications. The LIBS results also demonstrated uniform coat ingredient distribution. Therefore this process may also be useful for coating of drug substances.

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