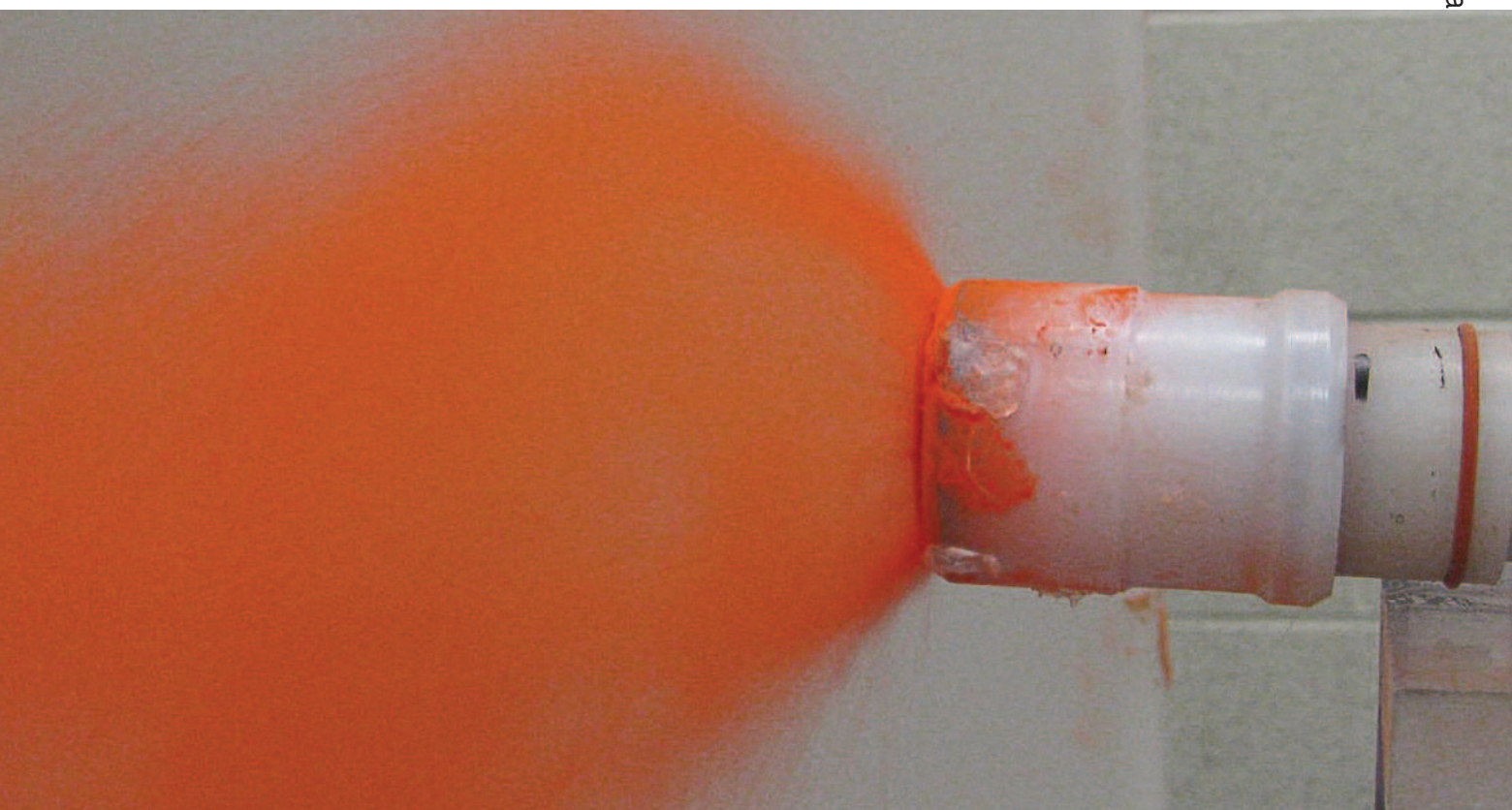

tablet coating

A METHOD FOR ELECTROSTATICALLY
POWDER COATING TABLETS

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This article describes a method of applying dry powder coatings to tablets using electrostatic technology. Powder coating may offer advantages over traditional liquid coating, including better environmental friendliness, efficiency, and cost effectiveness.

Most of today's pharmaceutical film coatings are aqueous polymer dispersions, while a small portion use organic solvents, which have several disadvantages, including toxicity, flammability, and cost. Although aqueous film coatings eliminate the disadvantages of solvents, they use a lot of energy to heat-cure the coatings, usually require long processing times, are potentially at risk for microbial contamination, and may be unsuitable for moisture-sensitive products.

These limitations are well known, and several methods have been proposed and tested to overcome them, including compression coating (tablet-in-tablet), hot-melt coating, dry power coating, and photo-curable coating. For a number of reasons, commercialization of these processes has been limited. One method of applying powder coatings came from Phoqus Pharmaceuticals [1, 2]. Its process applies electrostatically charged powders to tablets that are fixed in a holder that flips them to expose both sides to the coating. The coated tablets are then cured at 120°C using infrared radiation. While the process has shown promise, drawbacks include process complexity and the need for specialized equipment (no standard coating pan).

The powder coating method described here combines our fine-powder electrostatic coating process developed earlier with a traditional liquid coating pan [3, 4]. In fact,

the process itself mimics traditional liquid film coating: Tablets are loaded into a rotating pan, spray guns apply the coating, and heat cures the coating. The main difference is the use of powder instead of liquid for the final tablet coating and the application of an electrostatic charge to the coating powder. The fine powder (30 microns or less) helps obtain a smooth coated surface, as do additives that improve powder flowability, without which the fine powder is too cohesive to flow smoothly [5]. One of the advantages of this electrostatic powder coating method is its use of a retrofitted coating pan intended for liquid coating. Furthermore, it can apply a variety of coating materials to provide immediate, enteric, or extended release. The coatings included Opadry AMB and Acryl-EZE MP (Colorcon, West Point, PA) and Eudragit EPO, Eudragit L 100-55, and Eudragit RS/RL (Evonik, Parsippany, NJ), as well as an Ethocel (Dow Chemical, Midland, MI).

Process and equipment

Figure 1 shows the four phases of the dry powder coating process. To begin, the tablets are heated and the liquid plasticizer is applied, followed by application of the charged powder. Finally, heat is once again applied, fusing the powder into a film. The role of the liquid plasticizer is to reduce the glass transition temperature of the coating polymer so that that a film will form at temperatures less than 60°C.

Testing was conducted on a laboratory-scale system (Figure 2). The coating pan was electrically grounded, and an electrostatic powder spray gun (Nordson, Westlake, OH) was inserted through the front door of the coating pan. A volumetric screw feeder (Schenk AccuRate, Whitewater, WI) introduced the coating powder into the gun. A fluid dispensing and metering pump (Fluid Metering, Syosset, NY) fed the liquid plasticizer to an atomizing nozzle.

The first step is to heat the tablets, after which the liquid plasticizer is applied. Immediately thereafter, the powder gun delivers the negatively charged powder, which reaches the tablet surface by a combination of electrical attraction and the force of the carrier air. (Over the course of testing, it was sometimes beneficial to alternate application of the liquid and powder to achieve a thick coating.) Because the spray gun directs the powder toward the tablet bed, which completely covers the lower area of the coating pan, there is no obvious powder accumulation on the inner surface of the coating pan.

Effect of electrostatic charging on powder deposition

To investigate how electrostatic charging affected powder deposition on the tablet surfaces, three coatings were applied, first with a 60 kilovolt charge and then with no electrostatic charge. The results listed in Table 1 show that powders with an electrostatic charge produce thicker coats. Furthermore, because of the electrical field that develops between the charging gun and tablet bed, the negatively charged powder adhered better to the

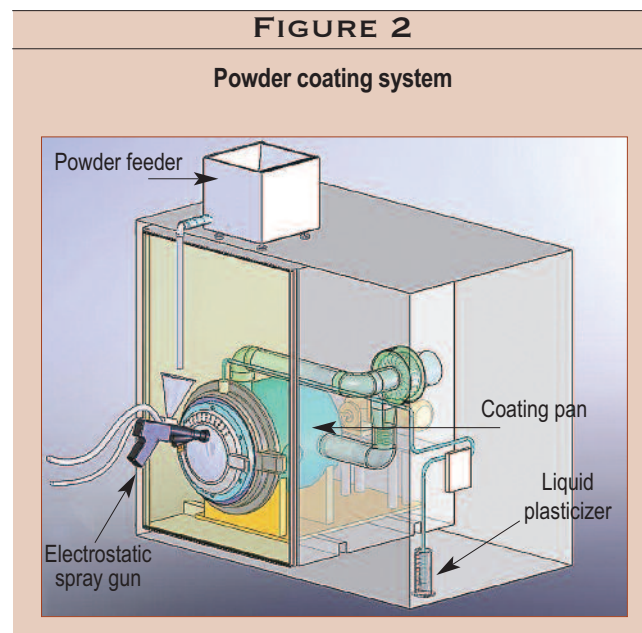
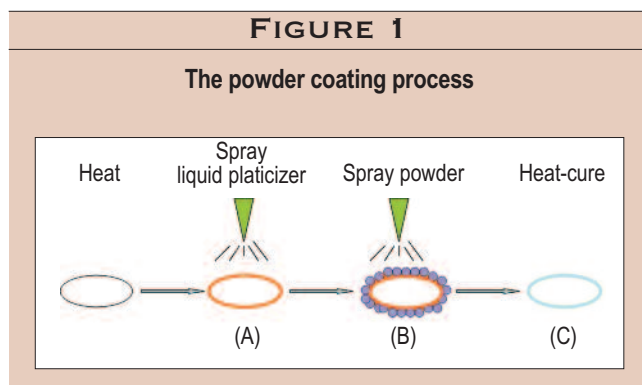


TABLE 1

Coating level of tablets coated with and without electrostatic charging

Coating material	Coating level (% weight gain)	
	60-kV charge	0-kV charge
Opadry AMB	3.8	2.4
Eudragit RS/RL	2.9	1.5
Eudragit EPO	3.1	2.1

tablet surfaces than the non-charged powders, reducing overspray. Without an electrostatic charge, powder adhesion was produced by capillary force (wicking) between the powder and liquid.

Coating thickness uniformity

The coated tablets in Figure 3 show smooth surfaces after coating with a variety of materials. The size of the coating particles ranged from 16.5 to 25.1 microns.

Laser-induced breakdown spectroscopy, or LIBS (PharmaLIBS 250, Pharma Laser, Boucherville, QC Canada), was used to measure the uniformity of coating.

FIGURE 3

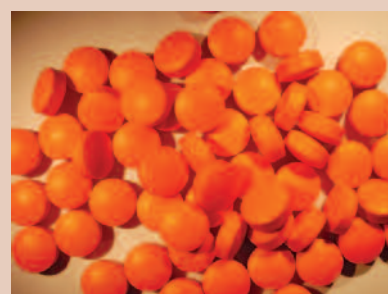
Powder-coated tablets



a. Opadry AMB



b. Eudragit EPO



c. Eudragit L 100-55



d. Acryl-EZE MP



e. Eudragit RS/RL



f. Ethocel

LIBS analysis permits the acquisition of data at multiple sites across each tablet. At each site, the laser bores a hole into the tablet, releasing coating and tablet core particles that undergo spectroscopic analysis. In this way, LIBS can identify the specific elements that reside at different depths within the tablet. Titanium (Ti) was the target element in this case because it was found in all of the coatings, but in none of the tablet cores. By monitoring the Ti emission line from the LIBS, it was possible to determine the uniformity of coating thickness.

Table 2 shows the relative standard deviation (RSD) of Ti emissions between multiple sites across each tablet and across different tablets. The inter-tablet RSD indicates that the thickness uniformity of several liquid-coated tablets (Motrin, McNeil Consumer Healthcare, Fort Washington, PA) varied more than that of tablets that

were powder coated. The inter-site average RSD shows that coating thickness uniformity of individual tablets was comparable whether coated with liquid or dry powder.

Dissolution testing

Ibuprofen tablets bearing four different coatings (Eudragit EPO, Opadry AMB, Eudragit L 100-55, and Acryl-EZE MP) were used to test in vitro drug release profiles. The dissolution tests were performed according to USP General Chapter <711> (paddle method). For tablets coated with Eudragit EPO or Opadry AMB, a pH 1.0 hydrochloric acid (HCl) solution was used. For tablets coated with Eudragit L 100-55 or Acryl-EZE MP, a 0.1N HCl solution was used for 2 hours, followed by a pH 6.8 phosphate buffer solution. At predetermined intervals, 10-milliliter samples were withdrawn, replaced by an equal volume of fresh solution. The ibuprofen concentration was measured using a UV visible-light spectrophotometer (Model 8453, Agilent Technologies, Santa Clara, CA). Figures 4 and 5 show the release profiles.

Stability testing

Stability tests on the Eudragit EPO and Eudragit L 100-55 powder-coated tablets were also conducted. These tablets were put in a stability chamber for 3 and 6 months at 40°C and 75 percent relative humidity (RH) and for 12 months at 25°C and 60 percent RH. Their drug release profiles were then tested according to USP standards and, as figures 6 and 7 show, the profiles were little changed after 12 months.

TABLE 2

Coating thickness uniformity based on amount of titanium detected using laser-induced breakdown spectroscopy

Sample	Ti		
	Intensity	Inter-tablet RSD (%)	Inter-site average RSD (%)
Eudragit EPO	30	3.6	14
Acryl-EZE MP	241	2.7	20
Eudragit L 100-55	26	6.2	18
Motrin	2,074	14	13

FIGURE 4

Dissolution tests of tablets with immediate-release coating

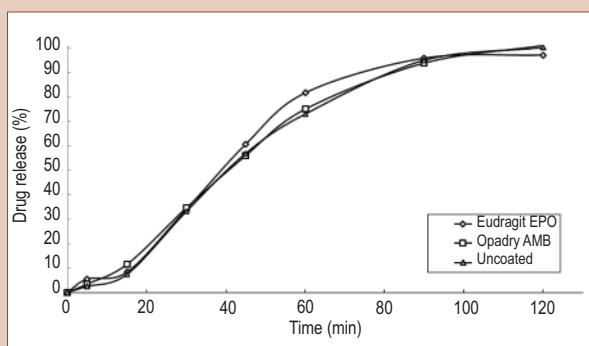


FIGURE 7

Dissolution tests of tablets with delayed-release coating (Eudragit L 100-55)

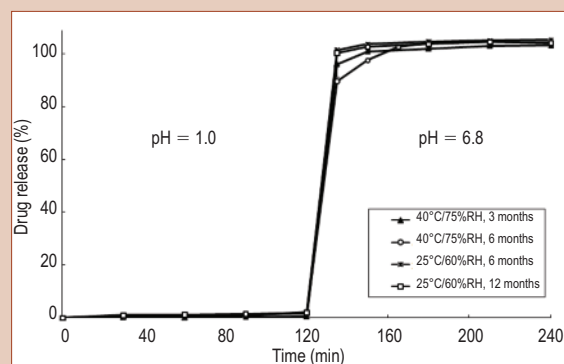


FIGURE 5

Dissolution tests of tablets with delayed-release coating

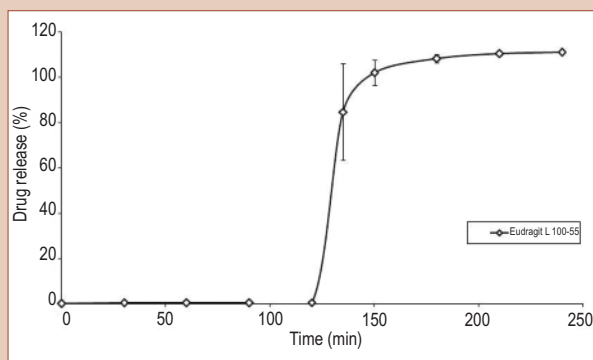
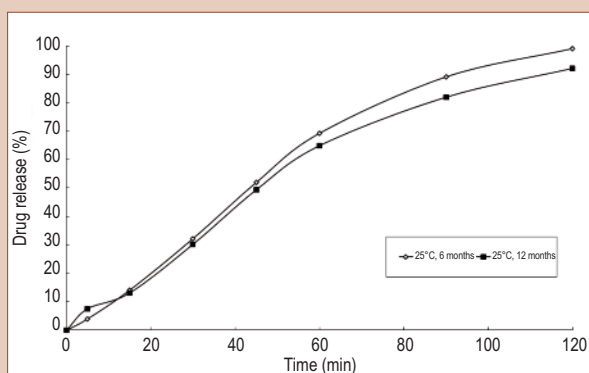


FIGURE 6

Dissolution tests of tablets with immediate-release coating (Eudragit EPO)



Conclusion

All of the test results described above indicate that electrostatic dry powder coating is a promising technology for pharmaceutical applications, and we are preparing to commercialize the method. We have already succeeded in coating 3-kilogram batches of placebo tablets with Acryl-EZE MP in a 15-inch-diameter coating pan. Weight gain was 9 percent after 2.5 hours. T&C

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