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Research Paper

Applying a novel electrostatic dry powder coating technology to pellets

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ABSTRACT

The present study aimed to apply a novel dry powder technology to coat pellets with different coating materials grounded into fine powders. Piroxicam, a non-steroidal anti-inflammatory drug, was used as the active pharmaceutical ingredient (API). Eudragit® EPO, Eudragit® RS/RL and Acryl EZE were used as the coating materials to achieve immediate release, sustained release and delayed release, respectively. Three steps including preheating, powder adhesion and curing were carried out to form the coating film while liquid plasticizers were used to decrease the glass transition temperature of coating powders and also served to reduce the electrical resistance of pellets. Results of SEM indicated coating film could be better formed by increasing curing temperature or extending curing time. Dissolution tests showed that three different drug release profiles, including immediate release, sustained release and delayed release, were achieved by this coating technology with different coating formulations. And the dry powder coated pellets using this developed technology exhibited an excellent stability with 1 month at 40 °C/75% RH. The coating procedure could be shortened to within 120 min and the use of fluidized hot air was minimized, both cutting down the overall cost dramatically compared to organic solvent coating and aqueous coating. All results demonstrated that the novel electrostatic dry powder coating method is a promising technology in the pharmaceutical coating industry.

1. Introduction

In the pharmaceutical industry, solid dosage forms including tablets and pellets are commonly coated to achieve taste masking, chemical and physical protection and modification of drug release characteristics. Presently, liquid coating is most widely used, where the coating materials are dissolved/dispersed into organic solvent/water to form a solution/suspension, then sprayed onto solid dosage forms to achieve a coating film. Organic solvent based coating can make the film formation faster and more uniform due to the dissolved nature of coating polymers. However, the toxicity of organic solvent does decrease the safety of the drug and cause environmental related problems. As a result, aqueous coating, where water is used as the solvent, started to dominate in 1990s and remains the preferred approach in the pharmaceutical industry. Nevertheless, aqueous coating still possesses many limitations such as longer processing time and higher energy consumption. Also aqueous coating is not appropriate for the moisture sensitive APIs.

Driven by these issues, many efforts have been made to develop alternative coating techniques to reduce or avoid the use of organic solvent as well as water [1–5]. Details of each coating technology can be found in the following reviews [6–8].

Powder coating has gained tremendous attention owing to their distinct characteristics, such as highly valued for energy savings, environmental friendliness, low overall operation cost and significant reduction of coating time [9,10]. Some of the earlier attempts used liquid plasticizers in the coating process to wet the dosages surface, promoting the adhesion of coating powders. Also the liquid plasticizer could reduce the glass transition temperature of coating materials to enhance the film formation under a lower temperature [10–14]. However, surplus plasticizer can possibly lead to very soft or sticky film, so that careful balance needs to be reached between the plasticizer concentration for a sufficient coat thickness and that for a flexible and dry coat. Cerea et al. [15] developed a dry powder coating technology without using any solvent or plasticizer. In this coating technology, a laboratory-scale spheronizer was used as the coater with a motorized single screw powder feeder and an infrared lamp positioned on the top of the spheronizer as a heating source. Coating powders were continuously spread onto the tablets by the powder feeder and film formation was completed in a following curing step in a static oven at 80 °C for 12 h. The advantage of this technology is

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that there is no sticky film due to the absence of liquid plasticizer, while the long curing time (12 h) and high curing temperature (80 °C) make it hard to apply in the industry.

Electrostatic coating has gained tremendous attention as a promising alternative to liquid coating in many industries, owing to its advantages in energy saving, high transfer efficiency, and environmental friendliness [16]. However, application of electrostatic coating in pharmaceutical industry is very limited due to the much weaker electrical conductivity of solid dosages. In order to overcome the limitations of those previous attempts, the authors' group developed a novel dry powder coating technology [17]. By spraying certain amount of liquid plasticizer onto the surface of the solid dosage forms, the electrical resistance can be dramatically decreased so as the electrostatic coating method can be adapted to form an electrical field between the electrostatic gun and the grounded substrate, which can direct the powder flow and enhance deposition of charged particles. And also a more uniform coating film could be promoted by this technology due to the better distribution of deposited particles caused by the repulsive force among the charged particles. This dry coating technology utilizes the same coating pan that was commonly used for solvent coating as well as aqueous coating, so that no major equipment change would be required with the shift to the new powder coating technology. This technology has been successfully applied on the larger solid dosage forms such as tablets for all common drug release profiles including immediate release [18], drug sustained release [19] and drug delayed release [20], respectively and was successfully demonstrated in an O'Hara Labcoat Model I [21].

On the other hand, coating of smaller solid dosage forms such as pellets, being solvent coating or aqueous coating, was carried out in a fluid bed coater in the present pharmaceutical industry [22], because those small pellets are very easy to agglomerate that prevents uniform coating. Although the fluidization of pellets aids in achieving a more uniform coating film, much more hot air is required compared to a pan coater to fluidize the pellets, bringing significantly high cost. Also longer processing time up to several hours or even days due to the low coating efficiency leads to an even larger amount of energy consumption. The objective of present study was to extend the novel electrostatic dry powder coating technology in a pan coater to pellets to modulate drug release profiles.

2. Coating equipment and process

2.1. Coating equipment

As shown in Fig. 1, the coating system includes a rotatory coating pan, a liquid plasticizer spray system, an electrostatic spray gun and a powder feeder. The rotatory coating pan, the same as commonly used for the organic/aqueous coating in the pharma industry, is electrically grounded. The liquid plasticizer spray system includes a metering pump and an atomizing nozzle. The electrostatic spray gun is applied to regulate and charge the coating powder and uniformly spray them onto the surface of the dosage forms preloaded in the pan.

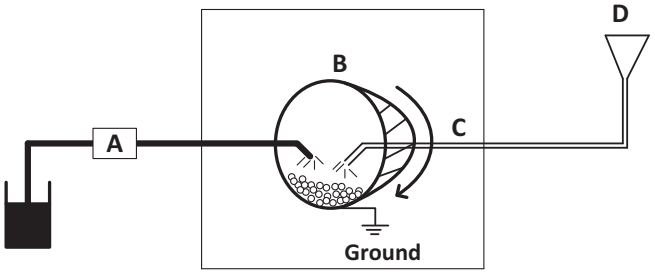

Fig. 1. Schematic of the electrostatic powder coating system. (A) Liquid plasticizer spray system, (B) coating pan, (C) electrostatic spray gun, and (D) powder feeder.

2.2. Electrostatic dry powder coating process

The coating process was performed in three steps. A batch of 100 g pellets were firstly loaded into the coating pan and preheated to a given temperature. Then a given amount of liquid plasticizer was sprayed onto the surface of the pellets. It is followed immediately by spraying dry coating powder. If necessary, repeat those two steps for several times until enough particles were deposited on the surface of the pellets. The temperature of coating pan was maintained as required until the particles deposited on the pellets were cured to produce a uniform coating film.

The coating level (%) of the pellets could be obtained from the weight gain of coated pellets divided by the weight of uncoated ones. The coating powders contain coating material, talc powder, nano silica and pigments.

3. Materials and methods

3.1. Materials

Piroxicam pellets with a particle size of 0.9–1.18 mm were provided by Gaocheng Biotech & Health CO., Ltd. Eudragit® EPO, Eudragit® RS/RL, Eudragit® L100-55 and Colloidal silicon dioxide (AEROSIL® 200 Pharma) were donated by Evonik Degussa Corporation (Germany). Acryl EZE was provided by Colorcon, Inc. (US). It is the enteric coating materials containing Eudragit® L100-55 developed by Colorcon, Inc. Talc powder was purchased from Mallinckrodt Baker Inc. (Canada). Triethyl citrate (TEC) and PEG 400 were obtained from Caledon Laboratories Ltd. (Ontario, Canada) and EMD Chemicals Inc. (Ontario, Canada), respectively.

3.2. Particle size reduction and analyses

Particle size reduction of coating materials was achieved by using a blade grind mill. A particle size analyzer (TSI Corporation, Model 3603, Shoreview, MN, USA) was used to confirm the particle size of the coating particles. The particle size at 50% of total weight fraction was used as the average particle size. Table 1 gives the average particle size of coating powder used in the present study.

3.3. Thermal analysis of coating polymers

Differential scanning calorimetry (DSC) analysis (Mettler Toledo, DSC822, Mississauga, Canada) was used to investigate the glass transition temperature of raw coating materials and the mixture of coating materials with plasticizers (TEC and PEG 400) of different weight ratio (plasticizer/coating materials). Samples with a weight of 10 mg were tested under nitrogen atmosphere with a heating rate of 2 °C/min over the temperature range of 20–200 °C.

Table 1
Average particle size of coating powder.

Coating powder	Average particle size (μm)
Eudragit® EPO	23.3
Eudragit® RS	48.7
Eudragit® RL	39.7
Acryl EZE	20.8
Talc powder	28.9