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Original Research Paper

Sustained drug release from electrostatic powder coated tablets with ultrafine ethylcellulose powders

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ABSTRACT

In the present study, tablets were successfully coated with ultrafine ethylcellulose powders by using an electrostatic dry powder coating technology and sustained drug release was successfully achieved. The angle of repose (AOR) of the ultrafine powders of ethylcellulose was significantly reduced by adding nano sized colloidal silicon dioxide, indicating a significant improvement of flowability. Variations in charging voltage of the electrostatic gun had a significant influence on the coating powder adhesion and coating efficiency. Lactose and triethyl citrate (TEC) were used as the solid and liquid plasticizers to reduce the glass transition temperature (T_g) of ethylcellulose. The presence of liquid plasticizer could also increase the electrical conductivity of drug tablets so as to promote the coating powder adhesion. Other factors that affect the film formation include curing time and curing temperature. Dissolution tests indicated that the drug release from electrostatic dry powder coated tablets could be altered by adjusting coating level or pore former ratio in the coating formulation.

1. Introduction

In pharmaceutical industry, solid dosage forms are commonly coated with polymers to achieve sustained drug release [1], to alleviate the side effects caused by the high drug plasma concentration due to the immediate release. Several polymers are commercially available for sustained release coating like acrylic acid derivatives, poly (vinyl acetate) and cellulose derivatives, such as ethylcellulose. Among those, ethylcellulose is particular appropriate for the sustained release coating due to its excellent robust properties such as nontoxic, nonallergenic and nonirritant [2,3]. It can be applied either from organic solvent solutions or from aqueous dispersions (Fig. 1). For solvent coating, ethylcellulose as well as other excipients are dissolved into an organic solvent to form a coating solution and then the solution is sprayed onto the surface of the solid dosage forms to form the coating film by evaporating the solvent. This method can obtain a very smooth and uniform coating film. However, the presence of the organic solvent could cause safety and environmental issues. For aqueous coating, ethylcellulose particles, pigments and additives are firstly milled into fine powders and mixed together and then they are dispersed into water to form a coating suspension, which is sprayed onto the surface of solid dosage forms to form a coating film by evaporating the water. Aqueous coating remains the preferred approach to obtain the coating film with ethylcellulose because it can eliminate those environmental related problems caused by the organic solvent. However, it still possesses many limitations such as higher energy consumption and longer processing time with hot air handling and equipment cleaning. Also aqueous coating is not suitable for the moisture sensitive drugs.

In order to overcome these limitations, several earlier attempts of dry coating methods have been reported, trying to coat solid dosage forms with ethylcellulose (EC). Lin et al. [4] used a direct compression method to coat tablets with micronized EC to form the out layer of the tablet core. In this coating process, the tablet core was precisely positioned in the center of the die, encapsulated by the EC powder and then they were compressed to form the out layer film. This is a total dry coating method without using any solvent or water and it could form a very thick coating film with very high coating efficiency. However, the thickness of the film was reported to be not uniform owing to the difficulty of placing the core tablet in the center of the die.

Different with Lin's work, Pearnchob and Bodmeier [5] developed a dry powder coating technology to coat pellets with micronized ethylcellulose particles, which was further optimized by Terebesi and Bodmeier [6]. In their technology, the coating formulation contained two components, one was a powder mixture

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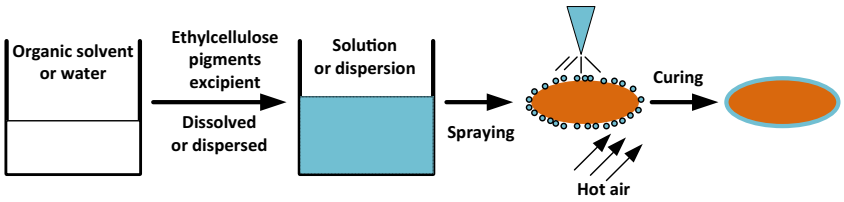

Fig. 1. Liquid coating process with ethylcellulose.

(coating polymer plus talc) and the other was a mixture of liquid materials (plasticizer plus binder solution). They were sprayed separately into a coating chamber of a fluidized bed coater, followed by an oven-curing step under different conditions (60–80 °C, 2–24 h). Although drug extended release was achieved by using this coating technology, it was unable to form a uniform coating film and acceptable surface morphology of the coated pellets. Also the oven curing temperature is too high (up to 80 °C) and the curing time is too long (up to 24 h), making it difficult for the industrial application.

Although there are some other dry coating technologies that have been reported recently such as hot-melt coating [7–9], supercritical fluid coating [10–13] and photocuring coating [14–16], none of them is suitable for ethylcellulose owing to its high glass transition temperature.

Researchers of Particle Technology Research Centre (PTRC) in Western University [17] developed an electrostatic dry powder coating technology by combination of plasticizer, electrostatic and heat to promote the coating powder adhesion and film formation under a lower curing temperature with a shorter processing time. The electrostatic coating method is adapted to create an electrical field between the electrostatic gun and grounded solid dosage forms, directing the flow of coating powders so as to enhance the coating powder adhesion on the solid dosage forms. Also the coating film is more uniform due to a better distribution of deposited coating powders resulting from the repulsive force among the charged particles. By using this electrostatic powder coating technology, different coating formulations have been successfully developed including Opadry® AMB and Eudragit® E PO [18], Eudragit® RS/RL [19] and Eudragit® L100-55 [20]. This electrostatic powder coating technology was also successfully applied to coat smaller dosage forms like pellets [21].

This study aims to apply this electrostatic powder coating technology to coat tablets with ultrafine ethylcellulose powders so as to achieve sustained drug release.

2. Materials and methods

2.1. Materials

Ethylcellulose was provided by Colorcon, Inc. (US). Talc powder was purchased from Mallinickrodt Baker Inc. (Canada). Triethyl citrate (TEC) was purchased from Caledon Laboratories Ltd. (Ontario, Canada). Lactose (monohydrate) was obtained from GlaxoSmithKline, Inc. (Canada). Colloidal silicon dioxide (AEROSIL® 200 Pharma) was donated by Evonik Degussa Corporation (Germany). Salbutamol sulfate was provided by Nanjing Pharmaceutical Factory (Nanjing, China). Avicel® Microcrystalline cellulose PH-102 was purchased from FMC Corporation (USA), plasdone K-29/32 was purchased from ISP technologies, INC. and Magnesium stearate was purchased from Alfa Aesar (Massachusetts, USA). Placebo tablets (diameter: 7.0 mm, thickness: 3.8 mm, weight: 0.16 g, hardness: 66 N) were obtained from Pathon (Ontario, Canada). PVA-g-PEG (PVA-PEG graft copolymer, Kollicoat® IR) was purchased from BASF (Ludwigshafen, Germany).

2.2. Particle size reduction and analysis

A blade grind mill was used to reduce the particle size of coating materials, after which a particle size analyzer (TSI Corporation, Model 3603, Shoreview, MN, USA) was used to confirm the particle size of the coating particles. The average particle size in this study is the size at 50% of total weight fraction, which is given by Table 1.

2.3. Angle of repose (AOR)

In order to characterize the flowability of coating powers and also to investigate the influence of nano sized additives (colloidal silicon dioxide) on the flowability of ultrafine powders, measurement of the angle of repose was carried out using a PT-N Hosokawa Powder Characteristic Tester, following the standardized testing procedures of ASTM D6369-08 (ASTM Standard D6369-08, 1999). During each test, a powder sample was first loaded onto a screen mounted with a vibrator. Under the screen there is a mounted funnel, which is used to let the powder sample fall through down to a plate which was aligned with the funnel. When the whole plate was covered with the powders, angle of repose was obtained by measuring the largest angle between the powder pile surface and the horizontal plane. In order to achieve an accuracy result, each test was repeated 3 times and the average was used.

2.4. Differential scanning calorimetry (DSC)

Glass transition temperature of pure ethylcellulose and the mixture of ethylcellulose with plasticizers (TEC and lactose) at different weight ratio (based on ethylcellulose) were investigated using the differential scanning calorimetry (DSC) analysis (Mettler Toledo, DSC822, Mississauga, Canada). The weight for each sample was 10 mg and nitrogen was used as the test atmosphere. The heating rate for the test was 2 °C/min over the temperature range of 20–200 °C.

2.5. Tablets preparation

The component of the tablets core, shown as Table 2, includes drug (salbutamol sulfate), microcrystalline cellulose, PLASDONE® K-29/32 (PVP) and magnesium stearate. A mixture of drug, microcrystalline cellulose and PLASDONE® K-29/32 (PVP) were dry granulated using a granulator (Mechanomill MM-20N, OKADA SEIKO Co. Ltd, Iwate, Japan) at 300 rpm for 6 min, then they were mixed with magnesium stearate (300 rpm for 3 min), after which the powder mixture was compressed into convex tablets with 5 mm

Table 1
Average particle size of coating materials.

Materials	Average particle size (μm)
Ethylcellulose	25.8
Lactose	29.1
PVA-g-PEG	21.8
Talc	28.6