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Sustained release coating of tablets with Eudragit® RS/RL using a novel electrostatic dry powder coating process

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ABSTRACT

The objectives of this study were to develop an electrostatic dry powder coating process for sustained coating tablets with Eudragit® RS/RL and to investigate the effects of various factors and operating conditions on the coating process and drug release profile. A liquid plasticizer (triethyl citrate) was sprayed onto the surface of the tablets followed by spraying coating powder by an electrostatic spray gun. The powder coated tablets were cured at elevated temperature for a film formation. Liquid plasticizer played important roles in lowering down the glass transition temperature (T_g) of the coating polymer and increasing the surface electrical conduction of tablet cores. Electrostatic assisted coating deposition was confirmed by the fact that higher coating level was obtained with electrical charging than the ones without it. The micrographs of scanning electron microscopy (SEM) of coated tablets showed that the film formation mainly occurred during the curing step. Higher curing temperature and longer curing time help enhance the film formation. The *in vitro* drug release profiles indicated that curing time, temperature, coating level and ratio of Eudragit® RS/RL were the main factors affecting the sustained release profile. The electrostatic dry powder coating process has been demonstrated to be an alternative for tablet sustained release coating with Eudragit® RS and RL.

Coating of pharmaceutical solid dosage forms is a common process to achieve taste masking, enhancement of stability, and modification of drug release behavior, to name a few. Modern pharmaceutical coating technology started with sugar coating and progressed through organic and aqueous-based film coating. Organic based film-coating technology suffers toxical, environmental, cost and safety-related disadvantages (Cole et al., 1995). The aqueous-based coating technology was developed to phase out organic based coating using water as solvent. However, the aqueous-based coating has the problems of slow drying rate of coating, high energy input, microbial contamination, etc. (Bose and Bogner, 2007). Furthermore, the presence of water during the coating process and residual moisture in the film may affect stability of certain water sensitive drugs (Plazier-Vercammen and De Neve, 1993; Amighi and Moes, 1996). The limitations of organic and aqueous film-coating techniques are principally associated with solvent, which is used to dissolve or disperse the coating materials. Therefore, a coating process without organic solvent or water being used is considered to be a solution to the above-mentioned problems.

Dry powder coating process, which eliminates solvents in the coating process, was recognized to be a further step-up for coating technology development and a promising technology to overcome the limitations associated with organic and aqueous-based film-coating techniques. Dry powder coating process for pharmaceutical dosage forms was first developed by Obara in the late 1990s (Obara et al., 1999). The coating materials particles are directly layered onto the surface of cores with a liquid plasticizer being sprayed simultaneously. Film formation occurs during the following curing phase at elevated temperatures. Pearnchob and Bodmeier used a modified fluidized bed Wurster process to coat pellets with different formulations of Eudragit® RS, ethylcellulose and shellac to achieve sustained and delayed release (Pearnchob and Bodmeier, 2003a,b,c). It was found that higher coating levels were required for this process but a shorter processing time, compared to conventional liquid-based coating process. The processes described above were not completely solvent free and small amounts of liquid plasticizer or polymer solution were used to facilitate the film formation. The completely liquid-free dry powder coating processes were developed by some researchers later on and applied to coat Eudragit® EPO (Cerea et al., 2004), Eudragit® RS/RL (Zheng et al., 2004) and Eudragit L® 100-55 (Sauer et al., 2007). Powder adhesion to the tablet is improved by a partially melted polymer that generates binding force between particles and tablet surface. In these processes, some polymers with higher glass transition temperature (T_g) like Eudragit® RS, Eudragit® RL and Eudragit L® 100-55 were pre-plasticized with liquid plasticizer using hot-melt extru-

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sion prior to coating in order to lower down T_g to generate binding force at certain operating temperature.

Electrostatic dry powder coating is an environmentally friendly coating technique that has been widely used within the paint and automobile industries. The first attempt of application of electrostatic dry powder coating to pharmaceutical tablets and medical devices was reported by Phocus Ltd. (Feather and Nelson, 2002; Whiteman et al., 2003). The reported electrostatic powder coating process involved the deposition of charged powders on each side of the ground tablets separately and heating at 120 °C for several minutes by IR radiation to allow for a film formation. However, the approach has been compromised by a complicated coating process and complex coating apparatus, off-setting the benefits of switching from liquid to powder coating. Furthermore, it has difficulties coating tablets with well-defined edges (Hallett, 2006).

A novel electrostatic dry powder coating technology for pharmaceutical dosage forms was developed by the authors at The University of Western Ontario in 2007 (Zhu et al., 2007). In contrast to Phocus' coating process, the technology combines electrostatic dry powder coating with a traditional liquid pan coater for the first time, making it more feasible for pharmaceutical coating. In comparison to the normal dry powder coating, electrostatic powder coating uses electrical field created by an electrostatic charging gun and grounded substrate to assist deposition of charged powder particles. The electrical attractive force between coating particles and tablets enhances the particle deposition on the tablets. The electrical repulsive force among the charged particles promotes the uniform particle deposition and uniform coating film. As a result of that, electrostatic powder coating offers better particle deposition and coating film.

The objective of the current study was to develop an electrostatic dry powder coating process in a liquid pan coater system for coating Eudrgait® RS/RL on tablets. Eudragit® RS and Eudragit® RL are copolymers derived from esters of acrylic and methacrylic acid developed by Evonik-Degussa for sustained release coating of pharmaceutical dosage forms. The effects of liquid plasticizer and curing conditions on the coating process and sustained release profile were also investigated.

1. Materials and methods

1.1. Materials

Eudragit® RL and Eudragit® RS were provided by Evonik Degussa Corporation (Germany). Ibuprofen tablets and placebo tablets were obtained from Pathon (Ontario, Canada). Triethyl citrate (TEC) was purchased from Caledon Laboratories Ltd. (Ontario, Canada). Colloidal silicon dioxide (AEROSIL® 200 Pharma) was donated by Evonik Degussa Corporation (Germany). Talc was purchased from Mallinickrodt Baker Inc. (Canada).

1.2. Particle size reduction and analysis

Particle size reduction of Eudragit® RL, Eudragit® RS and Talc was conducted separately by a jet mill, prior to use. Particle size of the powder was confirmed by a Particle Size Distribution Analyzer (TSI Corporation, Model 3603, Shoreview, MN, USA). The particle size at 50% of total weight fraction was used as average particle size. The average particle size of Eudragit® RL, Eudragit® RS and Talc was 18.4, 16.5 and 28.9 μm, respectively.

1.3. Differential scanning calorimetry (DSC)

The glass transition temperature (T_g) of the Eudragit® RL, Eudragit® RS polymers and mixture of polymers and liquid plasticizer (TEC) with various ratios were examined by thermomechanical analysis (DSC822, Mettler Toledo, Mississauga, Canada). The samples of 10–15 mg were accurately weighted into aluminum pans and then sealed. The samples were tested at a heating rate of 5 °C/min over the temperature range of −20 to 100 °C under nitrogen atmosphere.

1.4. Electrical resistance test

A batch of 20 g of ibuprofen tablets and 60 g of placebo tablets were preheated in the coating pan for 10 min followed by spraying liquid plasticizer (0.3 g/min). Three tablets were taken out to test their electrical resistance by an electrometer (Keithley 610B, Keithley instruments, Inc., USA) at different spraying time points (0, 1, 2, 3 and 4 min) and right after spraying coating powder. The guarded method was employed to test the resistance of the tablets. The tablet was placed between two poles connecting to the INPUT of the electrometer and GROUND terminal, respectively. The tablet and poles are in a guarded chamber which is connected to ground point of the INPUT. Then the zero check button was unlocked and the resistance was read from the meter directly. The electrical resistance test of tablets was performed in duplicate.

1.5. Electrostatic powder coating process

The powder coating process was conducted in a laboratory scale electrostatic dry powder pan coater system comprising a coating pan with a maximum loading of 200 g (stainless steel, 14-cm diameter), a liquid spray nozzle, an electrostatic spray gun and a powder feeder (Fig. 1). The inside wall of the coating pan was mounted with four aluminum baffles, 90° apart, promoting a good tumbling movement of the tablets. The tablets (60 g placebo tablets and 20 g ibuprofen tablets) were loaded in the pan and preheated at certain temperature (30–60 °C) for 10 min before the coating started. The feeding of liquid plasticizer and coating powder were carried out alternately. First, liquid plasticizer (TEC) was regulated (flow rate, 0.3 g/min) by a fluid metering pump (Fluid Metering Inc., USA) and sprayed onto the tablet surface through a liquid atomizing nozzle for 2 min while the pan was rotating at speed of 30 rpm. Afterwards, a certain amount of coating particles was sprayed by an electrostatic spray gun (Nordson Corporation, USA). After feeding the liquid and powder, the tablets were further cured for 2 h to allow film formation. The coating powder contained 50% (w/w) of Eudragit® RL and Eudragit® RS and 49% of talc and 1% of pigment. The coating level (%) was calculated from the weight gain of coated tablets divided by the weight of uncoated tablets. Placebo tablets were used to conserve ibuprofen tablets while maintaining the volume of substrates.

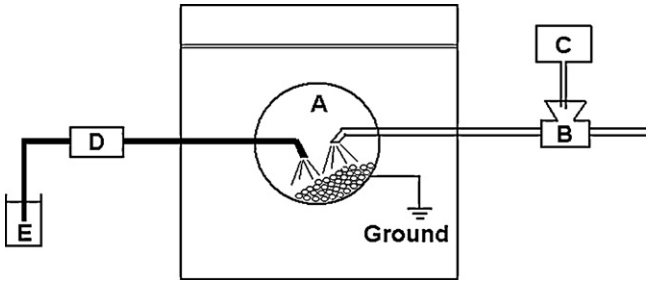

Fig. 1. Schematic of the electrostatic powder coating system. (A) Coating pan, (B) electrostatic spray gun, (C) powder feeder, (D) liquid metering pump, (E) liquid plasticizer.

1.6. Scanning electron micrographs

The surface morphology of the powder coated tablets at different curing temperatures (30–60 °C) and curing time (0, 60, 120 min) were examined by scanning electron microscopy (SEM). The samples were sputter coated with gold for 120 s under an argon atmosphere using Emitech K550 sputter coater (Emitech Ltd., Ashford, UK), and then were observed with a scanning electron microscope at 5.0 kV ×3.0k (S-2600 N Hitachi, Ontario, Canada).

1.7. Dissolution tests

In vitro release kinetics of ibuprofen from uncoated and Eudragit® RL/RS coated tablets were studied using United States Pharmacopeia (USP) apparatus (Apparatus 2, paddle; Huanghai Rcz-6c2, Shanghai, China). The drug release experiments (six tablets) were performed in a phosphate buffer (pH 7.2, 900 ml) at 37 °C with paddle rotating speed of 50 rpm. At predetermined time intervals, 10 ml of samples were withdrawn from each chamber using a syringe and replaced with fresh release medium. The samples were filtered and assayed using a UV–visible Spectrophotometer (8453, Agilent Technologies, Mississauga, Canada) at a wavelength of 222 nm.

2. Results and discussion

2.1. The glass transition temperature

As reported in the previous literature, the film formation of dry powder coating process conforms to the dry sintering theory of polymers, where the film formation occurs because of polymer particles deformation and viscous flow at elevated temperature higher than the glass transition temperature (T_g) of the polymer (Kablitz and Urbanetz, 2007). Due to the liquid plasticizer's abilities in reducing the T_g, brittleness and viscosity as well as improving flexibility and flow, it has been widely used to plasticize and improve the performance of polymer in dry powder coating process. T_g of the plasticized polymers was also considered as a key parameter in dry powder coating for adjusting curing temperature to achieve functional film formation (e.g. enteric release coating or sustained release coating) (Kablitz and Urbanetz, 2007).

T_g of pure Eudragit® RL and Eudragit® RS polymers and blends of polymer with liquid plasticizer (TEC) were examined by DSC to investigate the plasticizing effect of TEC on the polymers (Fig. 2). The T_g of pure Eudragit® RL and Eudragit® RS polymers was 62.5 and 58.0 °C, respectively, and were seen to decrease with higher concentrations of TEC in the blends. These results demonstrated that TEC was an effective plasticizer for Eudragit® RL and Eudragit® RS polymers. In dry powder coating process, effective plasticizer is critical for film formation. A low T_g of plasticized polymer allows a complete film formation under a relatively low curing temperature. For coating polymers like Eudragit® RL and Eudragit® RS that have relatively low T_gs, attention should be paid not to use too much plasticizer in the coating process. Sticky film and aging phenomenon will probably occur if the T_g of the coating polymer is lowered down below the room temperature.

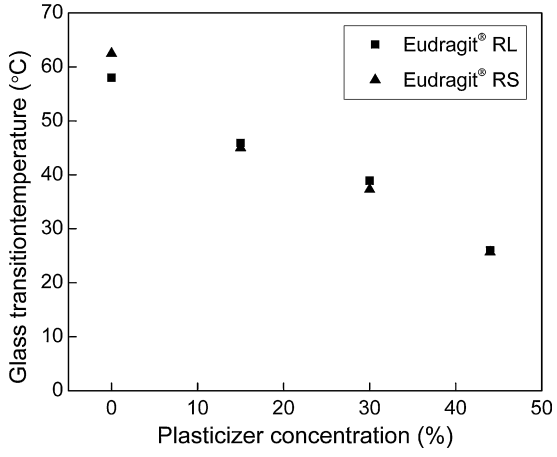

Fig. 2. The effect of plasticizer concentration on the glass transition temperatures of Eudragit® RL and Eudragit® RS.

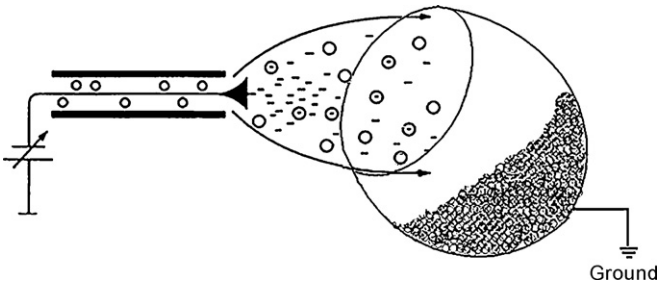

Fig. 3. The mechanism of electrostatic powder coating process. (A) Electrostatic spray gun, (B) coating pan.

2.2. Electrostatic dry powder coating process

2.2.1. Electrostatic assisted powder deposition

The mechanism of the electrostatic assisted powder deposition is shown in Fig. 3. The coating particles are first negatively charged at the tip of an electrostatic spray corona charging gun by a high voltage. An electrical field is generated between the tip of the gun and grounded coating pan. Then, the charged particles will follow the direction of electrical force and adhere onto the tablet surface under the electrical attractive force between the charged particles and grounded tablets. Based on the above-mentioned mechanism, the tablets are required to be electrically conductive to dissipate the negative charge brought by the coating particles. Otherwise, the negative charge will build up on the tablet surface, quickly reach the same electrical potential and repel the oncoming particles (back ionization), leading to poor particle deposition. As a result of that, tablets with low electrical conductivity cannot be successfully coated by electrostatic powder coating process.

Unfortunately, tablets are intrinsically not electrically conductive enough for electrostatic coating due to the high resistance of excipients used for compressing them (Grosvenor and Staniforth, 1996). It was recommended that pharmaceutical dosage forms with electrical resistance lower than 1×10^9 Ωm was suitable for electrostatic powder coating process (Bose and Bogner, 2007). In this study, the electrical conduction property of the tablets was enhanced by spraying liquid plasticizer. Fig. 4 shows the variation of tablet electrical resistance as a function of liquid plasticizer (TEC) spraying time. Before spraying the liquid plasticizer, the tablets showed high electrical resistance above 1×10^{13} Ωm. The resistance of tablet cores dropped quickly from 2×10^{13} Ωm to 3.7×10^{10} Ωm in the first 2 min, and then slowly down to 2×10^{10} Ωm in another 2 min, indicating that the surface conductivity of the tablet cores were greatly increased due to the surface wetting by liquid plasticizer. Even though the electrical resistance was slightly higher than the recommended value (1×10^9 Ωm), the tablets were more likely to be subject to electrostatic coating process. The resistance of the tablets marginally increased (up to 3.3×10^{10} Ωm) after spraying coating powders due to the coverage of dry powders on tablet surface. Increased tablet resistance will probably impede further powder deposition on tablet.

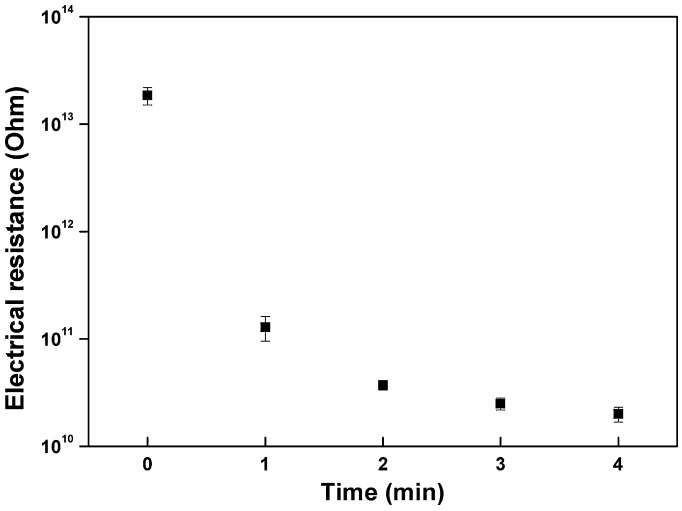

Fig. 4. The effect of liquid plasticizer on electrical resistance of tablets. (Liquid plasticizer: TEC, flow rate: 0.3 g/min, temperature: 50 °C.)

The most distinguished difference between the electrostatic powder coating and normal dry powder coating is that the electrical attractive force is introduced to assist particle adhesion in the coating process. In order to elucidate the effect of electrical attractive force in the particle adhesion, the tablets were coated with electrical charging (60 kV) and without it under same operating conditions. Higher coating level was obtained by coating tablets at 60 kV than that at 0 V ($3.0 \pm 0.17\%$ vs. $1.6 \pm 0.18\%$, $n = 3$), indicating that the electrical attractive force was able to enhance the adhesion of coating particles on tablet surface. In normal dry powder coating, particle adhesion to tablet surface was facilitated by the capillary force created by liquid plasticizer or other additives (Kablitz et al., 2008; Klar and Urbanetz, 2009). Sometimes, a large amount of liquid plasticizer or additive was used to obtain high coating level, which more likely produces a relatively low T_g of coating polymer and cause sticky coating film. Compared to normal dry powder coating, the developed electrostatic powder coating process has an additional electrical attractive force to improve particle adhesion. For some coatings where higher coating level are needed, the electrostatic coating more likely avoids a sticky coating film due to use of less liquid plasticizer or additives than normal dry powder coating. Another benefit is that the electrostatic powder coating produces smooth and uniform coating film. The same negative charge carried by the coating particles promotes uniform particle deposition due to the electrical repelling force.

2.2.2. Curing

In dry powder coating process, curing is the step that deposited particles coalesce into a film. The effect of curing time and temperature on film formation was observed by a scanning electron microscope (SEM). The SEM micrographs of the coated tablet at different curing time intervals are shown in Fig. 5. Before the curing started, the tablet surface was characterized as mainly voids and non-fused powder particles with a small portion of partially coalesced particles (Fig. 5A). The slight film formation occurred before curing started most likely because of the relatively high content of TEC in the initial powder deposition stage which leads to premature particle coalescence. After curing for 60 min (Fig. 5B), most of voids and non-fused powder particles had disappeared, indicating that film was formed to a large extent. However, the surface of the film was still rough. After 120 min (Fig. 5C), the large voids on the surface were barely visible and the surface was smoother in comparison to those at 60 min, indicating that more particles were

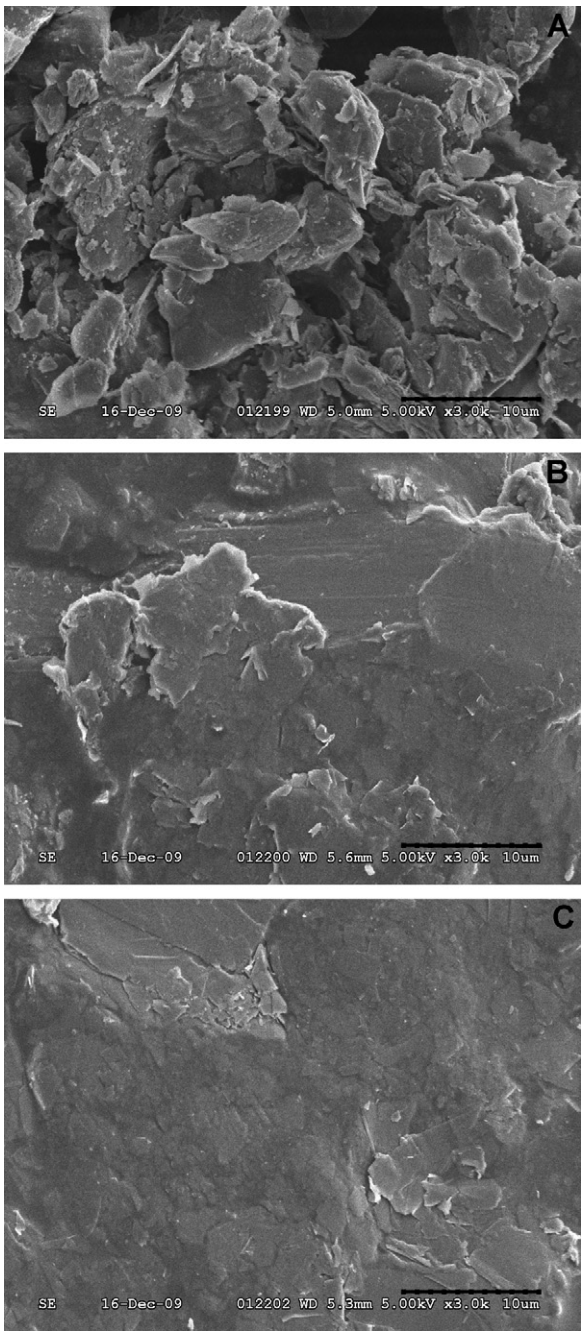

Fig. 5. SEM micrographs of Eudragit® RS/RL powder coated tablets curing at 50 °C for different time intervals: (A) 0 min, (B) 60 min, (C) 120 min.

fused into a film. Still, a few cracks were observed in the film. This indicated that longer curing time or higher curing temperature was needed to obtain a more complete film. The SEM micrographs of the coated tablet cured at 30, 40 and 60 °C for 2 h are shown in Fig. 6. Relatively more porous and rough films at lower curing temperatures of 30 °C (Fig. 6A) and 40 °C (Fig. 6B) were observed in contrast to the films formed at higher curing temperatures of 50 °C (Fig. 5C) and 60 °C (Fig. 6C).

2.3. In vitro drug release from dry powder coated tablets

The sustained release behavior of dry powder coated tablets with Eudragit® RS/RL was further investigated by *in vitro* drug release studies. It can be expected that curing time and temper-

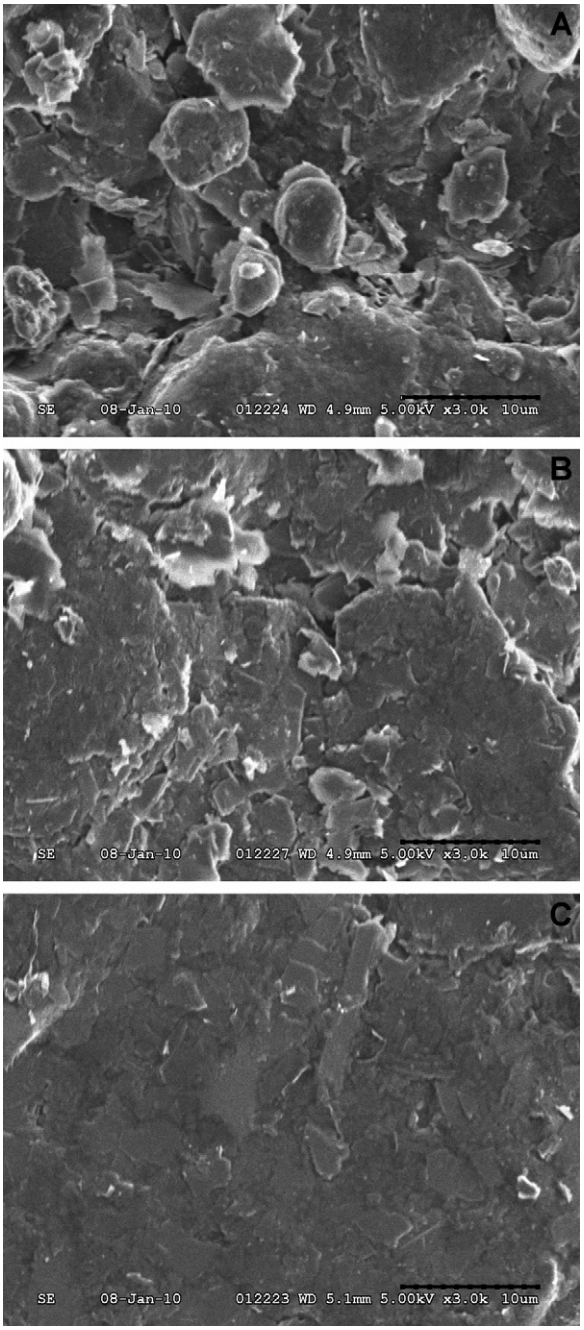

Fig. 6. SEM micrographs of Eudragit® RS/RL powder coated tablets curing for 120 min at different temperatures: (A) 30 °C, (B) 40 °C, (C) 60 °C.

ature would affect drug release profile since they influence the film formation and film's completeness. Fig. 7 shows the effect of curing time on drug release profile at curing temperature of 50 °C. Clearly, the release rate was significantly retarded by extending the curing time. The uncured coated tablets showed a rapid and complete drug release in only 2 h, and extending the curing time to 1 and 2 h showed merely 11% and 4.8% drug release in the same time period. Compared to the uncoated tablets, the dry powder coated tablets without being subject to curing already had a slower drug release, indicating a partially film formation during the powder deposition step. In the very beginning of feeding coating powder, the first layer of coating particles were probably softened and partially coalesced due to the relatively high plasticizer concentration on the tablet surface.

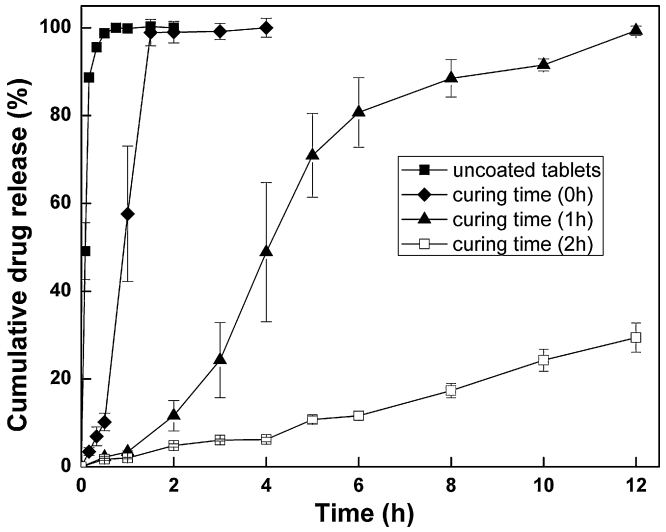

Fig. 7. The effect of curing time on drug release profiles. (Curing temperature: 50 °C, coating level: 3%, Eudragit ® RS/RL ratio: 2/1.)

The effect of curing temperature on drug release profile is shown in Fig. 8. Higher curing temperature clearly decreased the drug release rate. The dry powder coated tablets cured at 30, 40 and 50 °C showed 29%, 53% and 66% drug release in the period of 12 h. The dissolution tests were not performed on dry powder coated tablets cured at 60 °C due to the observable film-coating defects on the edge. It was noted that the relationship between drug release and time showed good linearities ($R^2 > 0.98$) when using linear regression analysis, indicating that the drug release from the coated film followed zero-order kinetics for all cases. The drug release profiles corresponded well with the film morphology shown by SEM microphotographs, where the lower curing temperature produced the film with more voids left by the uncompleted coalesced particles. These voids became the micro-channels for drug diffusion from the tablet core, resulting in faster drug release rate.

The effect of coating level on the drug release profile was investigated with a Eudragit® RS/RL ratio of 2:1 (Fig. 9). Dry powder coated tablets with a coating level of 3.0% showed much slower drug release than the ones with lower coating levels (2.0% and 2.5%). For the film controlled drug release, the mechanical stabil-

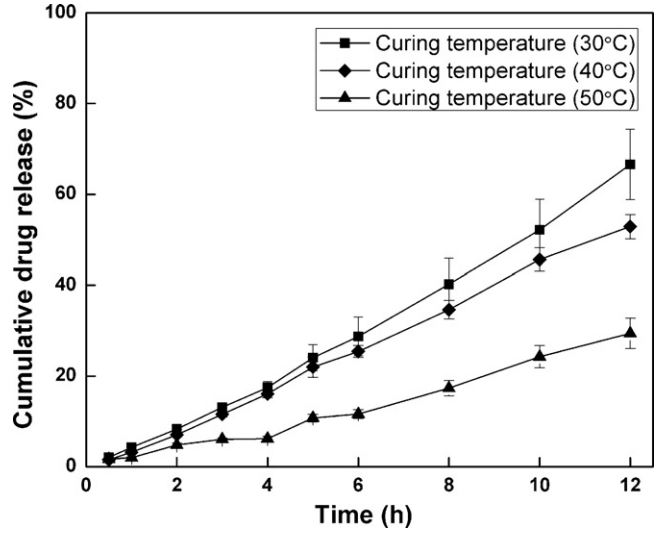

Fig. 8. The effect of curing temperature on drug release profiles. (Curing time: 120 min, coating level: 3%, Eudragit ® RS/RL ratio: 2/1.)

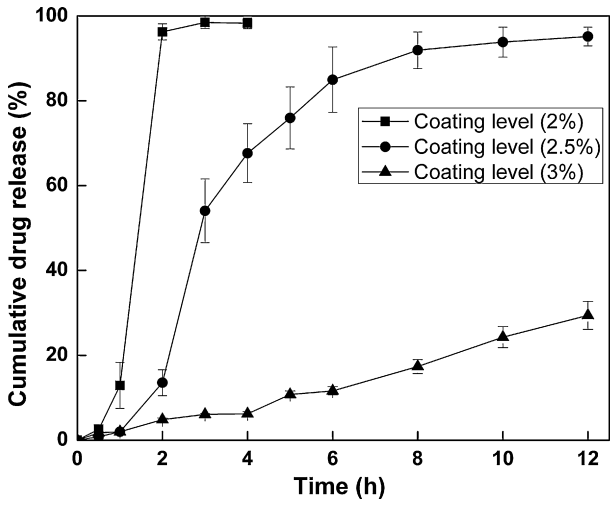

Fig. 9. The effect of coating level on drug release profiles. (Curing temperature: 50 °C, curing time: 120 min, Eudragit ® RS/RL ratio: 2/1.)

ity of the film coatings and the hydrostatic pressure determined whether or not crack occurs in the polymeric membranes (Schultz and Kleinebudde, 1997; Lecomte et al., 2003). Upon the tablet contacting with aqueous media, water diffused into the tablet core and generated a monotonically increasing hydrostatic pressure inside the tablet. If this hydrostatic pressure exceeds the mechanical stability of the film coating at a given time point, crack formation in the film was induced. The film coating of tablets with lower coating levels (2.0% and 2.5%) could not withstand the hydrostatic pressure built up inside the tablet core, leading to the premature formation of cracks during the dissolution test. After the cracks formation, the drug release was primarily controlled via diffusion through water-filled channels rather than polymeric film. The resulting release rates can be much higher than that through the intact polymeric film networks (3%, coating level).

The effect of copolymer ratio of Eudragit® RS and RL in coating formulation on drug release profile is shown in Fig. 10. A wide range of drug release behaviors could be obtained by simply changing the ratios of Eudragit® RS/RL in the formulation. With the weight ratio of Eudragit® RS increased, the drug release rate significantly decreased. Tablets coated with Eudragit® RS/RL (0/1) released 97% of drug in 4 h, while tablets coated with Eudragit® RS/RL (1/2, 1/1 and 2/1) showed 67%, 16% and 6% drug release in the same time interval. This was attributed to the difference of permeability of

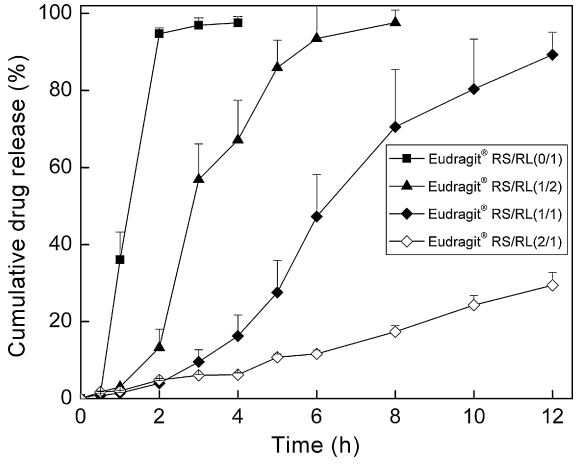

Fig. 10. The effect of Eudragit® RS/RL ratio on drug release profiles. (Curing temperature: 50 °C, curing time: 120 min, coating level: 3%.)

Eudragit® RS and Eudragit® RL film. Eudragit® RL copolymer possesses higher amount (50 mequiv./100 g polymer) of hydrophilic quaternary ammonium groups in the molecular structure than Eudragit® RS (25 mequiv./100 g polymer) (Lehman, 1997). Therefore, higher amount of Eudragit® RS in the formulation produced less permeable coating film and subsequently lower drug release rate.

3. Conclusion

The novel electrostatic dry powder coating process employing a liquid pan coater was developed and applied to sustained release coatings with Eudragit® RS and RL. Liquid plasticizer was found to increase the surface electrical conduction of the tablets besides its primary function of decreasing T_g of the coating polymers. The deposition of coating particles on the tablet surface was promoted by the attractive electric force. The deposited coating particles were cured into a film at elevated temperature. Curing time, temperature, coating level and ratio of Eudragit® RS and RL were found to affect the drug release profile. The electrostatic dry powder coating technique has been demonstrated to be a promising alternative for liquid based sustained release coating with Eudragit® RS and RL.

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References

Amighi, K., Moes, A., 1996. Influence of plasticizer concentration and storage condition on the drug release rate from Eudragit RS30D film-coated sustained release theophylline pellets. Eur. J. Pharm. Biopharm. 42, 29–35.
Bose, S., Bogner, R.H., 2007. Solventless pharmaceutical coating processes: a review. Pharm. Dev. Technol. 12, 115–131.
Cerea, M., Zheng, W., Young, C.R., McGinity, J.W., 2004. A novel powder coating process for attaining taste masking and moisture protective films applied to tablets. Int. J. Pharm. 279, 127–139.
Cole, G., Hogan, J., Aulton, M. (Eds.), 1995. Pharmaceutical Coating Technology. Taylor and Francis, London, pp. 1–5.
Feather, D.H., Nelson, D.H., 2002. Electrostatic application of powder material to solid dosage forms in an electric field. WO Patent Publication 049771, 27 June.
Grosvenor, M.P., Staniforth, J.N., 1996. The influence of water on electrostatic charge retention and dissipation in pharmaceutical compacts for powder coating. Pharm. Res. 13, 1725–1729.
Hallett, M.D., 2006. Method and apparatus for applying powder in a pattern to a substrate. US Patent Publication 20,060,099,350.
Kablitz, C.D., Kapplb, M., Urbanetza, N.A., 2008. Parameters influencing polymer particle layering of the dry coating process. Eur. J. Pharm. Biopharm. 69, 760–768.
Kablitz, C.D., Urbanetz, N.A., 2007. Characterization of the film formation of the dry coating process. Eur. J. Pharm. Biopharm. 67, 449–457.
Klar, F., Urbanetz, N.A., 2009. The role of capillary force promoters in dry coating procedures – evaluation of acetylated monoglyceride, isopropyl myristate and palmitate. Eur. J. Pharm. Biopharm. 71, 124–129.
Lecomte, F., Siepmann, J., Walther, M., MacRae, R.J., Bodmeier, R., 2003. Blends of enteric and GIT-insoluble polymers used for film coating: physicochemical characterization and drug release patterns. J. Control. Release 89, 457–471.
Lehman, K., 1997. In: McGinity, J.W. (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, 2nd ed. Marcel Dekker, New York, pp. 101–176.
Obara, S., Maruyama, N., Nishiyama, Y., Kokubo, H., 1999. Dry coating: an innovative enteric coating method using a cellulose derivative. Eur. J. Pharm. Biopharm. 47, 51–59.
Pearnchob, N., Bodmeier, R., 2003a. Dry powder coating of pellets with micronized Eudragit RS for extended drug release. Pharm. Res. 20, 1970–1976.
Pearnchob, N., Bodmeier, R., 2003b. Dry polymer powder coating and comparison with conventional liquid-based coatings for Eudragit RS, ethylcellulose and shellac. Eur. J. Pharm. Biopharm. 56, 363–369.
Pearnchob, N., Bodmeier, R., 2003c. Coating of pellets with micronized ethylcellulose particles by a dry powder coating technique. Int. J. Pham. 268, 1–11.
Plazier-Vercammen, J.A., De Neve, R.E., 1993. Evaluation of water and organic coating formulations for the protection of tablets against humidity. Pharmazie 48, 441–446.
Sauer, D., Zheng, W., Coots, L.B., McGinity, J.W., 2007. Influence of processing parameters and formulation factors on the drug release from tablets powder-coated with Eudragit L 100-55. Eur. J. Pharm. Biopharm. 67, 464–475.

Schultz, P., Kleinebudde, P., 1997. A new multiparticulate delayed release system. Part I: dissolution properties and release mechanism. J. Control. Release 47, 181–189.

Whiteman, M., Hallett, M.D., Feather, D.H., Nelson, D.H., Gazza, J.M., 2003. Electrostatic application of powder material to solid dosage forms. WO Patent Publication 061841, 31 July.

Zheng, W., Cerea, M., Sauer, D., Mcginity, J.W., 2004. Properties of theophylline tablets powder-coated with methacrylate ester copolymers. J. Drug Deliv. Sci. 14, 319–325.

Zhu, J., Luo, Y., Ma, Y., Zhang, H., 2007. Direct coating solid dosage forms using powdered materials. US Patent Publication 2007-0128274, June 7.