

Solventless Coating Technology for Solid Pharmaceutical Dosage Forms

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ABSTRACT

Dry coating is a coating technology for solid pharmaceutical dosage forms derived from powder coating of metals. In this technology, powdered coating materials are directly coated onto solid dosage forms without using any solvent and then heated and cured to form a coat. As a result, this technology can overcome such disadvantages caused by solvents in conventional liquid coating as serious air pollution, high time- and energy-consumption and expensive operation cost encountered by liquid coating. Several dry coating technologies, including plasticizer-dry-coating, electrostatic-dry-coating, heat-dry-coating and plasticizer-electrostatic-heat-dry-coating have been developed and extensively reported. This review summarized the fundamental principles and coating processes of various dry coating technologies, and thoroughly analyzed their advantages and disadvantages as well as commercialization potentials.

Keywords: Coating technology, plasticizer-dry-coating, electrostatic-dry-coating, heat-dry-coating.

INTRODUCTION

Typically in the pharmaceutical industry, drug products exist in two dosage forms, solid and liquid dosage forms. Included in solid dosage forms are tablets, pellets, pills, beads, spherules, etc. These solid dosage forms are often coated for various reasons, such as odor or taste masking, prevention from moisture, light and/or air, protection from destruction by gastric acid or gastric enzymes, enhanced mechanical strength, aesthetics or controlled release including controlling release sites and/or release rate.

At present, the commercially used technology for coating solid dosage forms is the liquid coating technology. Generally, a mixture of polymers, pigments and excipients is dissolved in an appropriate organic solvent (for water insoluble polymers) or water (for water soluble polymers) to form a solution, or dispersed in water to form a dispersion, and then sprayed onto the dosage forms and dried by continuously providing heat until a dry and smooth coating film is formed.^[1-2] A typical liquid coating process is carried out in a rotary pan coater for larger size solid dosages such as tablets, or in a fluidized bed coater for smaller size dosage forms such as pellets or pills. The liquid coating process and equipment have been well established and widely adopted by

the pharmaceutical industry. The liquid coating technology can obtain exceptionally uniform smooth lustrous coating surface. However, the inherent disadvantages caused by using organic solvents or water have become increasingly obvious.^[3-5] Firstly, vaporizing organic solvents or water is energy consumptive, which adds a large bill to the coating cost; secondly, long processing time up to hours and even days is essential for liquid coating to get a dry, uniform, and smooth coating surface; in addition, using organic solvents results in environmental pollution, solvent recycling cost and operation dangers of explosion; finally, organic solvent itself imposes another cost to the coating process in addition to the energy-consumption and long processing time.

In order to overcome these limitations of the liquid coating technology, new efforts have been made in recent years to develop solventless coating technologies. The developed solventless coating technologies include hot-melt coating, supercritical fluid spray coating, photocuring coating and powder coating.^[6] Among these solventless coating techniques, powder coating technique, which is often termed as "dry coating" in the pharmaceutical coating fields, is the most widely studied one and has not been elaborated. The aim of this review is to introduce and discuss the current status and future development of various dry coating technologies.

PRINCIPLES OF POWDER COATING TECHNOLOGIES

Concept of powder coating technologies

The concept of powder coating originated in the USA in 1950s^[7] and significant growth has been achieved in the

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metal and wood finishing industries over the last two decades. More and more liquid coatings are being replaced by powder coatings due to the drawbacks of liquid coatings similar to those described above. The principle of the powder coating technology involves spraying of a mixture of finely ground particles and polymer onto a substrate surface without using any solvent, and then heating the substrate in a curing oven until the powder mixture is fused into a coating film. Four different powder coating processes have been developed for the metal and wood finishing industry during the last 30 years: electrostatic spraying, fluidized bed coating, electrostatic fluidized bed coating and flame spray, among which electrostatic spraying is the most common process used for application of powder coating in metal finishing.

The basic principle of electrostatic spraying concerns propulsion of the dry powder by compressed air through a spray gun, by which it becomes electrically charged and then moves and adheres to the earthed substrate surface. A successful electrostatic spraying should satisfy several requirements: a powder charging/dispensing unit, an earthed conductive substrate and powder particles able to be charged. There are two types of spraying units, generally in the form of powder charging guns, according to the charging mechanisms:

Corona charging and tribo charging

Corona charging guns are characterized by electrical breakdown and thereafter ionization of air by imposing a high voltage on a sharp pointed needle-like electrode (i.e., charging pin) at the outlet of the gun, and the powder particles picking up the negative ions on their way from the gun to the substrate, while tribo charging guns make use of the principle of frictional charging associated with the dielectric properties of solid materials and therefore no free ions and electrical field will be present between the spray gun and the grounded substrate. The movement of the particles between the charging gun and the substrate is mainly governed by a combination of electrical and mechanical forces. The mechanical forces are produced by the air that blows the powder towards the substrate from the spray gun.

For corona charging guns, the electrical forces are derived from the electrical field between the charging pin of the spray gun and the earthed substrate, which push the charged particles towards the grounded substrate and from the repulsive forces between the charged particles. For tribo charging guns, the electrical forces are only regarded to the repulsive forces between the charged particles.

For both corona and tribo spraying processes, when the charged particles move into the space adjacent to the substrate, the attraction forces between the charged particles and the grounded substrate will make the particles to deposit on the substrate. Three steps for the charged powder particles to absorb onto the substrate surface are involved^[8]: firstly, charged particles are uniformly sprayed onto the earthed substrate in virtue of mechanical forces and electrostatic attractions; thereafter, particles accumulate on the substrate before the repulsion force of the deposited particles against the coming particles increases and exceeds the electrostatic attraction of the earthed substrate to the coming particles finally, once the said repulsion becomes equivalent to the said attraction, particles cannot adhere onto the substrate any more, and the coating thickness does not increase any more. Compared with the traditional liquid coating technology, the powder coating technology is highly valued for energy and

time savings, nearly 100 % utilization of the coating materials, long shelf life, environmental friendliness, safety and therefore low overall operation costs.^[3-5, 9] Furthermore, the coating process is simplified because important parameters of liquid coating processes have not to be considered, e.g., evaporation parameters. Applications of the powder coating technology have been successful in metal and wood finishing, which has enlightened new application in the pharmaceutical industry to coat solid dosage forms.

Liquid coating vs. powder coating

Fig 1 describes some basic step of liquid coating and powder coating. In liquid coating huge energy is use for evaporating solvent, while in case of powder coating; energy savings can be achieved due to absence of liquid evaporation step is not required.^[10-11]

Procedure for dry powder coating

Fig 2 describe how powder coating take place .it include different steps like heating source for preheat solid dosage form, then liquid atomizer to spray plasticizer. If there is no need of Plasticizer then spraying charged powder material on the earthed dosage form by electro static spray gun and finally curing the product.^[12]

Role of particle size in powder coating technologies

Based on the above-mentioned basic principle of powder coating technology, it is reasonably deduced that particle size of the powdered coating materials is a key parameter to control coating quality.

In 1973, Prof. Geldart of Bradford University in England proposed to divide all powders into four groups according to (Fig 3) particle size, Geldart Groups A–D.^[13] Geldart Group A and B powders are in the range of about 25–35 μm to 700–900 μm and both can be easily fluidized. Geldart Group D powders are about 700–90 μm to several millimeters in size. Geldart Group C powders are those with diameters smaller than about 22–30 μm and are often termed as ultrafine powders. Typical characteristics of ultra fine powders include strong cohesive forces and agglomeration arising mainly from Van der Waals attraction, leading to poor flowability and non uniform coating surfaces when used for powder coating. This is the major hurdle that has prevented the effective usage of ultrafine powders in the dry coating of solid pharmaceutical dosage forms, even in the powder coating of metals.

According to the following equation^[8]:

$$\text{Charging efficiency} = \left(\frac{q}{m} \right)_{\max} = \frac{3\varepsilon_0 E}{(\rho_0)a} \left(1 + 2 \frac{\varepsilon_r - 1}{\varepsilon_r + 1} \right) \quad (1)$$

Where ε_0 is the permittivity of free space, ε_r is the relative permittivity of powder particles, a is the particle radius, ρ_0 is the density of the particle and E is the electric field to which the particles are subjected, a smaller particle could get a higher charging efficiency.

In addition, a smaller particle has a larger specific surface area, and can be more easily wetted by liquid and softened or melted by heat. In fact, fine powder with a diameter generally less than 100 μm is a pre requisite for powder coating.

Application of ultrafine powders could produce more uniform and thickness-controllable coat compared with other fine powders with bigger particle size once the poor flowability is conquered. An effective method to improve the flowability of ultrafine powders is addition of a flow agent with nanoscale sizes. Using this technology, 10–20 μm powder coatings have been successfully developed and

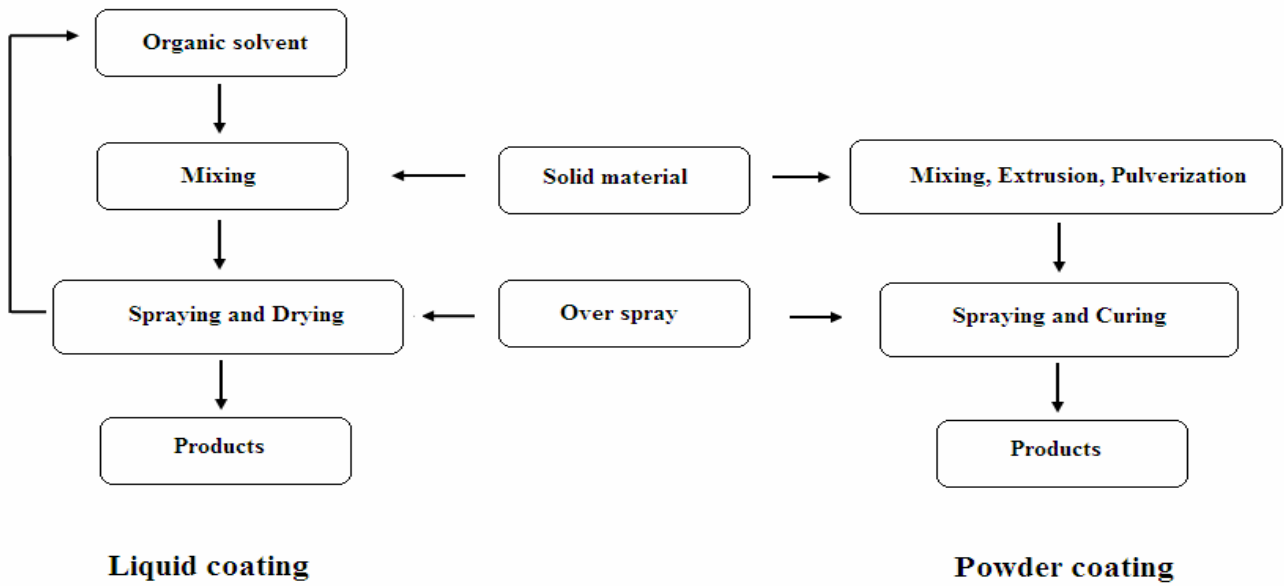


Fig. 1: Difference between liquid coating and powder coating

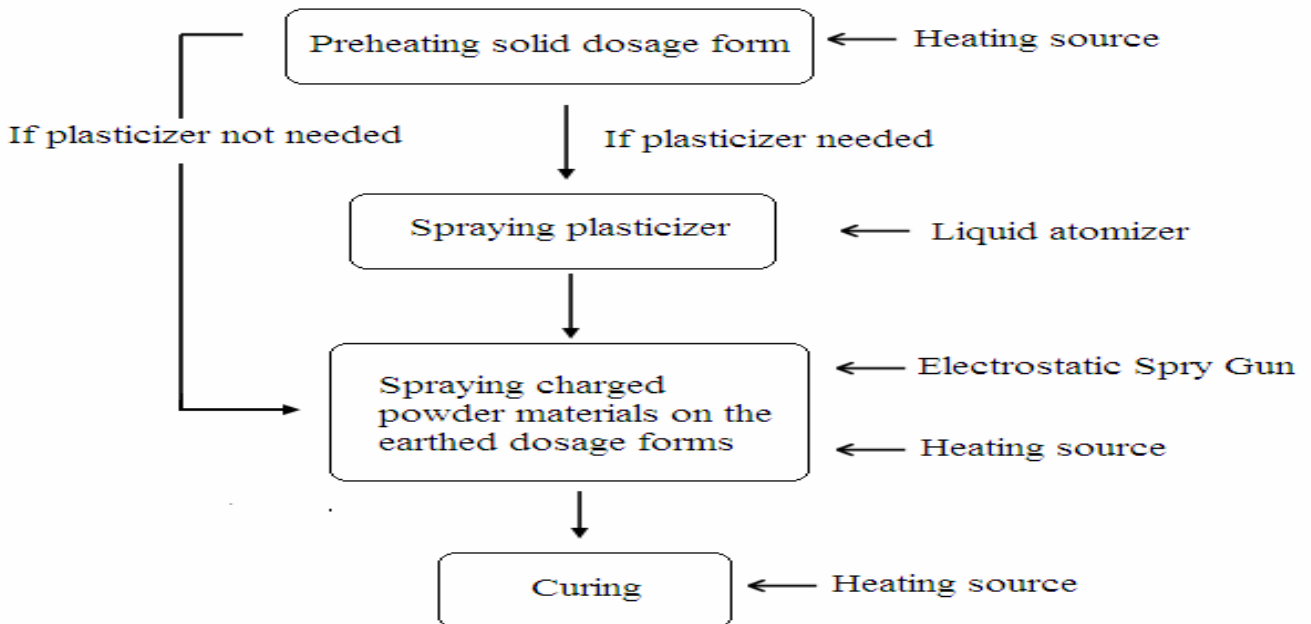


Fig. 2: Flow chart for dry powder coating

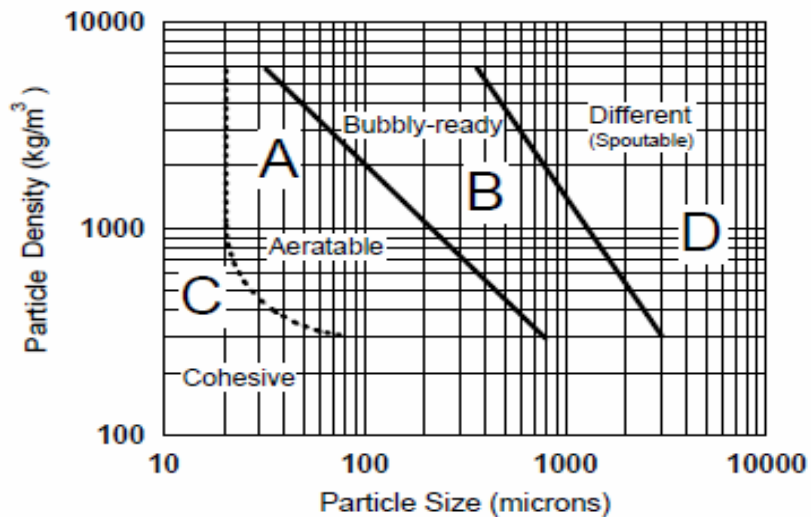


Fig. 3: Gledrt's classification of powder according to fluidization properties

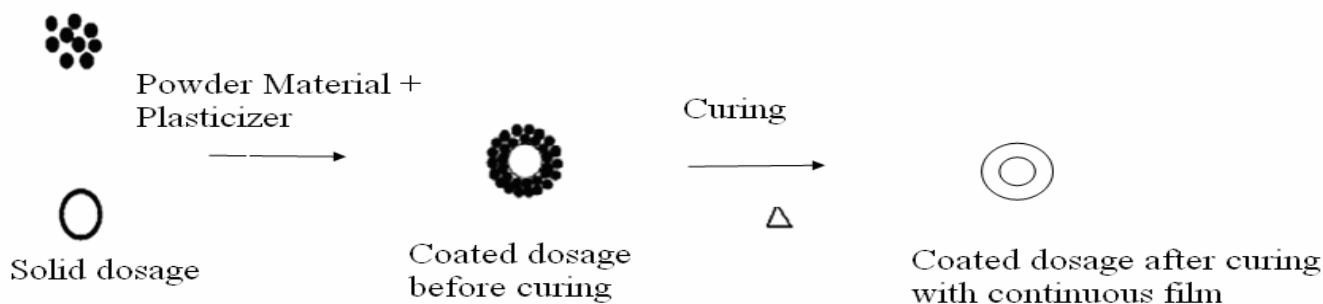


Fig. 4: Schematic illustration of the film formation in the plasticizer-dry-coating

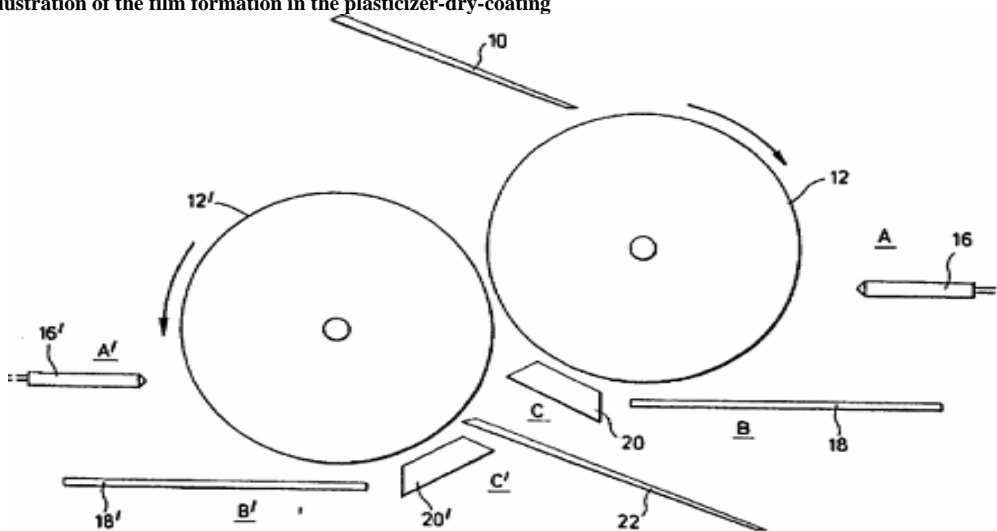


Fig. 5: Schematic diagram of an electrostatic coating apparatus for solid dosage forms. (10) tablet feeding chute; (12, 12') rotary drum; (16, 16') electrostatic spraying gun; (18, 18') tray to hold particles; (20, 20') infrared ray heater; (22) tablet collection chute; (A) preconditioning station; (B) coating station; (C) fusing station.

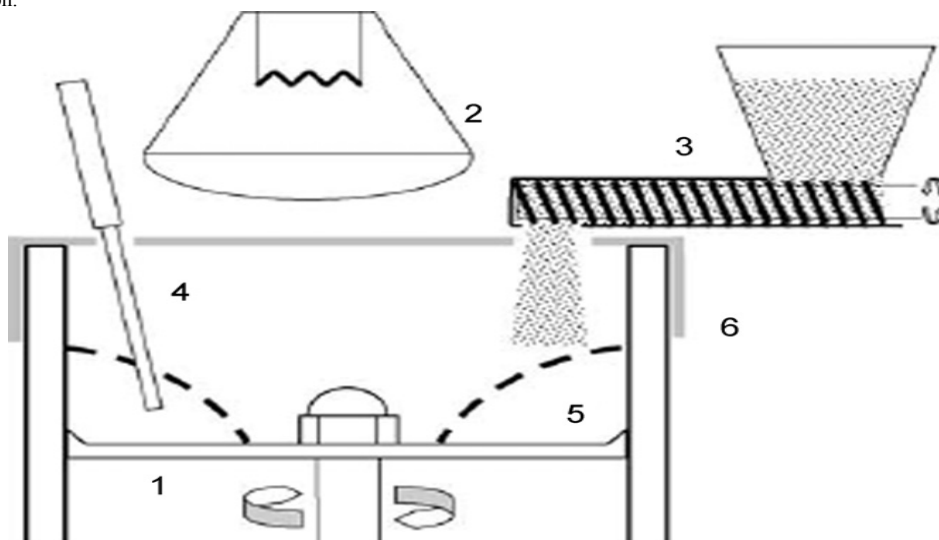


Fig. 6: Schematic representation of the heat-dry-coating apparatus and process for tablet coating: (1) rotating disk; (2) infrared lamp; (3) powder feeder; (4) temperature probe; (5) coating tablets; (6) glass cover(Cerea *et al.*, 2004).

practiced to coat metals in Links Coatings Inc., an Ontario powder coating company.

PRINCIPLES AND PROCESSES OF CURRENT DRY COATING TECHNOLOGIES

In pharmaceutical industries, powder coating technologies are termed as dry coating technologies, in which powdered coating materials are directly coated onto solid dosage forms without using any solvent, and then heated and cured to form a coat. Solid dosage forms are different in several aspects from those metal substrates.

Solid dosage forms are with weak electrical conductivity while metal substrates are very electrically conductive. Besides, film-forming polymers for solid dosage forms are exclusively thermoplastic. For thermoplastic film-forming polymers, plasticizers are often added to lower the softening temperature (T_s) or glass transition temperature (T_g) of the polymers, allowing film formation at a reduced temperature and improving the flexibility and tensile strength of the obtained coat. The majority of plasticizers are liquid organic chemicals with small molecular weight and low volatility.

Generally, T_s or T_g decreases with the increase of plasticizer/polymer ratio. When plasticizer/polymer ratio is increased to an extent that the reduced T_s or T_g is close to or below the room temperature, the polymer film will become soft and sticky, having no practical values.

Based on the above information, several dry coating technologies have been developed, including plasticizer-dry-coating, electrostatic-dry-coating, heat-dry-coating and plasticizer-electrostatic-heat-dry-coating. The classification is schemed according to the main factor, from each of the technologies, that attributes to the adhesion of particles onto solid dosage forms.

Plasticizer-dry-coating

The first dry coating technology is mainly based on the usage of plasticizers. Here, this technology is referred to as “plasticizer-dry-coating”. For solid dosage coating, low T_s or T_g of the film-forming polymer is essential to protect active pharmaceutical ingredients (APIs) in the dosages from being damaged at a high temperature.

This necessitates the use of plasticizers. For example, cellulose derivatives such as hydroxypropyl methylcellulose acetate succinate (HPMCAS), a commercial cellulosic enteric coating polymer, and ethylcellulose, an extended release agent, depend on plasticizers of acetylated monoglyceride (AMG), acetyltributyl citrate (ATBC) or triethyl citrate (TEC) to bring their T_g or film-forming temperature from more than 100 °C down to 60 °C or less. [14-16]

In plasticizer-dry-coating technology, powdered materials are sprayed onto dosage surface simultaneously with the plasticizer spraying from separate spraying nozzle. The sprayed liquid plasticizer would wet the powder particles and the dosage surface, promoting the adhesion of particles to dosage surfaces. The coated dosages are then cured for a predetermined time above the T_g of the polymer, forming a continuous film. The schematic illustration of the film formation in the plasticizer-dry-coating is shown in Fig 4. The adhesion of particles to dosage surface is mainly the result of the said wetting of particles and dosage surfaces by plasticizers, and the film formation is the combined response of improved viscous flow and particle deformation resulted from plasticizer and heat. [17] In addition, capillary forces exerted by liquid plasticizer prior to its uptake into the polymer particles may also contribute to the particle deformation in the interstitial capillary system between particles and thus to the film formation [14, 17-18] reported that, in their plasticizer-dry-coating process, spraying a small amount of water or hydroxypropyl methylcellulose (HPMC) solution to their HPMCAS-coated spheres could obviously improve the film quality. [15] Moisture would significantly accelerate the film formation and optimize the film smoothness and integrity of ethylcellulose-coated pellets during the heat curing phase.

These phenomena are similar to those observations for film formation of aqueous dispersions. [19, 21] For these cases, water or water in the polymer solution plays a role of coalescing solvent or plasticizer promoting the interdiffusion of polymer chain, and the evaporation of water may also provide a driving force to fuse the polymeric particles based on the film formation mechanism proposed for aqueous latex systems. [18-20, 21-22]

By means of the plasticizer-dry-coating technology both tablets and pellets could be coated. The former were

generally coated in a pan coater. However, for the latter a fluidized bed coater is required in order to avoid formation of agglomerates caused by the smaller size and higher specific surface area of pellets and thus strong interactions [15-16, 22] coated pellets in a fluidized bed with micronized ethylcellulose particles, Eudragit® RS particles (a copolymer of methacrylic acid ester and triethylaminoethyl methacrylate chloride) and shellac, respectively, by means of the plasticizer-dry-coating technology. Based on the same technology [14, 17] employed HPMCAS as film-forming polymer to coat beads in a fluidized bed and pellets in a rotary fluidized bed, respectively. In addition, in a pan coater also coated tablets with HPMCAS. [14] The effects of plasticizer types and concentrations and curing temperatures and time on the film formation, surface morphology and controlled release profiles of the obtained coats were thoroughly investigated. The results indicated that the coating thickness or coating level (coating level is referred to the weight gain based on the uncoated dosage weight) could be regulated by the amount of plasticizer feeding [14-16, 22] Compared with liquid coating, a much more amount of plasticizer even up to a plasticizer/polymer ratio of 50 % is required for the adhesion of enough particles to dosage surface in order to gain a coat thick enough for sufficient protection, gastric resistance or proper controlled release. [14-16, 22-23] Commonly, coat thickness increases with increasing plasticizer concentration. Adversely, surplus plasticizer possibly leads to very soft or sticky films. It is hard to balance the plasticizer concentration for a sufficient coat thickness and that for a flexible and dry coat.

Electrostatic-dry-coating

Another dry coating technology is based on the electrostatic powder coating technology, here called “electrostatic-dry-coating”. Electrostatic coating of solid dosages with powdered materials is more difficult than coating of metals due to the much weaker electrical conductivity of solid dosages than metal substrates. For solid dosage forms, however, the electrostatic attraction between the charged particles and the solid dosages with weak conductivity or high electric resistance is typically weak, leading to difficulty in producing a thick coat. Despite this difficulty, the benefits of electrostatic-dry-coating including more uniform coat and more accurate control of coat thickness in comparison with the “plasticizer-dry-coating” have been encouraging researchers to devote efforts to surmount this difficulty of the electrostatic-dry-coating. Phoqus Pharmaceuticals Limited, an oral drug delivery and development company located in Kent, the United Kingdom, has been devoting great efforts in designing both apparatus and formulations of powdered coating materials in order to fulfill electrostatic coating of solid dosage forms, and many patents in this field have been produced.

There are several patents providing a similar apparatus for electrostatic application of solid pharmaceutical dosage forms, especially tablet cores with powdered materials [24-26, 27-30] The apparatus includes two occluding rotary drums, two electrostatic spray guns, two infrared ray-based fusion stations: infrared ray heater, two cooling stations, a tablet feeding chute and a tablet collection chute (Fig. 6). This special design aims at making every tablet effectively grounded, and directing and restricting the charged particles onto the tablet surface without spraying onto the surrounding, by which the coating efficiency is greatly improved.

Moreover, the two sides of a tablet may be coated with different color or different formulation.

However, this apparatus was found unable to focus all charged powder to the tablets but the drum also received some powder. This is wasteful of powder and also makes cleaning of the apparatus time consuming. It was also difficult to provide such a coating with a well-defined edge using this apparatus.^[31-32]

Based on the above mentioned and other patents, Phoqus has applied electrostatic-dry-coating technology for the preparation of its lead product Chronocort, a once-daily modified release hydrocortisone tablet for the treatment of adrenal insufficiency, and successfully completed the phase I clinical trials (Phoqus Group plc, 2006). The shining features of the electrostatic-dry-coating technology include uniform coating surfaces with controllable thickness and, if needed, with different color or formulation. So far, the published electrostatic-dry-coating technologies mainly focused on coating tablets. Endeavors are being made aiming to coat smaller solid dosage forms such as pellets or beads by means of the electrostatic-dry-coating.

Heat-dry-coating

The third dry coating technique was developed by Cerea *et al.*, 2004 known as “heat-dry-coating” since only heat was used as a “binding force” to realize the dry coating of tablets. In this coating technology, Eudragit EPO (a copolymer based on dimethylaminoethyl methacrylate and methacrylates) particles were continuously spread onto the tablets contained in a lab-scale spheronizer by way of a motorized single screw powder feeder, with an infrared lamp positioned on the top of the spheronizer as a heating source, without using any solvent and plasticizer (Fig. 7). Powder adhesion onto the tablet surface is promoted only by the partially melted polymer that generates binding forces between particles, and between particles and tablet surfaces. Because Eudragit EPO has a low T_g of about 50°C, and because the film of Eudragit EPO is sufficiently elastic, coating with Eudragit EPO generally requires no plasticizers. Accordingly, Eudragit EPO is a special example, and this coating process cannot directly apply those polymers with high T_g . For polymers with higher T_g such as Eudragit L 100–55 ($T_g = 120–129^\circ\text{C}$), Eudragit RS PO ($T_g = 67^\circ\text{C}$) and Eudragit RLPO ($T_g = 70^\circ\text{C}$)^[33], pre-plasticization was employed by blending polymers with plasticizers using a hot-melt extrusion process.^[34-35] The extrudates were subsequently cryogenically grounded into a micronized coating powder, and then applied to the solid dosage forms by means of the heat-dry-coating technology. The advantages of heat-dry-coating include abandoning plasticizer for lower T_g film-forming polymers or avoiding high concentrations of plasticizer because of pre-plasticization. However, it is still a challenge for heat-dry-coating technology to get a smooth, uniform and thick coating only by the help of the said heat-based adhesion.^[36]

Plasticizer-electrostatic-heat-dry-coating

Plasticizer-electrostatic-heat-dry-coating (PEH-dry-coating) is named here mainly because this technology is featured by combined usage of plasticizer, electrostatic and heat. In this technology, the coating process comprises the steps of^[37]: (1) positioning pre-heated solid dosage forms in a chamber of a rotatable, electrically grounded pan coater; (2) spraying powdered coating materials and plasticizer on the solid dosage forms in the pan coater during rotation thereof for a pre-selected length of time using an electrostatic spray gun

and (3) curing the coated solid dosage forms to form continuous, uniform and flexible coats. During the whole coating process, the solid dosage forms and the chamber are always kept in a hot state by heating the air in the coater or directly heating the coater. According to the coating process, PEH-dry-coating is characteristic of integration of five kinds of “forces”, including softening or melting effects of particles by heat, wetting of dosage surface by a plasticizer, electrostatic attraction forces, hydrodynamic force due to spraying and mechanical force due to the rotation of pan coater. They are combined to enhance the adhesion of powdered coating materials to solid dosage surface. Firstly, the movement of the powdered materials from the charged gun to the dosages is promoted by a combination of electrical and hydrodynamic forces, and the adhesion of powders onto the dosage surface is the synergic contribution of electrostatic attraction between the charged powders and earthed dosages, softening effects of the powders due to heat from pre-heating and heating during coating, and wetting effects by plasticizers. Secondly, the hydrodynamic forces from compressed air and the mechanical forces from the tumbling effect of the pan coater are both helpful to the adhesion of powder on the solid dosage surface. It should be noted that the adhesion of powdered materials to the dosage surface due to the synergic contribution of electrostatic attraction and heat- and wet-induced adhesions is so strong that it not only can withstand the tumbling and colliding of solid dosages with each other and with the inner surface of the coater, but the tumbling and colliding actually also help make the coating more compact and uniform. Finally, the repulsions between the same charged particles on the dosage surface promote the uniform distribution of the particles on the dosage surface and prevent the coalescence between solid dosage forms even between smaller dosage forms such as beads or pellets as well. By this way, a pan coater similar to the conventional pan coaters for liquid coating of tablets can be used for both larger solid dosage forms such as tablets and smaller ones. By means of the combination of the five “forces”, the coating thickness can be controlled by regulating the charging voltage and the plasticizer amount. Generally, a higher charging voltage produces a thicker coating if the charging voltage is not high enough to cause electric breakdown of the coating and to damage the coating quality. Regarding to the regulation of plasticizer amount, a higher amount of plasticizer in plasticizer-electrostatic-heat dry-coating technology authentically produces a thicker coating without resulting in a sticky coating which is the case for the plasticizer-dry-coating technique when a higher amount of plasticizer is used. Compared with the plasticizer-dry-coating technique, when the same amount of plasticizer is fed, the electrostatic attraction applied in this dry coating technique helps adhere much more particles to the dosage surface, hence giving a much lower plasticizer/ polymer ratio and avoiding a sticky coating.

Furthermore, the applicability of pan coaters for both larger solid dosage forms such as tablets and smaller ones such as beads, pellets and spherules avoids the utilization of fluidized bed coaters. Typically, fluidized beds are indispensably required in liquid coating and plasticizer-dry-coating for coating small size solid dosages such as beads, pellets and spherules^[23] which need a large quantity of compressed air for fluidizing these dosages. Consequently, the continuous application of similar pan coaters for liquid coating and the

elimination of fluidized beds not only reduce the cost for re-designing and fabricating new complicated coating equipment as the case in the electrostatic-dry-coating, but also get rid of bills for providing and heating compressed gas and for post disposing the discharged gas. This will definitely speed up the commercial application of this technology in the pharmaceutical industry.

By means of this PEH-dry-coating technique, conventional coating pharmaceutical polymers, such as such as Eudragit RS, Eudragit RL, Eudragit L, Eudragit E PO and Acryl-eze MP, in combination with standard excipients were successfully coated onto tablets and beads, and uniform and smooth coating surfaces comparable to the surfaces from liquid coating were generated.^[10, 12, 38] Taking account of the solid dosage forms always tumbling in the pan coater during the whole coating process, the PEH-dry-coating technology is particularly applicable for pharmaceutical coating with a single color. For tablet coating, sometimes the tablet surfaces need to be partially coated, or need to be coated with different colors or formulations for purposes of controlled drug release or delivery. In these cases, electrostatic-dry-coating rather than this technology, is a much better choice.

CONCLUSION

Among these four reported dry coating technologies, Plasticizer-dry-coating and heat-dry-coating have to overcome the difficulties in obtaining smooth and uniform coating surfaces with controllable coating thickness before commercial applications in the pharmaceutical industry. Electrostatic-dry-coating has advantages of well-confined coating particles on dosage surfaces and well controlled coating thickness by the help of well-designed coating apparatus. It is capable of applying different coating colors or formulations on the same surface, yet its applications are currently limited to tablets. Plasticizer-electrostatic-heat-dry-coating makes use of plasticizer, electrostatic and heat, capable of producing smooth and uniform coating surfaces with controlled coating thickness on both larger dosage forms and smaller ones in pan coaters. Its applications are limited to coating surfaces with a single color. However, before commercialization further work will be focused on scale-up tests, functional detections of coated solid dosage forms such as drug release profiles, and clinical tests.

REFERENCES

1. Felton LA, Shah NH, Zhang G, Infeld MH, Malick AW, McGinity JW. Physical-mechanical properties of film-coated soft gelatin capsules. *Int J Pharm* 1996; 127: 203-211.
2. Osterwald HP. Properties of film-former and their use in aqueous systems. *Pharmaceutical Research* 1985; 2(1): 14-18.
3. Wheatley TA, Steuernagel CR. Latex emulsion for controlled drug delivery. In: McGinity, J.W. (Ed.), *Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms*. Marcel Dekker, New York, 1997, pp. 1-54.
4. Leong KC, Lu GQ, Rudolph A. A comparative study of the fluidized-bed coating of cylindrical metal surfaces with various thermoplastic polymer powders. *J Mater Proc Technol* 1999; 89-90, 354-360.
5. Belder EG, Rutten HJ, Perera DY. Cure characterization of powder coatings. *Prog Org Coat* 2001; 42: 142.
6. Bose S, Bogner RH. Solventless pharmaceutical coating processes: a review. *Pharm Dev Technol* 2007; 12: 115-131.
7. Bailey AG. The science and technology of electrostatic powder spraying, transport and coating. *J. Electrostat.* 1998; 45: 85-120.
8. Mazumder MK, Sims RA, Biris AS, Srirama PK, Saini D, Yurteri CU, Trigwell S, De S, Sharma R. Twenty-first century research needs in electrostatic processes applied to industry and medicine. *Chem Eng Sci* 2006; 61: 2192-2211.
9. Misev TA. *Powder Coatings: Chemistry and Technology*. Wiley, Toronto, 1991, 23-32.
10. Luo YF, Ma Y, Zhang LQ, Huang J, Lum S, Chow K, Zhu J. Dry powder coating of pharmaceutical tablets by electrostatic pan coating. *Int J Pharm* 2006; .
11. Zhu J, Zhang H. Ultrafine powder coatings: an innovation. *Powder Coat. Int J Pharm* 2005; 16 (7): 39-47.
12. Zhu J, Luo YF, Ma Y, Zhang H. Direct coating solid dosage forms using powdered materials. *Int J Pharm* 2007; 25-32, 25.
13. Geldart D. Types of gas fluidization. *Powder Technol* 1973; 7: 285-297.
14. Obara S, Maruyama N, Nishiyama Y, Kokubo H. Dry coating: an innovative enteric coating method using a cellulose derivative. *Eur J Pharm Biopharm* 1999; 47: 51-59.
15. Pearnchob N, Bodmeier R. Coating of pellets with micronized ethylcellulose particles by a dry powder coating technique. *Int J Pharm* 2003a; 268: 1-11.
16. Pearnchob N, Bodmeier R. Dry polymer powder coating and comparison with conventional liquid-based coatings for Eudragit RS, ethylcellulose and shellac. *Eur J Pharm Biopharm* 2003b; 56: 363-369.
17. Kablitz CD, Urbanetz NA. Characterization of the film formation of the dry coating process. *Eur J Pharm Biopharm* 2007; 67: 449-457.
18. Toussaint A, De Wilde M. A comprehensive model of sintering and coalescence of unpigmented latexes. *Prog Org Coat* 1997; 30: 113-126.
19. Liu J, Williams III RO. Long-term stability of heat-humidity cured cellulose acetate phthalate coated beads. *Eur J Pharm Biopharm* 2002a; 53: 167-173.
20. Liu J, Williams III RO. Properties of heat-humidity cured cellulose acetate phthalate free films. *Eur J Pharm Sci* 2002b; 17: 31-41.
21. Williams III RO, Liu J. Influence of processing and curing conditions on beads coated with an aqueous dispersion of cellulose acetate phthalate. *Eur J Pharm Biopharm* 2000; 49: 243-252.
22. Pearnchob N, Bodmeier R. Dry powder coating of pellets with micronized Eudragit® RS for extended drug release. *Pharm Res* 2003c; 20: 1970-1976.
23. Ivanova E, Teunou E, Poncelet D. Encapsulation of water sensitive products: effectiveness and assessment of fluid bed dry coating. *J Food Eng* 2005; 71: 223-230.
24. Brown SR, Reeves LA, Stantiforth JN. Method and apparatus for the coating of substrates for pharmaceutical use. 2004;.
25. Brown SR, Reeves LA, Stantiforth JN. Method and apparatus for the coating of substrates for pharmaceutical use. 2005;.
26. Brown SR, Reeves LA, Stantiforth JN. Method and apparatus for the coating of substrates for pharmaceutical use. 2006;.
27. Hogan JE, Page T, Reeves L, Stantiforth JN. Powder coating composition for electrostatic coating of pharmaceutical substrates. 2002a;.
28. Hogan JE, Page T, Reeves L, Stantiforth JN. Method and apparatus for the coating of substrates for pharmaceutical use. 2003;.
29. Hogan JE, Page T, Reeves L, Stantiforth JN. Powder coating composition for electrostatic coating of pharmaceutical substrates. 2006a;.
30. Hogan JE, Page T, Reeves L, Stantiforth JN. Powder coating composition for electrostatic coating of pharmaceutical substrates. 2006b;.
31. Hallett MD. Method and apparatus for applying powder in a pattern to a substrate. 2006;.
32. Whiteman M, Hallett MD, Feather DH, Nelson DH, Gazza JM. Electrostatic application of powder material of powder material to solid dosage forms utilizing an electrically conductive shield. 2006;.
33. Nyamweya N, Bradley R, Annamalai M. Effects of thermal history and sample preparation on the glass transition temperature of polymethacrylate copolymers. 2005;.
34. Zheng W, Cerea M, Sauer D, McGinity JW. Properties of theophylline tablets powder-coated with methacrylate ester copolymers. *J Drug Deliv Sci Technol* 2004; 14: 319-325.
35. Sauer D, Zheng W, Coots LB, McGinity JW. Influence of processing parameters and formulation factors on the drug release from tablets powder-coated with Eudragit L 100-55. *Eur J Pharm Biopharm*. 2007; 67: 464-475.
36. Bodmeier R, McGinity JW. Dry coating of solid substrates with polymeric powders. *Drug Deliv Technol* 2005; 5: 70-73.
37. Zhu J, Zhang H. Fluidization additives to fine powders. U.S. Patent 6833185, 2004, December 21.
38. Ma Y, Zhang LQ, Luo YF, Zhu J, Chow K, Lum S, Huang J. Dry powder coating on pharmaceutical tablets. *Int J Pharm* 2007;.