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Mini review

Dry coating, a novel coating technology for solid pharmaceutical dosage forms

Yanfeng Luo [a,b,*], Jesse Zhu [b], Yingliang Ma [b], Hui Zhang [b]

[a] Department of Bioengineering, Research Center of Bioinspired Material Science and Engineering, Chongqing University, Chongqing 400030, China
[b] Department of Chemical and Biochemical Engineering, Faculty of Engineering, the University of Western Ontario, London, ON N6A 5B9, Canada

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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 mini-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.

1. 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 (Felton et al., 1996; Osterwald, 1985). 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 (Wheatley and Steuernagel, 1997; Leong et al., 1999; Belder et al., 2001): 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. Bose and Bogner (2007) gave an excellent review on these solventless coating techniques. 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 paper is to introduce and discuss the current status and future development of various dry coating technologies.

* Corresponding author at: Department of Bioengineering, Research Center of Bioinspired Material Science and Engineering, Chongqing University, Chongqing 400030, China. Tel.: +86 23 65102509.
E-mail address: yfluo@cqu.edu.cn (Y. Luo).

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2. Principles of powder coating technologies

2.1. Concept of powder coating technologies

The concept of powder coating originated in the USA in 1950s (Bailey, 1998), and significant growth has been achieved in the 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 coatings 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 (Misev, 1991): 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 (Wheatley and Steuernagel, 1997; Leong et al., 1999; Belder et al., 2001; Mazumder et al., 2006). 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 a new application in the pharmaceutical industry to coat solid dosage forms.

2.2. 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 particle size, Geldart Groups A–D (Geldart, 1973). 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 700–900 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 ultrafine 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 (Misev, 1991):

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

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 prerequisite 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 (Elbicki and Tardos, 1998; Valverde et al., 2000; Yang et al., 2005; Zhu and Zhang, 2004). Using this technology, 10–20 μm powder coatings have been successfully developed and practiced to coat metals in Links Coatings Inc., an Ontario powder coating company (Zhu and Zhang, 2004, 2005).

3. 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 other than thermosetting which is a common case for metal substrates. 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 for-

mation 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 dosages forms.

3.1. 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 (Obara et al., 1999; Pearnchob and Bodmeier, 2003a,b).

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. 1. 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 (Kablitz and Urbanetz, 2007). 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 (Kablitz and Urbanetz, 2007; Toussaint and De Wilde, 1997). Obara et al. (1999) 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; Pearnchob and Bodmeier (2003a) also suggested that 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 (Liu and Williams, 2002a,b; Williams and Liu, 2000). 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 (Chevalier et al., 1992; Liu and Williams, 2002a,b; Toussaint and De Wilde, 1997; Williams and Liu, 2000).

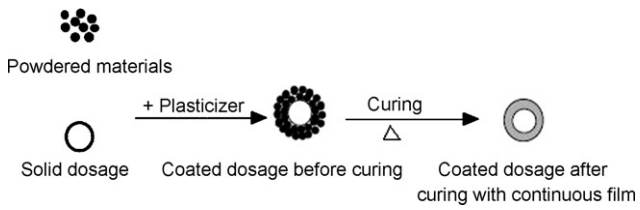

Fig. 1. Schematic illustration of the film formation in the plasticizer-dry-coating.

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. Pearnchob and Bodmeier (2003a,b,c) 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, Obara et al. (1999), Kablitz et al. (2006) and Kablitz and Urbanetz (2007) 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, Obara et al. (1999) also coated tablets with HPMCAS. 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 (Obara et al., 1999; Pearnchob and Bodmeier, 2003a,b,c). 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 dosages surface in order to gain a coat thick enough for sufficient protection, gastric resistance or proper controlled release (Obara et al., 1999; Pearnchob and Bodmeier, 2003a,b,c; Ivanova et al., 2005). 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 flexile and dry coat.

3.2. 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 metal substrates, the sufficiently strong electrostatic attraction between the charged particles and the grounded metal substrate makes particles to firmly adhere to the substrate surface, producing a coat with a desirable thickness. 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

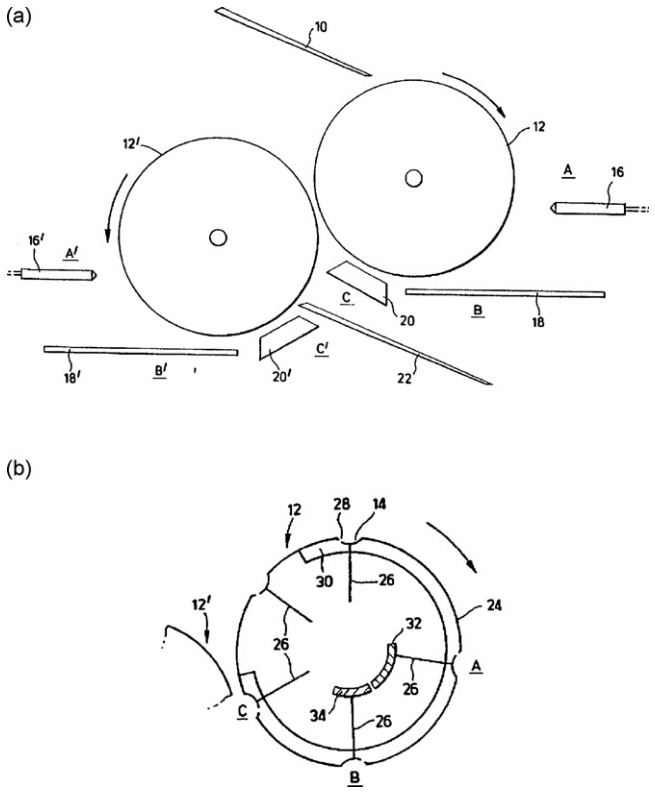

Fig. 2. Schematic diagram of: (a) an electrostatic coating apparatus for solid dosage forms. (10) tablet feeding chute; (12, 12′) rotary drum; (16, 16′) electrostatic spraying gun; (18, 18′) tray to hold particles; (20, 20′) infrared ray heater; (22) tablet collection chute; (A) preconditioning station; (B) coating station; (C) fusing station. (b) A cross-section of rotary drum 12 or 12′. (14) a depression; (24) rotating shell on the rotary drum; (26) pick-up drum; (28) a passage; (30) vacuum manifold; (32) an earthed arcuate stationary electrode; (34) an arcuate stationary electrode at a potential. (Hogan et al., 2000, 2002b, 2003, 2006c, reproduced with permission).

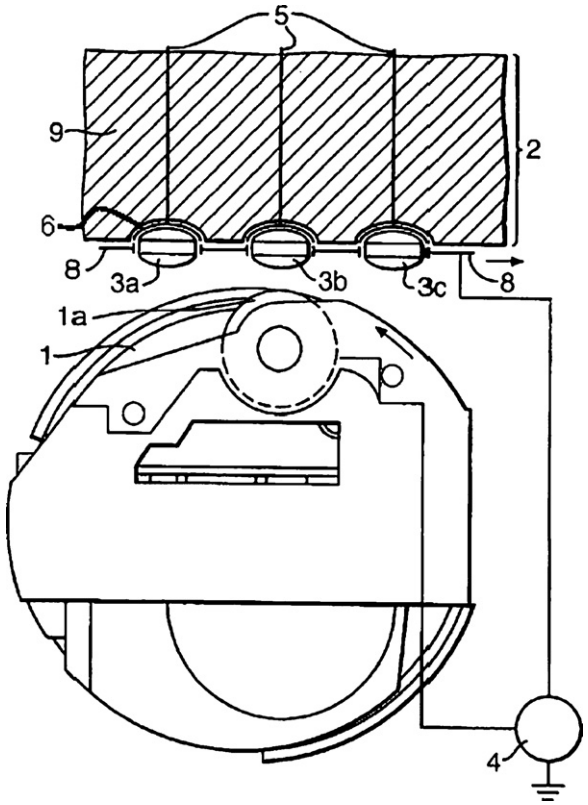

Fig. 3. Schematic diagram of an electrostatic coating apparatus for solid dosage forms with an electrically conductive shield. (1) source of charged powder material; (1a) electrically conductive roller; (2) supporting assembly; (3a, b, c) tablet; (4) voltage source; (5) electrically conducting member; (6) cupped tablet receiving part; (8) electrically conductive shield mounted just above (9); (9) electrically insulating body. (Hallett, 2006; Whiteman et al., 2006, reproduced with permission).

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 (Brown et al., 2004, 2005, 2006; Hogan et al., 2000, 2002b, 2003, 2006c). 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. 2(a)). 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 (Hallett, 2006; Whiteman et al., 2006).

In order to address these shortcomings, an improved new apparatus involving an electrically conductive shield was invented (Hallett, 2006; Whiteman et al., 2006). The typical schematic diagram of this apparatus is illustrated in Fig. 3. The shield 8 is electrically conductive and is coated with a layer of electrically insulating material. It is applied with the same voltage to the roller 1a but with different voltage to the tablet receiving part 6, providing both a physical barrier and an electrostatic barrier. In operation, the electric field, which provides the driving force for the charged powder, is cancelled out at some point between the powder source and the shield and is reversed in the immediate vicinity of the shield. Thereby powder is repelled from approaching the shield by virtue of the voltage potential of the shield and the charge on the powder. By this means, the charged powder is well confined to tablet surface without much deposition on the surroundings.

Quite recently, Newman et al. (2007) disclosed an improved electrostatic coating apparatus particularly practical for industrial production. This apparatus contains a platen which holds a plurality of tablets (Fig. 4). Therefore, handling of large numbers of tablets is greatly facilitated. US 6806017 (Reeves et al., 2004) describes another apparatus based on a photoconductive drum, by which charged powder material could be applied to the photoconductive drum, transferred to an intermediate belt and then to a solid dosage form.

Apart from great efforts in apparatus designing, Phoqus has been committing itself to composition designing of powdered coating materials in attempts to make the powder more easily charged or more suitable for the electrostatic-dry-coating and thus to improve coating quality (Hogan et al., 2002a, 2006a,b; Wei and Uang, 2002).

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 in 2006 (Phoqus Group plc, 2006). The shinning features of the electrostatic-dry-coating technology include uniform coating surfaces with controllable thickness and, if needed, with different color or formu-

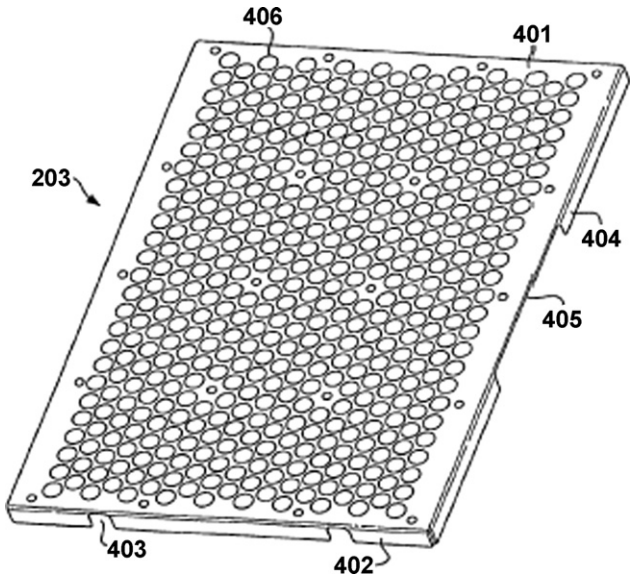

Fig. 4. Perspective view of a platen shield (Newman et al., 2007, reproduced with permission).

lation. 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.

3.3. Heat-dry-coating

The third dry coating technique was developed by Cerea et al. (2004). We name this technique 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 E PO (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 (see Fig. 5). Powder adhesion onto the tablet surface

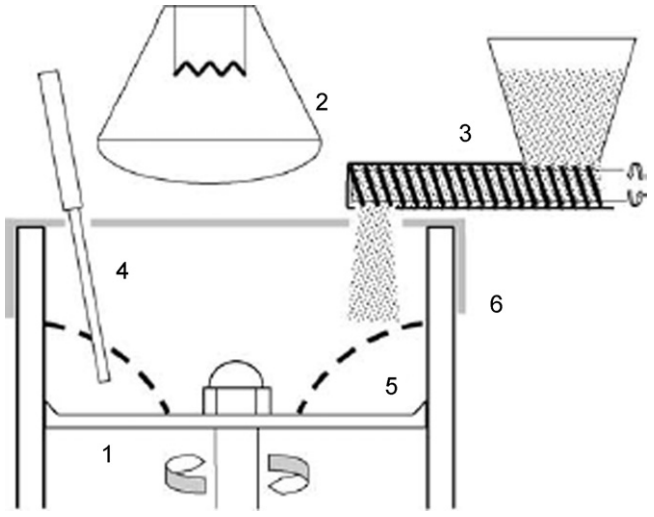

Fig. 5. Schematic representation of the heat-dry-coating apparatus and process for tablet coating: (1) rotating disk; (2) infrared lamp; (3) powder feeder; (4) temperature probe; (5) coating tablets; (6) glass cover (Cerea et al., 2004, reproduced with permission).

is promoted only by the partially melted polymer that generates binding forces between particles, and between particles and tablet surfaces. Because Eudragit E PO has a low T_g of about 50 °C, and because the film of Eudragit E PO is sufficiently elastic, coating with Eudragit E PO generally requires no plasticizers. Accordingly, Eudragit E PO 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 °C), Eudragit RS PO (T_g = 67 °C) and Eudragit RL PO (T_g = 70 °C) (Nyamweya et al., 2005), pre-plasticization was employed by blending polymers with plasticizers using a hot-melt extrusion process (Zheng et al., 2004; Sauer et al., 2007). 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. There is a mini-review describing plasticizer-dry-coating and heat-dry-coating by Bodmeier and McGinity (2005).

3.4. 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 (Zhu et al., 2007): (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 flexile 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.

In order to make use of ultrafine powder in PEH-dry-coating, Zhu's group added additives with nanoscale size into the powdered formulation, significantly improving the ultrafine powder flowability (Zhu and Zhang, 2004; Zhu et al., 2007). By using ultrafine particles, a higher charging efficiency can be obtained according to Misev (1991). As a result, the higher charging efficiency together with lighter weight and larger specific surface area increases the electrostatic attractions and reduce the inertial force and the possibility of particles rebounding back off the dosage surface, resulting in an easier and stronger adhesion and evener distribution on the dosage surface. Again, with finer particles, much easier wetting by plasticizer and softening by heat, thus much stronger adhesion and smoother coating surfaces can be obtained compared with coarse particles.

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 (Felton et al., 1996; Pearnchob and Bodmeier, 2003a,b,c; Ivanova et al., 2005) 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 (Luo et al., 2006; Ma et al., 2007; Zhu et al., 2007). The further studies and scale-up tests of this technology are being carried out at the University of Western Ontario together with a pharmaceutical company in Toronto.

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.

4. Conclusions

Plasticizer-dry-coating, electrostatic-dry-coating, heat-dry-coating and plasticizer-electrostatic-heat-dry-coating are four extensively 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. Both electrostatic-dry-coating and ultrafine powder-dry-coating technologies are promisingly commercialized, realizing little air pollution, low time- and energy-consumption and small operation cost. 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.

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