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The effect of spray mode and chamber geometry of fluid-bed coating equipment and other parameters on an aqueous-based ethylcellulose coating

Shirley T. Yang, Gary Van Savage, Jay Weiss and Isaac Ghebre-Sellassie

Parke-Davis Pharmaceutical Research Division, Warner-Lambert Co., Morris Plains, NJ 07950 (USA)

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Summary

Propranolol HCl pellets were prepared in a rotor-granulator by layering the drug powder onto nonpareil seeds. They were then coated with Aquacoat® (an aqueous dispersion of ethylcellulose) in fluid bed coating machines, i.e., Aeromatic Strea I or Glatt GPCG-1, using different spray modes and/or chamber geometries. Dissolution data and morphology studies of coated pellets indicated differences in the nature of the coatings. This phenomenon may be attributed to differences in the particle motion in the bed, particle distribution and density in the coating zone, as well as the direction and the distance the sprayed droplets traverse prior to impinging on the particles. In addition, bed load and substrate friability also appeared to affect the deposition of coating. Therefore, it is essential that for controlled-release coatings, the optimization of the fluid bed process be preceded by a careful evaluation of the spray mode and chamber geometry for a given piece of equipment.

Introduction

Fluidization is a process in which a bed of small solid particles is suspended and agitated by a rising stream of gas which enables a thorough gas-solid contact throughout the bed. The technology has been used in a number of industries for diversified applications, ranging from limestone calcination, preparation of synthetic gasoline, petrochemicals, and even in the design of nuclear reactors (Zenz, 1980). During the last 30 years, fluid-bed technology has increasingly been utilized by the pharmaceutical industry in various unit operations, including drying, granulation, pelletization and coating (Mehta, 1989; Olsen, 1989).

In a fluid-bed coating or granulating process, a liquid feed is sprayed onto a bed of solid particles either for film deposition on each particle or for the growth of particle size. The liquid feed can be applied by using one of the three spray modes: top spray, bottom spray or tangential spray.

Correspondence to: S.T. Yang, Parke-Davis Pharmaceutical Research Division, Warner-Lambert Co., Morris Plains, NJ 07950, U.S.A.

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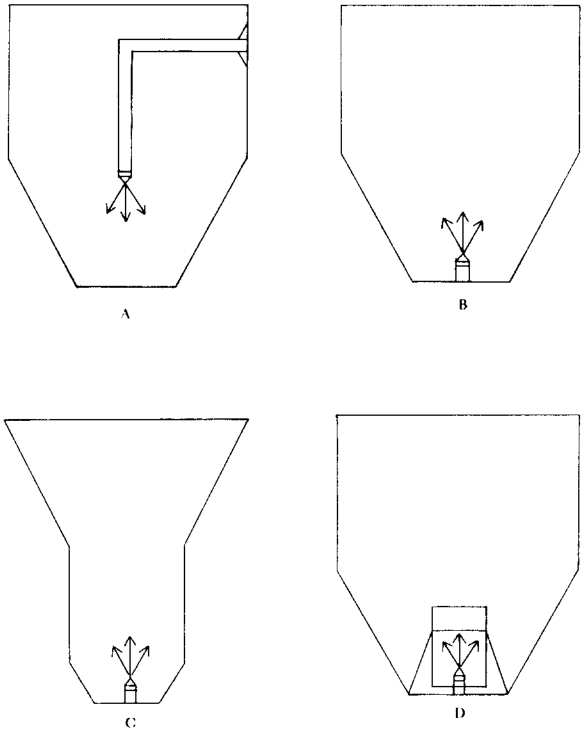

Fig. 1. (A) Top spray in the granulation chamber; (B) bottom spray in the granulation chamber; (C) bottom spray in the coating chamber; (D) bottom spray in the Wurster chamber of Aeromatic Strea I.

The top spray mode may be used for granulating or coating. The geometry of a granulator is very similar to that of a top spray coater. Each consists of a product container and an expansion chamber. The spray nozzle is located in the expansion chamber, and the sprayed droplets travel countercurrently to the fluidization air. The only difference in the geometry of a granulator and a top spray coater lies in the shape of the expansion chambers. In a top spray coater, the expansion chamber is longer to allow higher fluidization, and has a conical shape instead of a cylindrical shape (as in a granulator) to reduce the velocity of particles as they reach the section near the filter.

In the bottom spray mode, the nozzle is placed in the center of the gas distributor plate and liquid is sprayed concurrently with the fluidization air. The processing chamber for laboratory size equipment such as the Strea I, has a narrow diameter in the product-containing area which facilitates well organized particle motion, and therefore, reproducible coating results can be obtained. However, as the chamber becomes larger, particle motion loses its regular and circulatory pattern and becomes disorganized. As a result, a Wurster. chamber is commonly used for bottom spraying to produce an organized flow of particles similar to that observed in a spouted bed (more pronounced upward motion in the center and downward motion near the perimeter). With a Wurster chamber, a cylindrical partition is mounted in the center and slightly above the gas

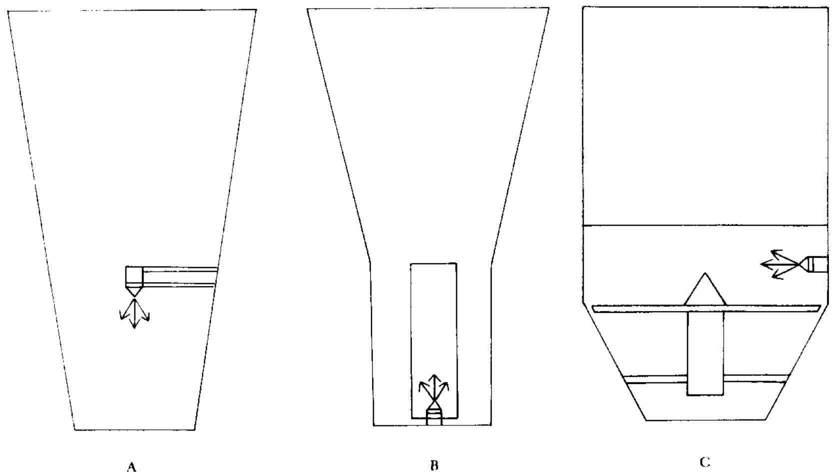

Fig. 2. (A) Top spray, (B) bottom spray, and (C) tangential spray of Glatt GPCG-1.

TABLE 1

The spray mode and corresponding chambers

Spray mode	Corresponding chambers	
	Strea I	GPCG-1
Bottom	Wurster chamber	Wurster chamber
Bottom	Granulation chamber	
Bottom	Bottom spray coater	
Top	Granulation chamber	Top-spray chamber
Tangential	N/A	Rotor insert

distributor plate. The design of the plate is such that more air enters the partition than the surrounding area to generate a circulatory motion of particles. The fluidized particles enter the partition, travel upward through the spray zone and into the expansion chamber. Then the particles decelerate and fall into the area outside the partition, from where they are driven horizontally back into the bottom of the partition to start the next circulatory cycle.

In the tangential spray mode, the spray gun placed on the side of the product chamber sprays the liquid tangentially to the rotating bed of particles. The product chamber contains a rotating disk which coupled with the fluidization air, generates centrifugal, gravitational and vertical forces that uniquely maximize the efficiency of the machine. The magnitude of each of these forces depends upon the fluidization air volume, the slit width and the rotation speed of the disk.

Since the spray mode determines not only the spray pattern of the coating formulation, but also how the sprayed droplets impinge and spread on the substrates, it is expected to have a significant impact on the film structure (Mehta et al., 1985).

TABLE 2

Coating conditions

Parameters	Strea I	GPCG-1
Spray rate (g/ml)	3–5	6–12
Atomizing pressure (bar)	0.5	1.0
Bed temperature (°C)	32–36	32–36
Air velocity (m^3/h)	50–90	110–200
Partition height (inch)	0.5	0.5
Rotor speed (rpm)	N/A	700

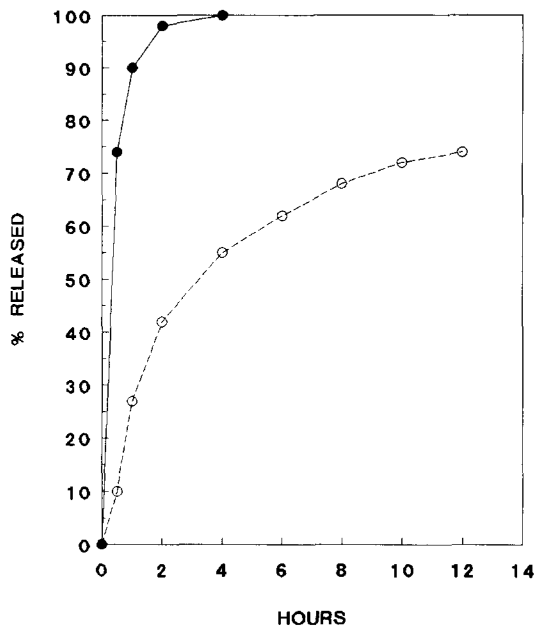

Fig. 3. The release profiles of pellets coated using top spray in the granulation chamber of Aeromatic Strea I. (●) Nozzle positioned above bed; (○) nozzle positioned in bed.

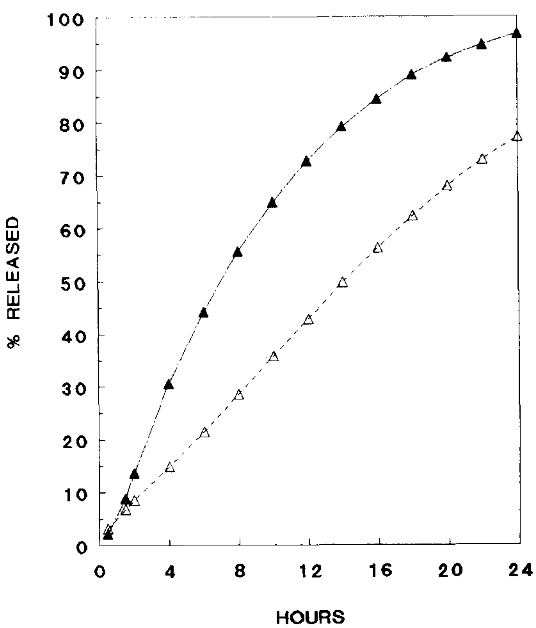

Fig. 4. The release profiles of pellets coated using bottom spray (△) and top spray (▲) in the granulation chamber of Aeromatic Strea I with 600 g bed load.

Although the effect of spray modes on some enteric coatings was previously reported (Mehta et al., 1986), the release profiles that were obtained cannot definitively characterize the film structure or properties owing to the all or none dissolution characteristics of enteric coatings. If the release behavior of the coated products is to be used to characterize film structure, an insoluble polymeric coating of sustained-release properties should be examined. In addition, since the chamber geometry determines the density and distribution of particles in the spray zone, it is also expected to influence the spray deposition and film formation. Therefore, the objective of this work was to examine the effect of spray mode and chamber geometry on the film structure and release properties of pellets coated with an aqueous-based ethylcellulose dispersion, i.e., Aquacoat®.

Materials and Methods

Materials

Aquacoat® ECD-30 (FMC, Philadelphia, PA), triethyl citrate (Morflex Chemical Co., Greensboro, NC), nonpareil seeds (Ozone Confectioners & Bakers, Elmwood Park, NJ) and talc (Cyprus Minerals Co., Englewood, CO) were used as received. Propranolol HCl (Flavine International, Inc., Closter, NJ) was milled through N000 screen (0.020 inch) using a Fitzmill (The Fitzpatrick Company, Elmhurst, IL) set with impact forward at high speed prior to use.

Preparation of pellets

Propranolol HCl pellets were prepared by a powder layering technique in rotary granulators (CF-Granulator, Freund Industrial Co., Ltd, Tokyo, Japan, and Glatt GPCG-5, Glatt Air Techniques Inc., Ramsey, NJ) using nonpareils as the starter seeds. The drug-loaded pellets were then screened to provide the 14–20 mesh fraction.

Coating process

A coating formulation consisting of Aquacoat® (38% w/w), triethyl citrate (3.5% w/w), talc (0.3% w/w) and water (58.2% w/w) was used to coat pellets to 8% weight increase in fluid-bed coating machines (Strea-I, Aeromatic, Towaco, NJ, and GPCG-1, Glatt Air Techniques Inc., Ramsey, NJ). A peristaltic pump (Cole-Parmer Instrument Co., Chicago, IL) was used for spraying the coating formulations during all coating processes. The spray modes and chambers employed are listed in Table 1 and the coating conditions are summarized in Table 2.

Drug release study

The release of drug from coated pellets into water (maintained at 37°C) was studied using a USP Dissolution Apparatus II at 50 rpm (Hanson Research, Northridge, CA) interfaced with a diode-array spectrophotometer (Hewlett-Packard, Avondale, PA) set at 290 nm wavelength.

Results and Discussion

The effects of spray modes and chamber geometry on film properties were examined using a bench-top coating machine (Strea-I) which can provide top spray and bottom spray modes. The effect of spray modes on film properties using another laboratory-size coating machine (GPCG-1) was also examined. In addition, the effect of two frequently neglected processing variables, bed load and substrate friability, were studied. The diagrams of the spray modes and the corresponding chambers are shown in Figs 1 and 2, respectively.

Effect of spray mode

In the study of spray mode effects, the granulation chamber was used for both top spray and bottom spray modes to keep the chamber geometry constant (Fig. 1A and B). For top-spray mode, spraying above the bed with a short spray gun results in blow back of droplets, loss of coating materials, and consequently, poor coating efficiency and fast release of drug (Fig. 3). Therefore, a long-shaft spray gun was used for the study of top spray mode to allow the nozzle to be immersed in the bed during fluidization. The release profiles of pellets coated under similar

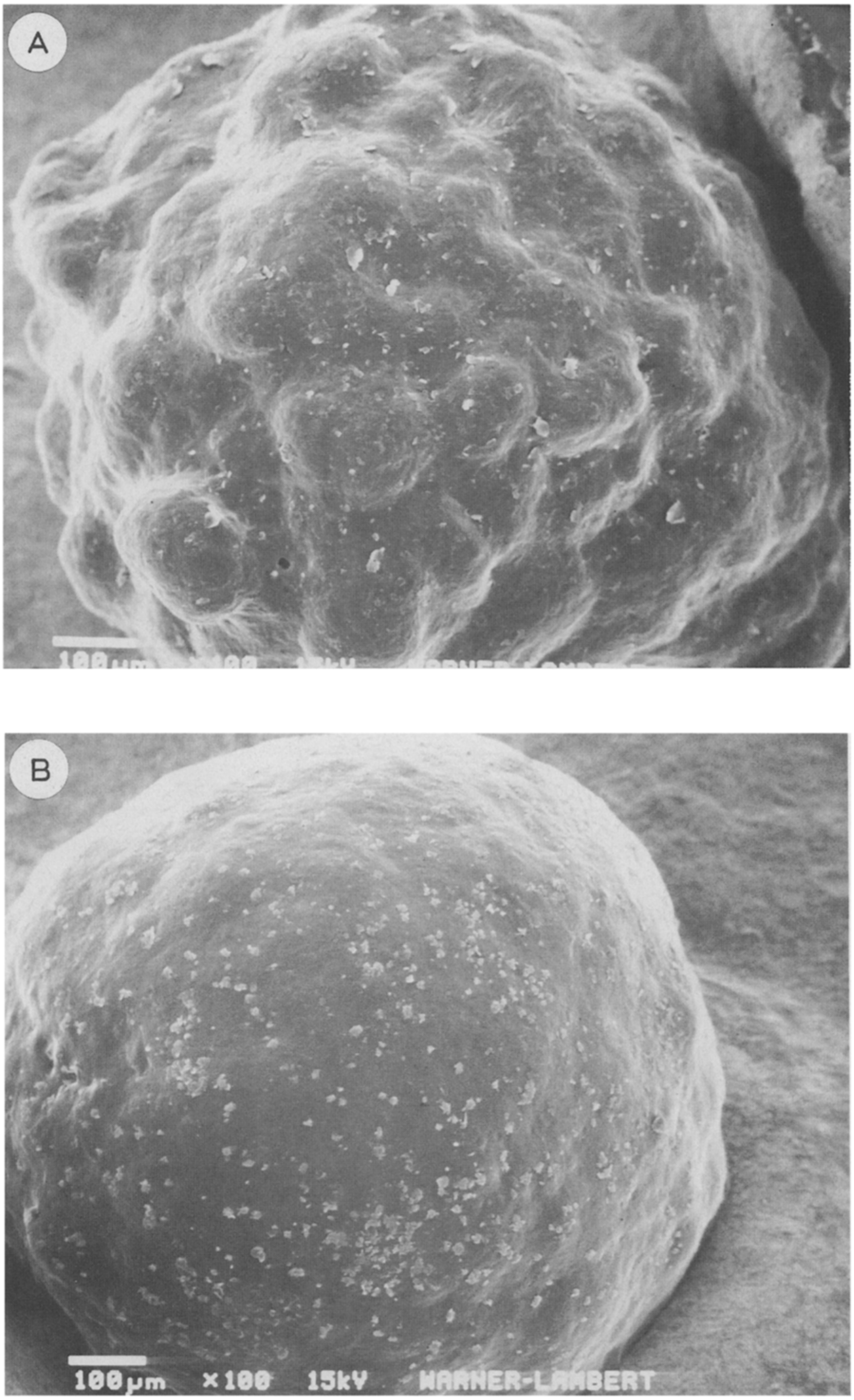

Fig. 5. SEM of pellets coated using (A) top spray and (B) bottom spray in the granulation chamber of Aeromatic Strea I with 600 g bed load each.

conditions using the two spray modes indicated that the bottom-spray coated pellets released the drug at a slower rate than the top-spray coated pellets (Fig. 4). Since the assay values showed that the amount of materials coated on the pellets using the two spray modes was similar, the difference in the release rates may be attributed to the physical properties and deposition of the spray droplets and hence, the film structure.

In a top spray process, the atomizing air travels countercurrently to the fluidization air; the spray liquid may evaporate to a large extent before impinging on the particles (i.e., spray drying effect), and hence, liquid spreading over the particle surface may be somewhat limited. In addition, a regular motion of particles in and out of the coating zone is essential for an evenly distributed coating throughout the bed. Although the particle motion in a fluid-bed is random, the top spray mode may make it even more irregular due to the countercurrent atomizing air, as a result, more variation in the residence time of particles in the coating zone can be expected. These factors either alone or in combination may lead to inadequate spreading of coating on the particle surface, more variation in coating thickness and, possibly, imperfection in film integrity. In such cases, faster release of drug is expected. Such speculation of the physical properties of the film was confirmed by an examination of the surface morphology of coated pellets. The scanning electron photomicrographs (SEM) clearly exhibit a rough and flaky appearance of top-spray coated pellets, as compared to a smooth and even surface of bottom-spray coated pellets (Fig. 5). However, the same processing parameters were used for both spray modes without being optimized for each individual spray mode. Therefore, it is very likely that some of the coating parameters favored the bottom spray but not the top spray mode. By identifying and optimizing these parameters, it may be possible to obtain sustained-release coatings of satisfactory properties using the top spray process.

The effect of spray mode on the film properties was also examined using another piece of laboratory-size coating equipment, i.e., Glatt GPCG-1. The top-spray coated pellets were found

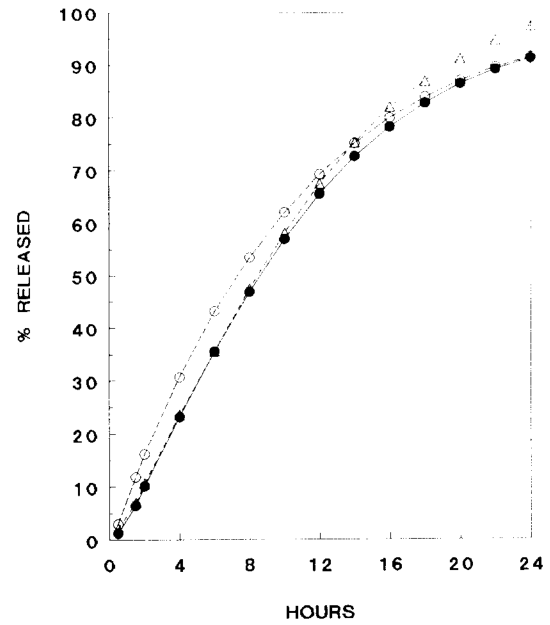

Fig. 6. The release profiles of pellets coated using bottom spray in the coating chamber (●), Wurster chamber (○) and granulation chamber (△) of Aeromatic Strea I with 300 g bed load.

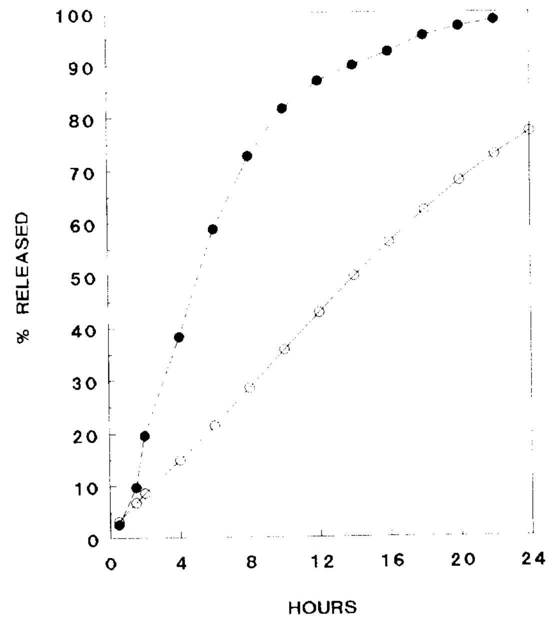

Fig. 7. The release profiles of friable (●) and less friable (○) pellets coated using bottom spray in the granulation chamber of Aeromatic Strea I.

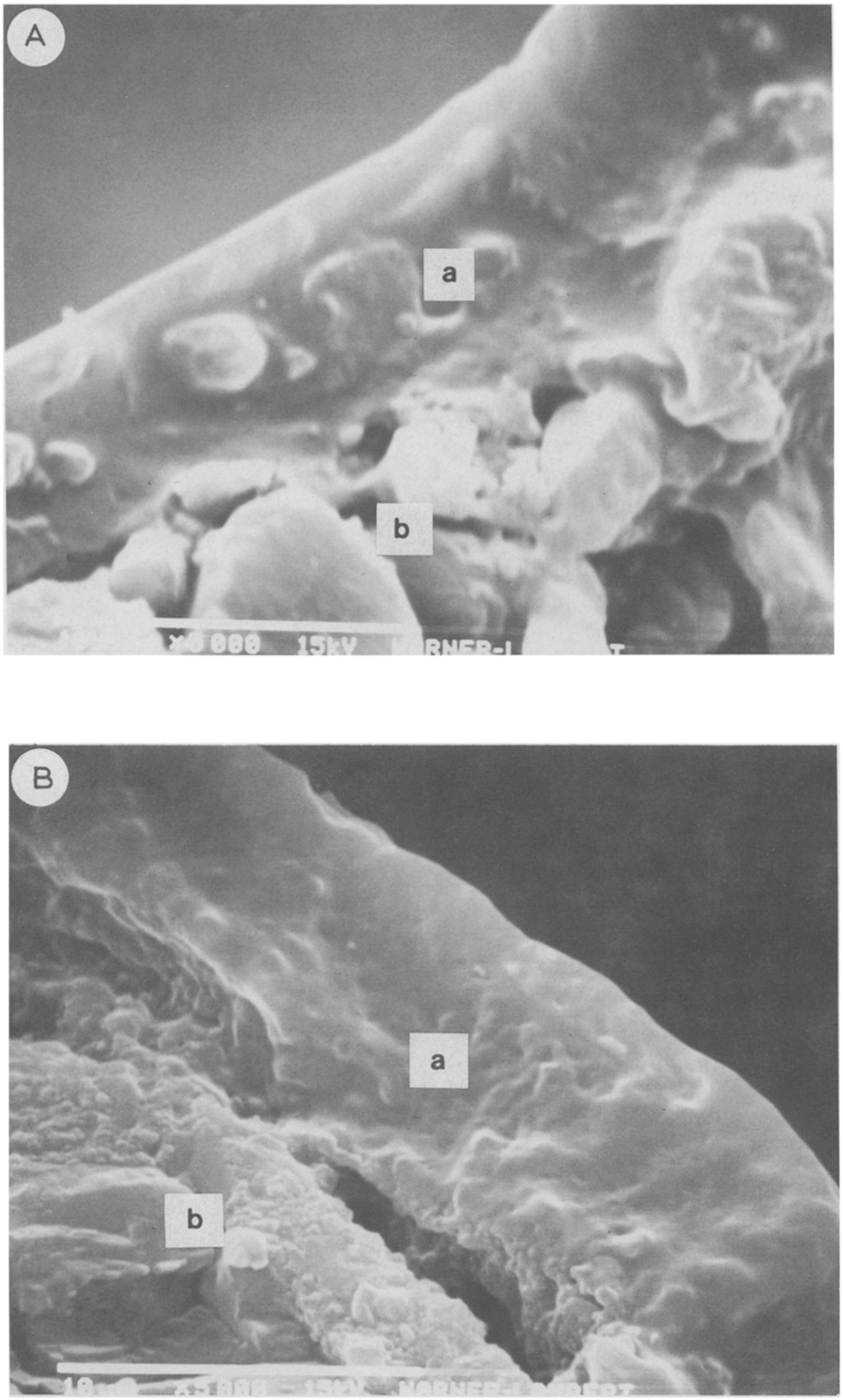

Fig. 8. SEM of cross-sectional view of (A) friable pellets and (B) less friable pellets coated using bottom spray. (a) Coating layer; (b) drug layer.

to release the drug at a faster rate than the bottom-spray coated and tangential-spray coated pellets. Once again, similar coating conditions were used for the three processes, and they may favor one spray mode over the others. In addition, the chamber geometry for each spray mode is different as shown in Fig. 2. Consequently, the differences in the release profiles cannot be attributed to spray mode alone.

Effect of chamber geometry of Strea I

In the study of chamber geometry using the Strea I machine, pellets were coated using the bottom spray mode in the granulation chamber, the coating chamber or the Wurster chamber, as shown in Fig. 1B–D. There is very little difference in the release rates of the pellets coated in the three chambers as indicated by the release profiles (Fig. 6). Due to the small sizes of these chambers, a near spouted bed can be maintained in all cases by properly adjusting the fluidization air velocity. Therefore, the particle residence time in the coating zone of these chambers is expected to be quite uniform. This in turn leads to a uniform distribution of coating material on the particle surface. However, for larger chambers of larger coating machines, it will be difficult to maintain an organized particle flow pattern without using Wurster partitions.

Effect of friability of core pellets

During the preliminary studies of the coating process, the friability of core pellets was found to affect the release rates of coated pellets. One batch of core pellets manufactured prior to process optimization showed high friability (10–12% weight loss after a coating process of about 1.5–2 h as opposed to 1–2% weight loss for the optimized batches used throughout this work), and was used to demonstrate this effect. A dramatic increase in the release rate was observed for the more friable pellets coated with the same process (Fig. 7). The SEM of the cross-section of a pellet from this friable batch clearly shows chunks of drug particles embedded in the coating (Fig. 8A). During the coating process, drug particles appeared to slough off the drug layer, adhere to the pellet surface and become embedded in the coat-

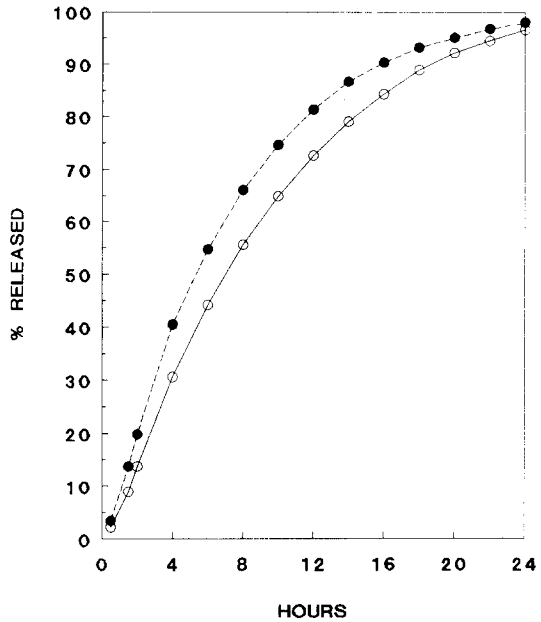

Fig. 9. The release profiles of pellets coated using top spray in the granulation chamber of Aeromatic Strea I with 600 g (○) and 300 g (●) bed load.

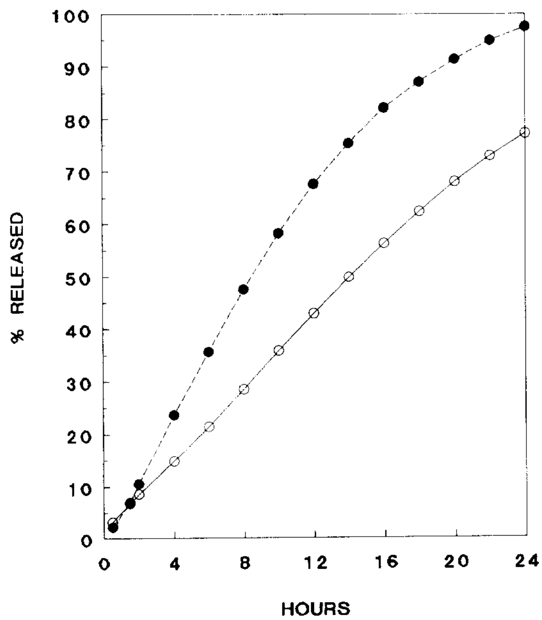

Fig. 10. The release profiles of pellets coated using bottom spray in the granulation chamber of Aeromatic Strea I with 600 g (○) and 300 g (●) bed load.

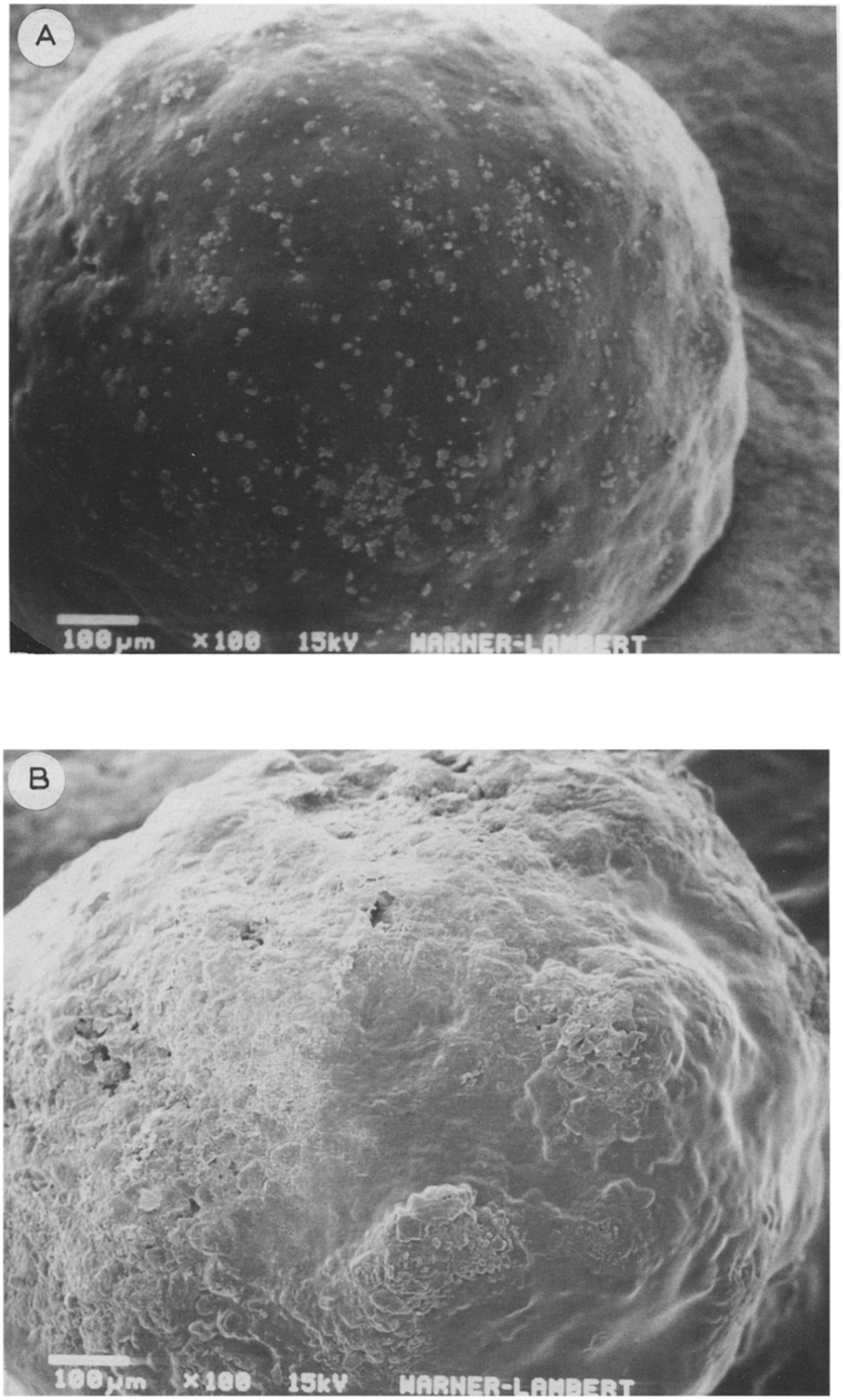

Fig. 11. SEM of pellets coated using bottom spray in the granulation chamber of Aeromatic Strea I with (A) 600 g and (B) 300 g bed load.

ing. In contrast, there is no apparent sign of drug particles in the coating layer of the less friable pellets (Fig. 8B). The fast release of the coated friable batch may be attributed to the presence of drug in the coating.

Effect of bed load

During the initial optimization process, the bed load was also found to affect the release profiles of coated pellets, but not to the same extent in each spray mode or chamber. Pellets coated from a bed load of 600 g with the top spray mode and the granulation chamber in Strea I released the drug at a slightly slower rate than similarly coated pellets from a bed load of 300 g (Fig. 9). However, for the bottom spray mode using the same chamber, the bed load was found to have dramatic effects on the release profiles of the coated pellets (Fig. 10). It appears that bed load is a parameter that needs to be considered for the bottom spray coating process.

Although the particle motion is random in fluidized beds, the countercurrent atomization in the top-spray mode may produce a less organized movement of the particles and increasing the bed load may not improve the particulate motion. Consequently, the distribution of coating materials and the uniformity of the film is not significantly affected by changing the load. In contrast, increasing the bed load from 300 to 600 g with the bottom spray mode, a near spouted bed was observed. Therefore, the distribution of coating materials on the pellet surface was expected to be more even and homogeneous. The surface morphology of these batches was also examined using SEM. Coated pellets from a bed load of 600 g demonstrated smoother surface characteristics compared to those from a 300 g bed load (Fig. 11). This observation further confirms that the particle flow pattern can influence the deposition of the coating material on the particle surface.

For the bottom spray mode conducted in the narrow coating chamber, the release profiles of coated pellets from 300 g bed loads are almost superimposable with those of 600 g bed loads (Fig. 12). Because of the narrow product-containing area in the coating chamber, a load of 300 g may be adequate to provide uniform movement

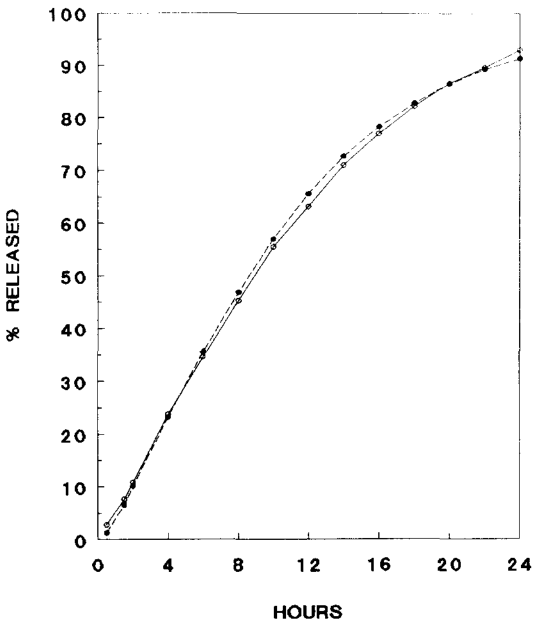

Fig. 12. The release profiles of pellets coated using bottom spray in the coating chamber of Aeromatic Strea I with 600 g (○) and 300 g (●) bed load.

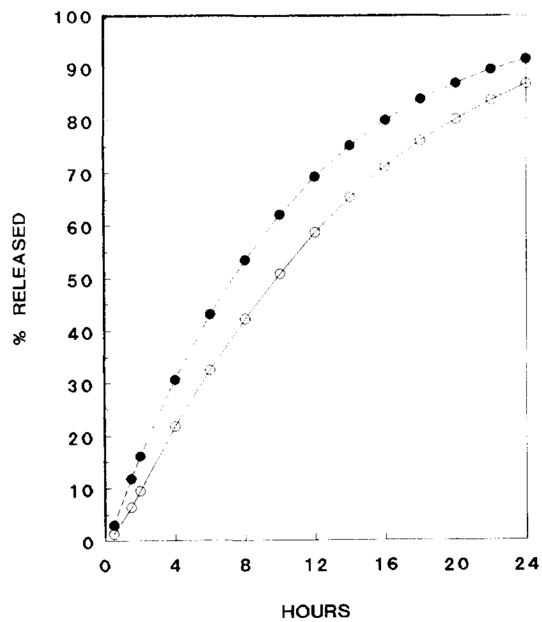

Fig. 13. The release profiles of pellets coated using bottom spray in Wurster chamber of Aeromatic Strea I with 600 g (○) and 300 g (●) bed load.

of pellets in the bed and regular motion in the coating zone.

Since the Wurster chamber is often used for bottom spray, especially in larger coating equipment, the effect of bed load on the release rates of pellets coated in the Wurster chamber was also examined. Increasing the bed load from 300 to 600 g resulted in a slight reduction in the release rates of the coated pellets (Fig. 13). Both chambers are similar in geometry, but the presence of the partition in the Wurster chamber produces a more organized movement of particles which is affected by bed load to a lesser extent. However, the load should still be kept constant in order to obtain batch-to-batch reproducibility.

The effect of bed load on the release rates of pellets coated in GPCG-1 with a Wurster insert was also examined. Increasing the load from 300 to 600 g slightly reduced the release rates of the coated pellets, a trend that was observed with the Strea I (Fig. 13). In addition, the release rates of pellets coated in GPCG-1 were also found to be influenced by the friability of core pellets, i.e., more friable core pellets lead to faster drug release.

In addition, the effect of bed load on the release rates of pellets coated in a larger piece of equipment, Glatt GPCG-5 with tangential spray, was examined. Increasing the bed load from 5 to 8 kg did not appear to have any significant effect on the release profiles (Fig. 14). However, since this equipment is usually used for development work, it would be more desirable to keep the bed load constant if batch-to-batch comparison is to be made.

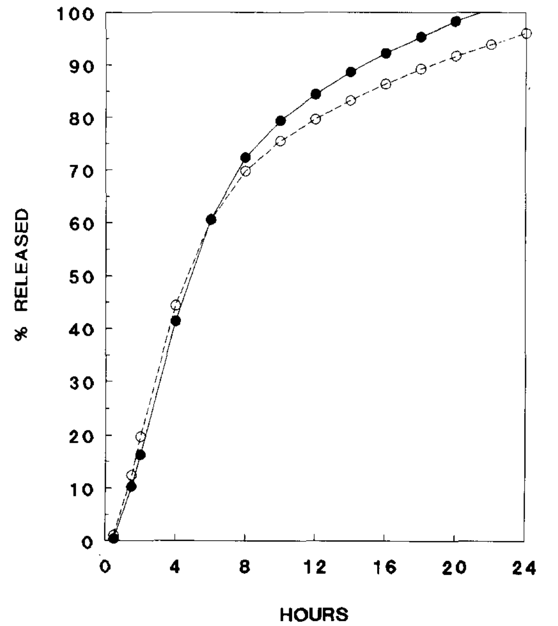

Fig. 14. The release profiles of pellets coated using tangential spray in Glatt GPCG-5 with 5.0 kg (●) and 8.0 kg (○) bed load.

Conclusions

Spray mode directly affects the impingement of spray droplets on the substrates, and hence, the structure of the film. Chamber geometry influences particle motion and distribution, and therefore, affects the deposition of coating materials on the substrate. When the spray mode is changed, the corresponding chamber geometry is often different, as a result, the differences in the product release profiles may be attributed to the effects of both the spray mode and the chamber geometry. Since the dimensions and geometry of coating chambers may vary from one machine to another even for the same spray mode, it is essential that the coating conditions be optimized on a case by case basis.

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