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# Air Suspension Coating

Reprinted from PHARMACEUTICAL TECHNOLOGY ENCYCLOPEDIA Jan. 1988

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In pharmaceutical solid dosage form development, many products require coating to provide the desired release characteristics [1]. Recent advances in film coating equipment have made it possible to coat particles ranging from crystals to tablets reproducibly. Films may be applied to provide sustained or controlled release, taste masking, enteric release, improved stability, or aesthetics. For many products, development of aqueous-based coating materials has eliminated the safety hazards and emissions problems related to flammable organic solvents. Additionally, these materials have higher solids concentrations and tend to be easier to apply than films from solution.

## Fluidized Bed Equipment Types

The fluidized bed is well known for its drying efficiency, as it has been used for drying and granulating for many years. It has recently been given increased interest owing to its ability to apply virtually any type of coating system (solution, suspension, emulsion, latex, and hot melt) to a wide range of particle sizes. Coatings can be applied to fluidized particles by a variety of techniques, including spraying from the top, from the bottom, or tangentially. For a given product, the resulting finished product release characteristics may significantly differ. In addition to a working knowledge of the formulation variables used in product development, an understanding of these types of processing techniques is essential.

The gas fluidization and bubble characteristics have been defined in the literature [2–9]. They are affected by the properties of the materials being fluidized and the design characteristics of the equipment being used, which varies with equipment vendors. Only the fundamentals of these phenomena will be described for each processing technique because of this dependence. Figure 1 illustrates typical fluidization characteristics encountered in air suspension coating. The air distribution plate design determines the size and number of bubbles, which in turn affects the mixing characteristics of the bed (Fig. 2). Machines are typically designed to maximize the number of bubbles to result in effective mixing; Fig. 3 illustrates how mixing occurs by rising bubbles.

The conventional top spray method shown in Fig. 4 has been used for more than a decade for coating. It evolved from the fluidized bed dryers commercialized more than 30 years ago. The substrate is placed in the product container (*A*), which is typically an unbaffled, inverted, truncated cone with a fine retention screen and an air or gas distribution plate (*B*) at its base. Preconditioned air is drawn through the distribution plate (*B*) and into the product. As the volume of air is increased, the bed no longer remains static but becomes fluidized in the air stream. The point at which the bed becomes just fluidized is known as *incipient fluidization*.

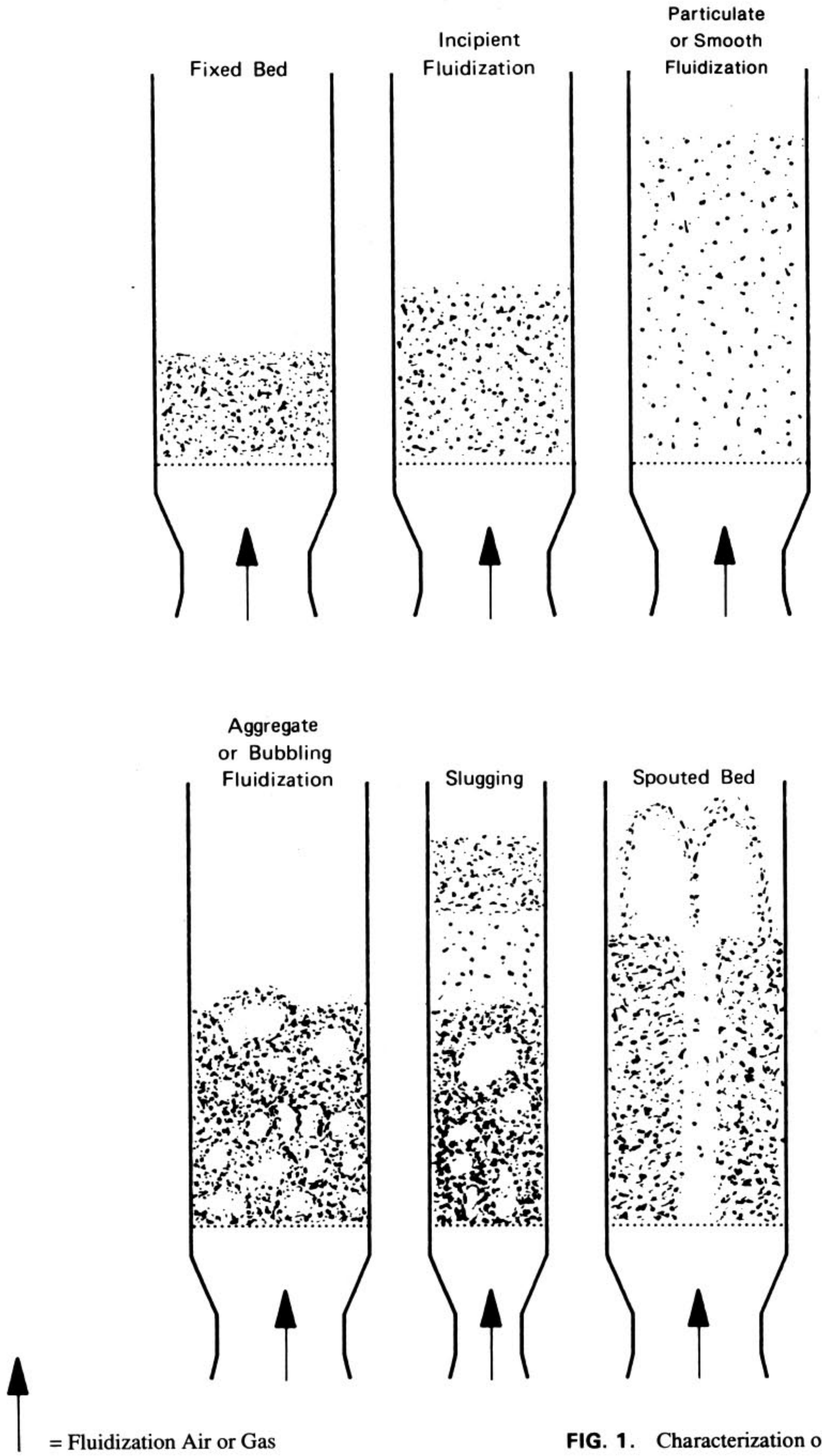

**FIG. 1.** Characterization of fluid beds.

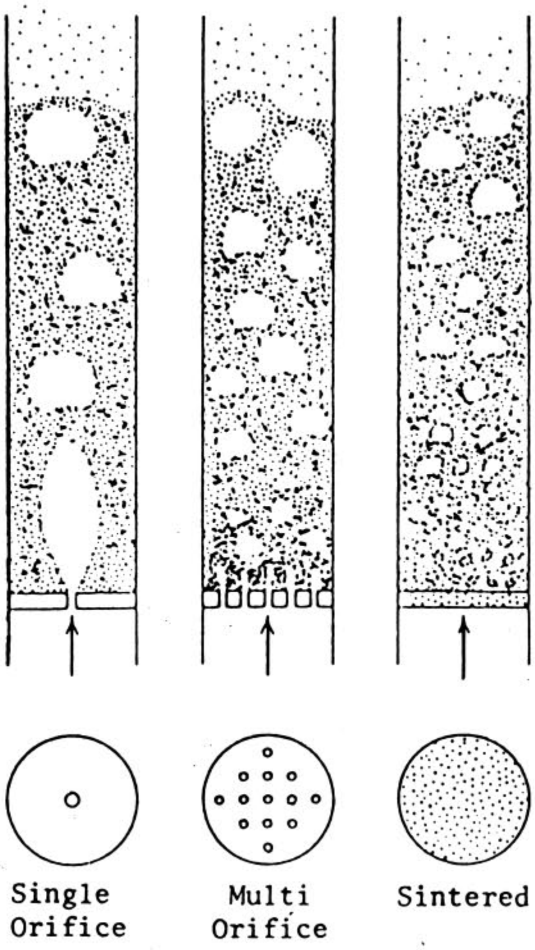

**FIG. 2.** Fluidization quality by gas distributor.

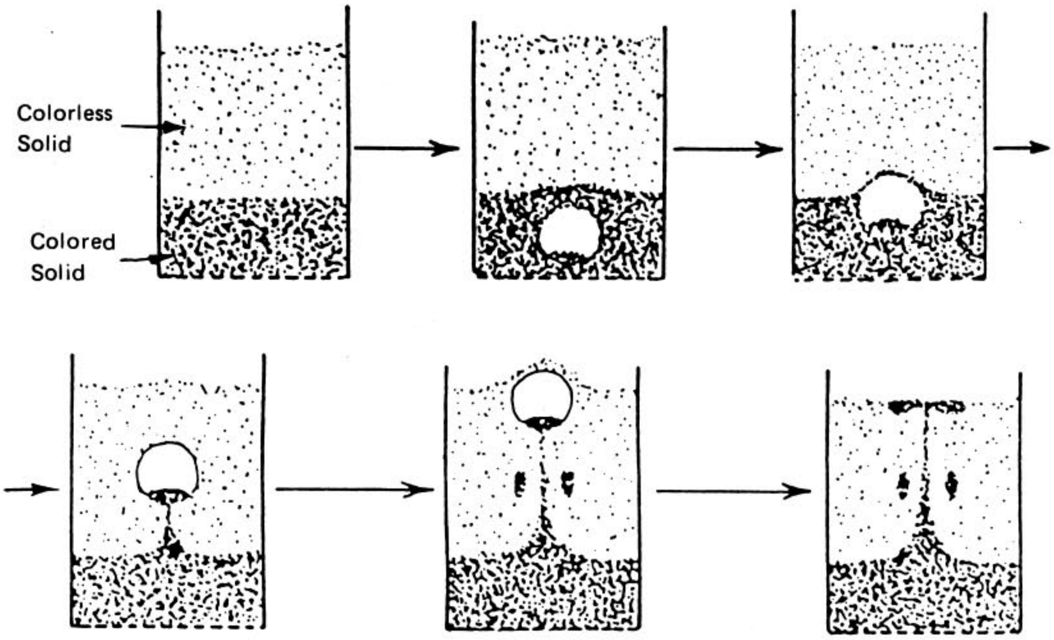

**FIG. 3.** Solids mixing by rising gas bubble.

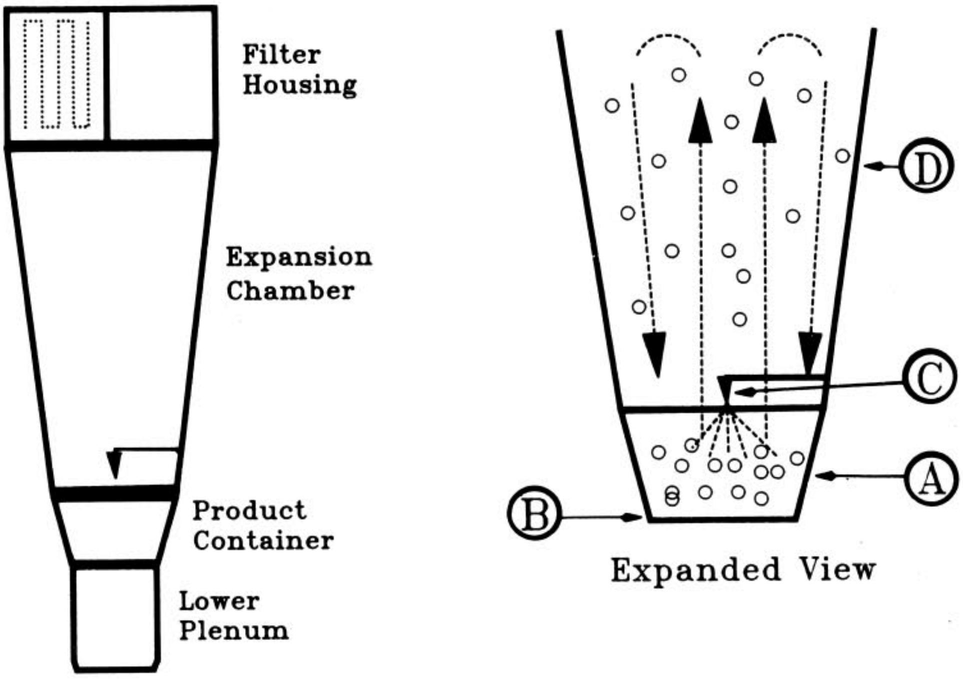

**FIG. 4.** Top spray coater: (*A*) Product container; (*B*) air distribution plate; (*C*) spray nozzle; (*D*) expansion chamber.

The velocity of particles in the bed under this condition is too low for efficient coating. Increasing the air volume (and hence particle velocity) results in a wider fluidization range known as *bubbling fluidization*, in which the bed can be defined as containing two phases: a particulate phase, containing particles and air, and a bubble phase, which contains the excess air.

The particles are accelerated from the product container past the nozzle (*C*), which sprays the coating liquid countercurrently onto the randomly fluidized particles. The coated particles travel through this coating "zone" into the expansion chamber (*D*), which is wider in diameter than the base of the product container; this results in a decreasing air velocity that allows deceleration of the particles to below entrainment velocity. The particles fall back into the product container and continue cycling throughout the duration of the process. The random mixing and evaporative efficiency, provided by bubbling fluidization, and the speed of recycling of the particles provide good uniformity in film thickness (Fig. 5).

In 1959, Dr. Dale Wurster, then at the University of Wisconsin, introduced an air suspension technique known as the *Wurster system* [10–13]. Originally designed to coat tablets, the process is now widely used for substrates as small as 100 $\mu$m. The components of the system are illustrated in Fig. 6. The coating chamber (*A*) is an unbaffled cylinder that contains another cylinder half its diameter known as a *partition* (*B*). At the base of the coating chamber is a fine screen and an air distribution (orifice) plate (*C*). In the center of the plate, a nozzle (*D*) is positioned to spray upwardly. The holes in the plate in the area beneath the partition are larger in diameter than those outside. Air passes through the plate at a high volume and velocity and pneumatically transports particles vertically through the partition and coating zone. This type of fluidization is characterized as a *spouting bed* (Fig. 1).

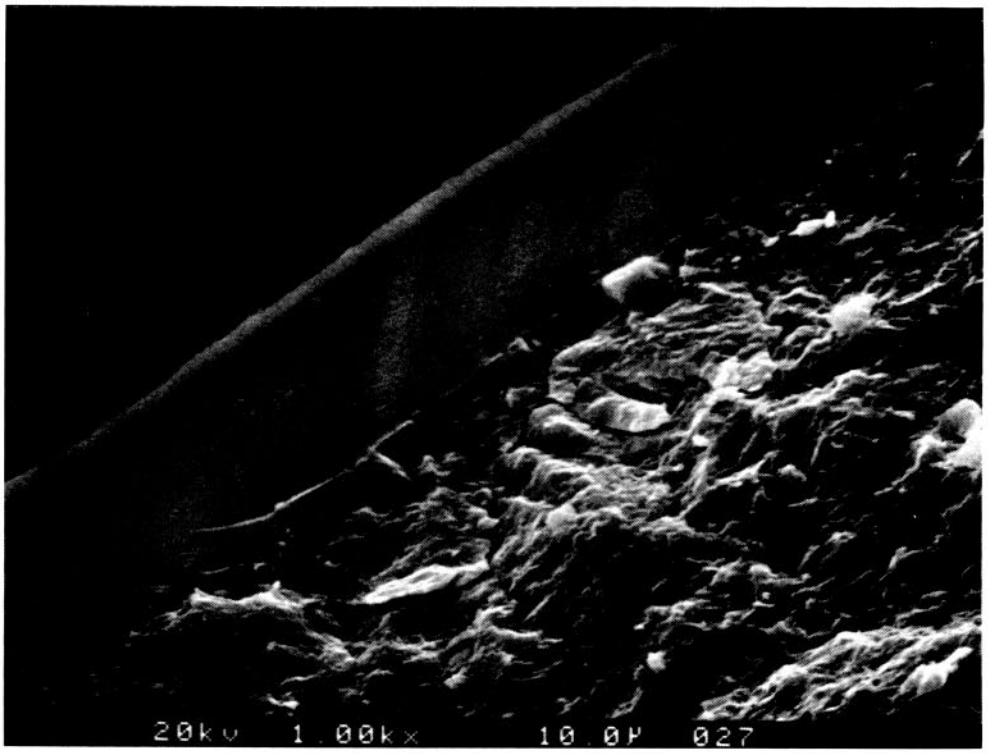

**FIG. 5.** Cross-section of particle coated by fluidized bed showing uniformity of applied film (magnification 1000×).

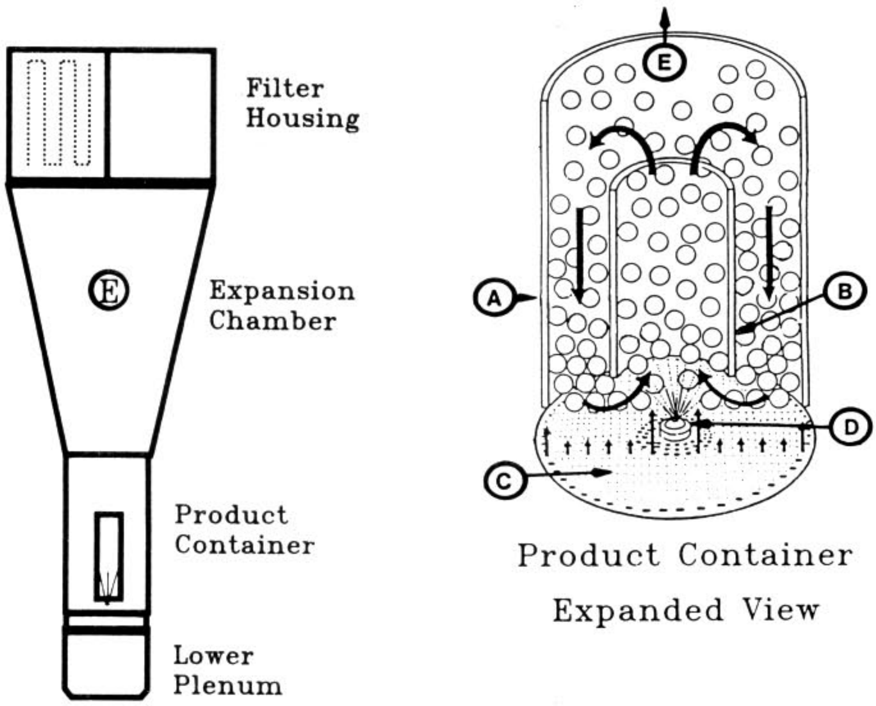

**FIG. 6.** Wurster bottom spray coater: (*A*) Coating chamber; (*B*) partition; (*C*) air distribution plate; (*D*) spray nozzle; (*E*) expansion chamber.

The coated particles exit the partition and begin to decelerate in the expansion chamber (*E*). When the air velocity is such that the particles can no longer be entrained, they drop into the area between the partition and the wall of the coating chamber known as the *down bed*. The air volume in the down bed depends on the size and number of holes in the orifice plate in the area outside of the partition. This air volume should be enough only to enhance downward motion, keeping the down bed in near-weightless suspension. The horizontal transportation of particles toward the coating zone, which completes the coating cycle, is accomplished by the proper selection of the distance between the base of the partition and the air distribution plate (known as *partition height*). Particles are recycled through the coating zone in a matter of seconds, as in the conventional, top spray technique, but by contrast, the fluidization pattern is much more controlled in the Wurster system.

A relatively new approach to coating is referred to as *tangential spray* or *rotary fluidized bed coating* (Fig. 7). Originally conceived for high-density fluid bed granulation [14], this technique is being used to produce high-dose pellets by applying a layer of drug particles to some type of seed material. The controlled release coating can subsequently be applied.

The product container consists of an unbaffled cylindrical chamber (*A*) with a solid, variable-speed disc (*B*) at its base. The disc and chamber are constructed such that during the process a gap (*C*) exists at the perimeter of the disc through which preconditioned air is drawn. During fluidization, three forces combine to provide a pattern best described as a spiraling helix. Centrifugal force causes the product to move toward the wall of the chamber, air velocity through the gap provides acceleration upward, and gravity cascades the product inward and toward the disc once again. The fluidization pattern may be characterized as smooth or particulate, as shown in Fig. 1. Beneath the surface of the rapidly tumbling bed, a nozzle (*D*) is positioned to spray the coating liquid tangentially to and concurrently with the flow of particles. The particle cycling time of this technique is very rapid; hence, the films are uniform in thickness, as are those applied using the processes discussed previously.

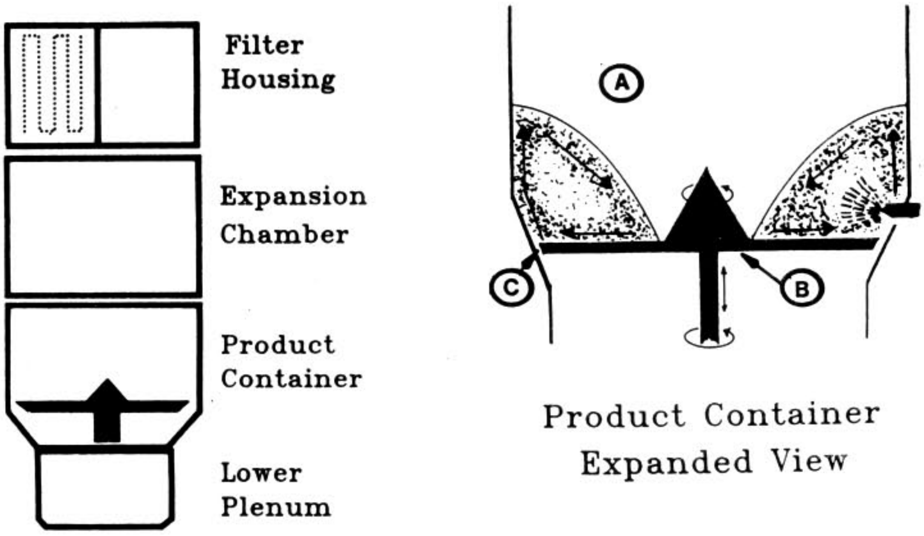

**FIG. 7.** Rotor tangential spray coater: (*A*) Product chamber; (*B*) variable-speed disc; (*C*) disc gap or slit; (*D*) spray nozzle.

## Fundamentals of Film Coating

Uniformity of distribution of the film and evaporative efficiency to inhibit core penetration by solvents or water are common to the three types of fluidized bed processing [15, 16]. However, each of the techniques has limitations, and they are by no means equivalent. Before examining each process in detail, a brief description of coating fundamentals and general process and product variables is necessary.

Application of a film to a solid is indeed very complex. A layer of coating does not occur during a single pass through the coating zone, but relies on many such passes to produce complete coverage of the surface. Droplet formation, contact, spreading, coalescence, and evaporation, as illustrated in Fig. 8, are occurring almost simultaneously during the process.

The nozzles typically used in the fluidized bed coating process are binary: liquid is supplied at a low pressure and is sheared into droplets by air. Droplet size and distribution are more controllable with this type of nozzle than with a hydraulic nozzle [17], especially at low liquid flow rates. However, the air used for atomization also contributes to evaporation of the coating solvent. This evaporation results in increasing the droplet's viscosity, thus inhibiting spreading and coalescence upon contact with the core material. Another factor affecting droplet viscosity is the distance that the droplets travel through the primary evaporation media (the fluidization air) before impinging on the core. This problem is amplified with the use of organic solvents that have much lower heats of vaporization than water (Fig. 9) and polymers whose viscosity is very sensitive to changes in solids concentration. In all three process techniques, the nozzle is positioned to minimize droplet travel distance.

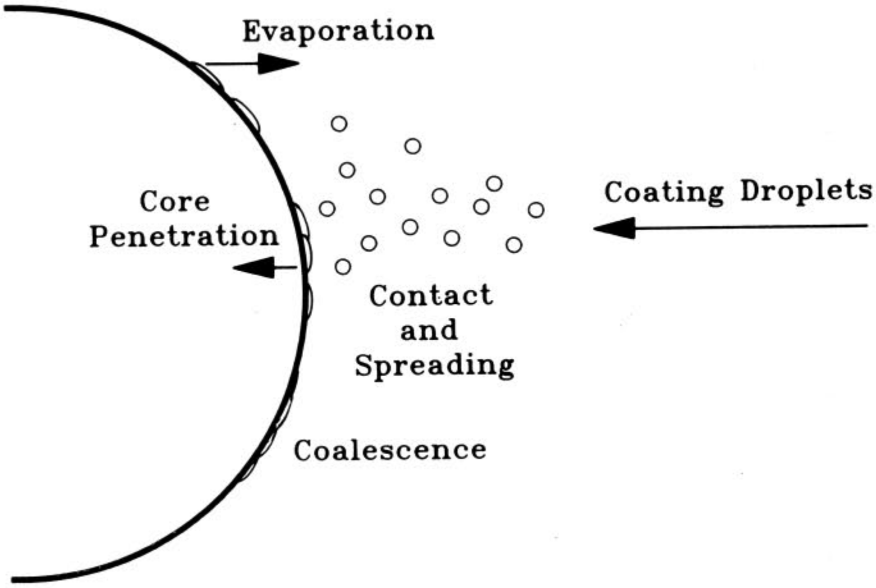

**FIG. 8.** Dynamics of film coating.

| Solvent | Boiling Point (°C) | Density (g/cc) | Heat of Vaporization (Kcal/ml) |
|---|---|---|---|
| Methylene chloride | 40.0 | 1.327 | 0.118 |
| Acetone | 56.2 | 0.790 | 0.103 |
| Methanol | 65.0 | 0.791 | 0.232 |
| Ethanol | 78.5 | 0.789 | 0.166 |
| Isopropanol | 82.4 | 0.786 | 0.132 |
| Water | 100.0 | 1.000 | 0.541 |

**FIG. 9.** Heats of vaporization for commonly used solvents.

## Process Variables

The most significant process variable is the selection of technique to be used. The majority of the remaining process variables are common to each type, however, and are listed in Fig. 10.

The rate of evaporation of the coating media can significantly affect film formation in both aqueous and organic solvent systems. Fluidization air volume, temperature, and humidity are the three components of this variable. Because the fluidization air volume affects particle velocity and, hence, the fluidization pattern, it should remain consistent from batch to batch. Drying capacity for aqueous coating systems is affected by the fluidization air temperature and specific humidity as illustrated in the psychrometric chart (Fig. 11). If a low temperature is chosen to accommodate a heat-sensitive polymer, drying capacity will fluctuate due to seasonal changes in the weather. An example illustrating this phenomenon follows:

> An aqueously applied thermoplastic polymer requires a fluidization air temperature of not more than 37°C. Assume that process variables such as fluidizing air volume and liquid spray rate are the same for both experiments.
>
> Day 1 Ambient Conditions:
> 8°C dry bulb
> 5°C wet bulb
> 1°C dew point, equivalent to 4 g $H_2O$ per kg dry air
>
> Day 2 Ambient Conditions:
> 26°C dry bulb
> 22°C wet bulb
> 20°C dew point, equivalent to 15 g $H_2O$ per kg dry air

Air heated to 37°C has a capacity of approximately 42 g of $H_2O$ per kg of dry air. On a humid summer day, such as day 2, drying capacity is eroded so significantly that the coating liquid application rate must be substantially reduced or agglomeration will occur. Specific humidity must be controlled to allow reproducible application rates.

- Evaporation
  - a. Fluidization air volume
  - b. Fluidization air temperature
  - c. Fluidization air humidity
- Solids application rate
  - a. Solution concentration
  - b. Liquid spray rate
- Droplet size

**FIG. 10.** General process variables.

For organic solvents, a low fluidization air temperature may be chosen to accommodate the solvent's low heat of vaporization. The danger in allowing specific humidity to vary is that enthalpy, which determines evaporation rate, increases at a given dry bulb temperature as the specific humidity increases. Additionally, if the specific humidity is high, evaporative cooling by the solvent in the coating zone may locally depress the air temperature below the dew point and cause condensation of water onto the substrate surface. If the film is incompatible with water, the film would not perform as desired.

Consistency in specific humidity is recommended, but removal of all moisture is not required. In fact, in many organic solvent coating processes, a quantity of moisture is usually helpful in dispelling static electricity, which develops after the surface of the particles is completely coated.

Coating uniformity is a result of the rapid cycling of particles or the number of times the particles are exposed to the spray. The rate at which the coating is applied (on a solids basis) is dependent on the solution concentration and the spray rate. Because the quantity of coating required for effective coverage of small particles is substantial, the tendency is to apply as concentrated a solution as possible to minimize the process time. However, the droplet size and spreading characteristics will be affected by the increased viscosity, and the resulting film may not perform as desired. Agglomeration of fine particles may also result.

Spray rate is dependent on three factors: (1) capacity of air for the solvent being used; (2) the tackiness of the coating being applied; and (3) the speed with which the particles travel through the coating zone. With most coating systems, the fluidizing air has excess capacity for the application media. The rate-limiting factor is generally the tackiness of the coating solution as it changes from a liquid to a solid. In the fluidized bed process, coating is applied to particles suspended in the air stream. However, particle-machine and particle-particle collisions do occur. If two particles collide where coating has just been applied, a bridge may form between them. If the mass of the particles (which decreases as particle size decreases) is not sufficient to disjoin the particles because of the tackiness of the coating substance, the bond will become permanent, resulting in agglomeration. It has been reported in the literature that coating solution tackiness can be altered [18–20]. Additionally, several coating system vendors have experience in this area.

Coating solution droplet size should be selected relative to the size of particles to be coated. Atomizing air volume and pressure determine droplet size; the higher these values, the smaller the droplets. High atomizing air volume and pressure are not necessary for coating tablets. For small particles (250 $\mu$m or smaller), however,

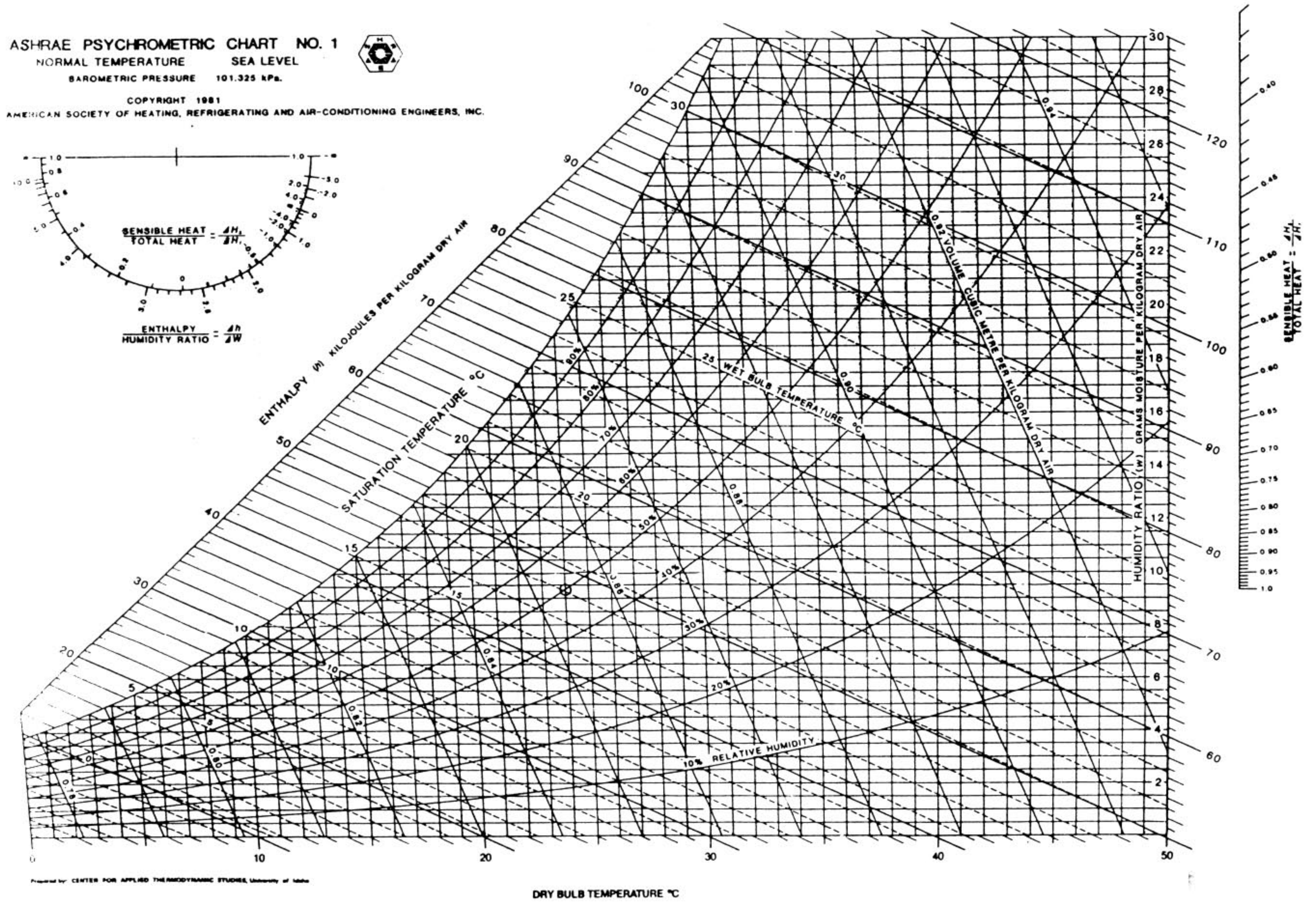

**FIG. 11.** Ashrae psychrometric chart no. 1. Normal temperature at sea level with barometric pressure 101.326 kPa. (Copyright 1981 by American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc.; used with permission.)

high pressure and volume may be necessary to attain droplets small enough to avoid the formation of liquid bridges between particles at contact points and thus avoid agglomeration.

Droplet size is also a function of characteristics of the coating solution such as viscosity and liquid surface tension. Each coating material or formulation will have different droplet sizes at a constant atomizing air volume and pressure. For this reason, droplet size is selected empirically rather than determined mathematically. However, several nozzle vendors do have droplet size histograms available to aid in understanding the nozzle's capability when using particular materials (typically water).

All the three processing techniques (top, bottom, tangential) are typically set up to maximize product density in the coating zone to minimize droplet travel. To increase the spray rate for any coating material, the machine can be adjusted to increase particle velocity such that particles pass through the coating zone quickly and receive only a small amount of spray. To increase the spray rate significantly, however, the number of coating zones must be increased. In pilot and production scale equipment, this is achieved by using multiple or multiheaded nozzles in the top spray method, multiple partitions and nozzles in the Wurster system, and multiple nozzles in the tangential or rotary fluidized bed coater.

## Product Variables

The scope of any coating development project must include an in-depth look at product-related variables. In many instances, trouble-shooting has traced problems in reproducibility to inconsistencies in the characteristics of the core and/or coating materials.

An early challenge formulators face is determining how much coating may be necessary to achieve desired finished product performance. Most coatings are applied as a percentage of weight of the starting material. Therefore, the thickness of the film depends on substrate particle size. Applied films should be thick enough to overcome various surface properties and perform as desired. Depending on the coating material, this thickness may vary from a few microns to more than 20. Assuming 10 $\mu$m as an average, Figure 12 shows amounts of coating substance required to cover particles ranging in size down to 325 mesh or 44 $\mu$m. As particle size decreases, the amount of coating required to achieve a 10-$\mu$m thickness becomes very high. Also, the coating substance must be applied using some medium, and solids concentrations in the liquid range typically from 10 to 30%, resulting in the need to apply large quantities of liquid relative to the uncoated product. A further complication is that as particle size decreases agglomeration becomes very dependent on the formulation of the coating liquid and nozzle limitations, and it may be unavoidable. For these reasons, it is advantageous to use the largest particle size that may reasonably yield the desired results.

The most stringent raw material requirements are found where sustained release is desired. If the rate of release is dependent on film thickness and quality, then surface area and integrity are of paramount importance. Surface area is controlled by

| | Uncoated Particles | | | Coated Particles | | |
|---|---|---|---|---|---|---|
| U.S. mesh | Diameter (mm) | Particles/ Gram | Surface Area/ Gram ($mm^2$) | Coated Diameter (mm) | Coating Added (%) | Coating in Production (%) |
| 5 | 4.00 | 23 | 1,157 | 4.02 | 1.2 | 1.18 |
| 10 | 2.00 | 183 | 2,312 | 2.02 | 2.4 | 2.34 |
| 18 | 1.00 | 1,468 | 4,610 | 1.02 | 4.7 | 4.49 |
| 35 | 0.500 | 11,764 | 9,235 | 0.520 | 9.6 | 8.75 |
| 60 | 0.250 | 94,340 | 18,490 | 0.270 | 20.0 | 16.7 |
| 120 | 0.125 | 751,880 | 36,917 | 0.145 | 43.3 | 30.2 |
| 200 | 0.074 | 3,663,000 | 63,004 | 0.094 | 82.3 | 45.1 |
| 325 | 0.044 | 17,543,860 | 107,018 | 0.064 | 163.5 | 62.0 |

**FIG. 12.** A comparison of the amount of coating required to apply a coating 0.01-mm thick onto particles of various sizes.

particle size, shape, porosity, density, and friability. Because coatings are applied on a weight basis, it is advantageous to have a core that has a narrow particle size range, is spherical, has a dense, strong surface, and does not vary in bulk density from batch to batch. An example of ideal surface characteristics is shown in Fig. 13. Surface integrity is important because any loose drug or core excipients that become reattached to the core via the coating may alter the solubility or permeability of the film. Note that all fluid bed coating techniques expose the product to some degree of mechanical stress.

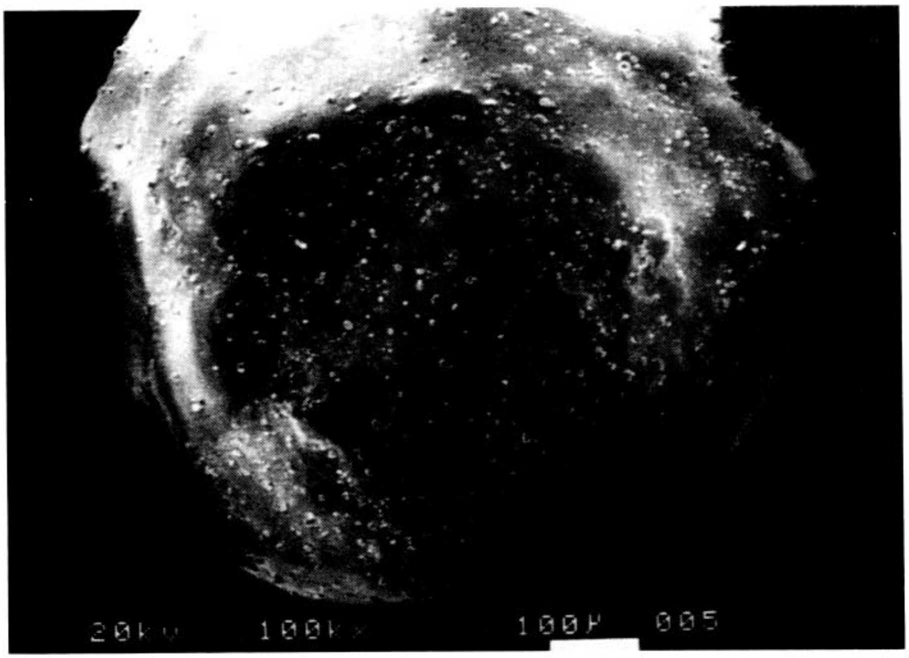

**FIG. 13.** Drug pellet with ideal surface characteristics for subsequent overcoating (magnification 100×).

Surface porosity may present a problem because a certain amount of film may be consumed in filling the pores and thus is not contributing to the overall film thickness. Additionally, large pores may never be covered, resulting in an imperfection in the film. Although such rigorous core material requirements may seem unrealistic, a formulator can help to minimize the effects of these substrate variables by avoiding the use of very thin films (less than 5 $\mu$m) in development work.

If performance does not rely on film thickness, as in sustained release, but is triggered by other mechanisms (such as pH change), the restrictions on substrate morphology are somewhat reduced. Then powders, crystals, and granules as well as pellets and tablets can be coated. Figure 14 shows a chilsonated aspirin granule coated for enteric release. The uncoated surface is very irregular and contains loosely attached aspirin crystals, which are immobilized in early layers of coating. When the coating process is complete, a uniform film is visible in both the surface and cross section views shown.

The total quantity of coating applied typically exceeds the minimum required for acceptable performance. This compensates for slight variations in substrate characteristics from lot to lot, such as particle size distribution, bulk density, and friability. However, these product characteristics should not be ignored.

For example, friability, a problem in tablet coating, is also a concern in particle coating. A film coating typically increases the strength of the core material. However, coating occurs in patches and complete coverage of a substrate takes time; therefore, the total surface area may be increasing during processing, as small particles detach from the surface. Additionally, achievement of small droplets is accomplished by using a high atomization air pressure, which yields a very high air velocity at the nozzle tip. A large velocity difference between the fluidization and atomization air may result in some pulverization of the substrate as it enters the coating zone.

To date, there is no standard method for determining friability of small particles. However, if friability is a suspected problem, an approach would be to conduct a sieve analysis or use a scanning electron microscope to characterize the particle size distribution and then fluidize a batch of substrate using desired processing conditions (without spraying the coating solution). After dry processing for 10 to 30 min, the material should again be checked for particle size distribution. A significant increase in fines (less than 100 $\mu$m) is an indication that the substrate may be a challenge to coat reproducibly.

With an awareness of general process and product variables, the capabilities and limitations of each of the three processing techniques may be examined.

## Top Spray Coating

The top spray system has successfully been used to coat materials as small as 100 $\mu$m. Smaller substrates have been coated, but agglomeration is almost unavoidable because of nozzle limitations and the tackiness of most coating substances. Batch capacities range from a few hundred grams to approximately 1500 kg. Typically, a single nozzle wand with up to six liquid delivery ports is used, but multiple nozzle systems have been applied.

**FIG. 14.** (*A*) Uncoated chilsonated aspirin granule (magnification 60×); (*B*) film-coated aspirin granule (magnification 60×); (*C*) film-coated aspirin granule cross-section (magnification 700×).

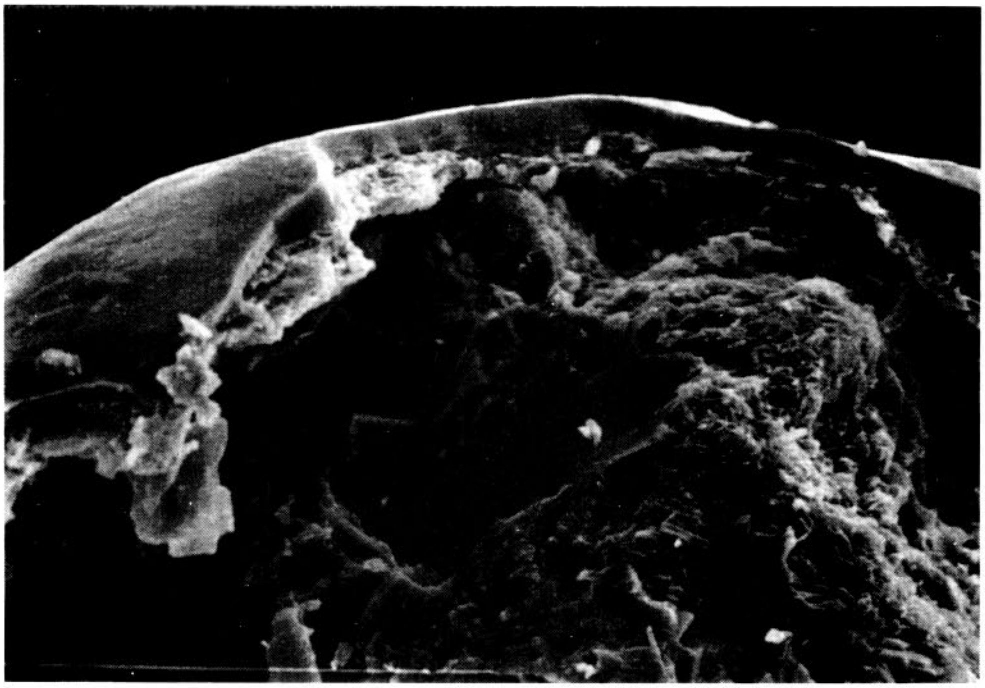

**FIG. 14. cont'd.** (*A*) Uncoated chilsonated aspirin granule (magnification 60×); (*B*) film-coated aspirin granule (magnification 60×); (*C*) film-coated aspirin granule cross-section (magnification 700×).

Fluidization is affected by batch size, and it is recommended that the bowl volume be completely occupied by the product upon completion of the coating process. Batch size can be determined by the following equation:

$$B = V \times D$$

B = batch size of the coated product in kg
V = total product container volume in L
D = bulk density of the coated product in g/cc

A minimum of 50% of the product container volume should be occupied by the uncoated material to allow an adequate fluidization pattern. Under these conditions, approximately 100% coating (based on starting weight) can be applied. Sustained-release coating is discouraged, as is most coating using organic solvents. However, top spraying is the system of choice for coating without any solvent (hot melt).

The most significant characteristic of the top spray method is that the nozzle sprays countercurrently or down, into the fluidizing particles. The fluidization pattern is random and unrestricted. As a result, controlling the distance the droplets travel before contacting the substrate is impossible. Figure 15 shows the surface of a pellet coated with ethylcellulose, a water-insoluble polymer, using ethanol. The coating is imperfect, and the core will dissolve rapidly when placed in water. By

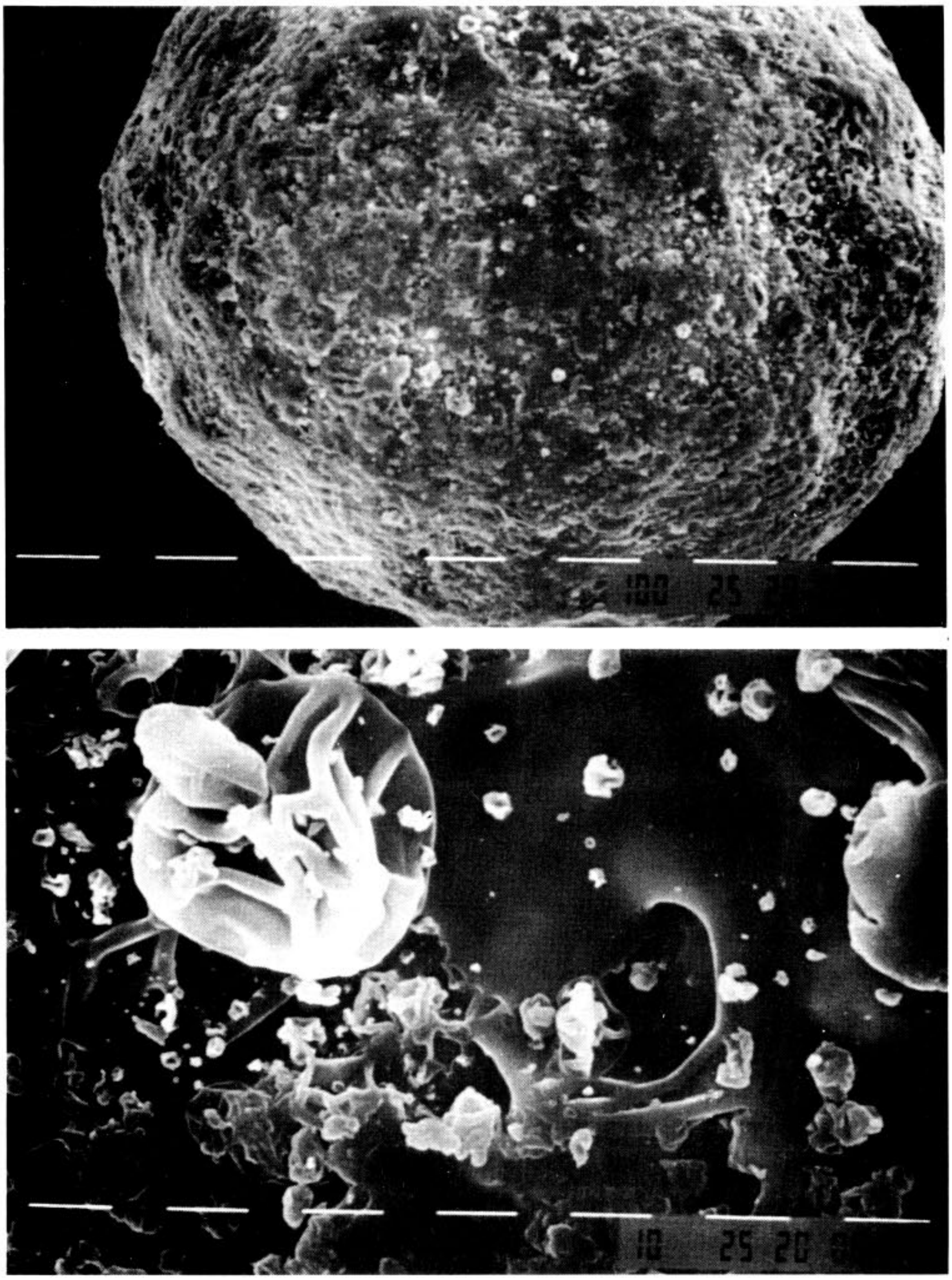

**FIG. 15.** Pellets coated with ethyl cellulose in an organic solution in a fluidized bed using the top spray method: (*A*) magnification 100×; (*B*) magnification 1000×.

contrast, the pellets shown in Figs. 16 and 17, coated in the Wurster and rotor (both immersed-nozzle, concurrent-spray techniques) using the same polymer system, show no imperfections and sustain the release of the core. The problem seems to be most severe with films applied from solutions, especially from organic solvents. When applying an enteric coating using an aqueously based latex film, the surface morphologies, cross-sections, and dissolution profiles of caffeine pellets appear similar (Figs. 18 and 19) with each of the three techniques. The problem previously described is probably forgiven by the low viscosity of the latex system and the high heat of vaporization of water.

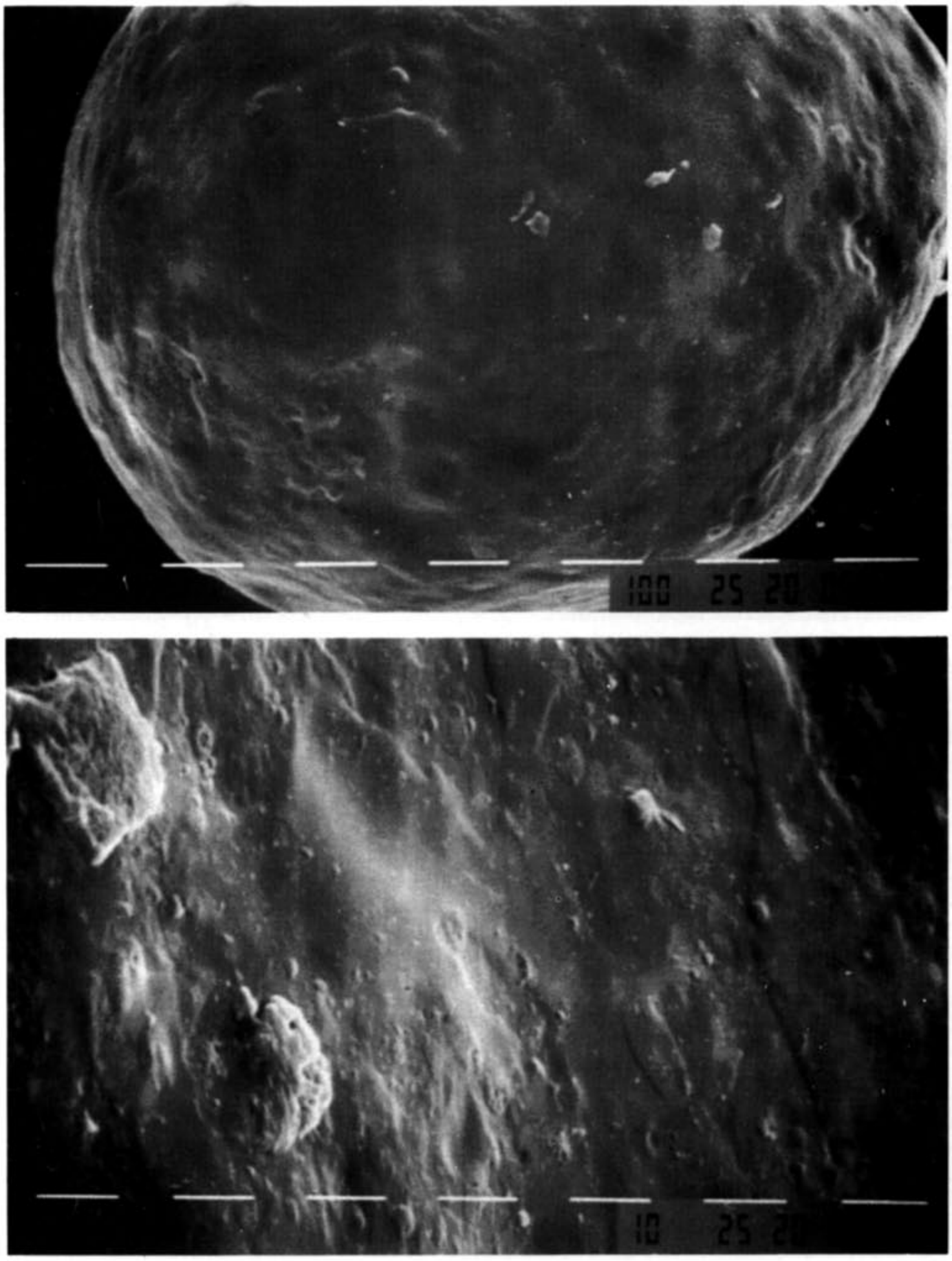

**FIG. 16.** Pellets coated with ethyl cellulose in an organic solution in a fluidized bed using the bottom spray method: (*A*) magnification 100×; (*B*) magnification 1000×.

The product container of the top spray system is designed for no restrictions to particle flow, an important consideration for the application of a hot melt coating. Materials with a melting point of less than 100°C can be applied to the fluidized particles by carefully controlling the liquid and atomizing air temperatures and the product bed temperature. The degree of protection offered by the coating is related to the rate at which it is applied and how slowly it congeals. Keeping the product temperature close to the coating's congealing temperature results in a significant increase in the viscous drag in the bed. For hot melt coating, therefore, the openness of the top spray product container is superior to the Wurster, which relies on a small

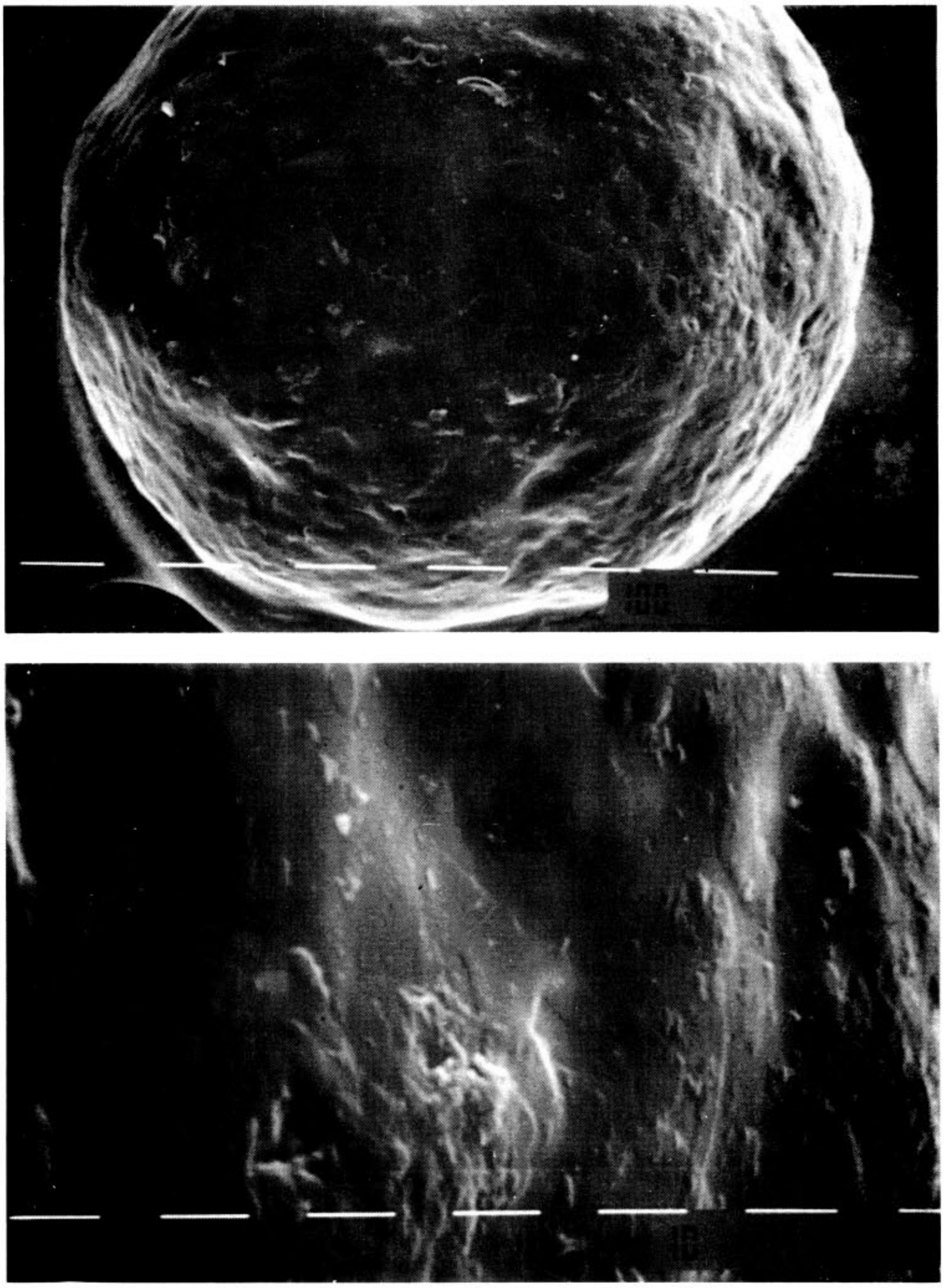

**FIG. 17.** Pellets coated with ethyl cellulose in an organic solution in a fluidized bed using the tangential spray method: (*A*) magnification 100×; (*B*) magnification 1000×.

gap between the partition and orifice plate for controlling the fluidization pattern and assuring coating quality. At this writing, only a minimal amount of hot melt coating has been attempted using the tangential spray method, and any comments on the results would be premature.

The top spray coating system is the least complicated of the three machines. It has the largest batch capacity, and downtime between batches can be only minutes. Its biggest disadvantage is that its applications are somewhat limited.

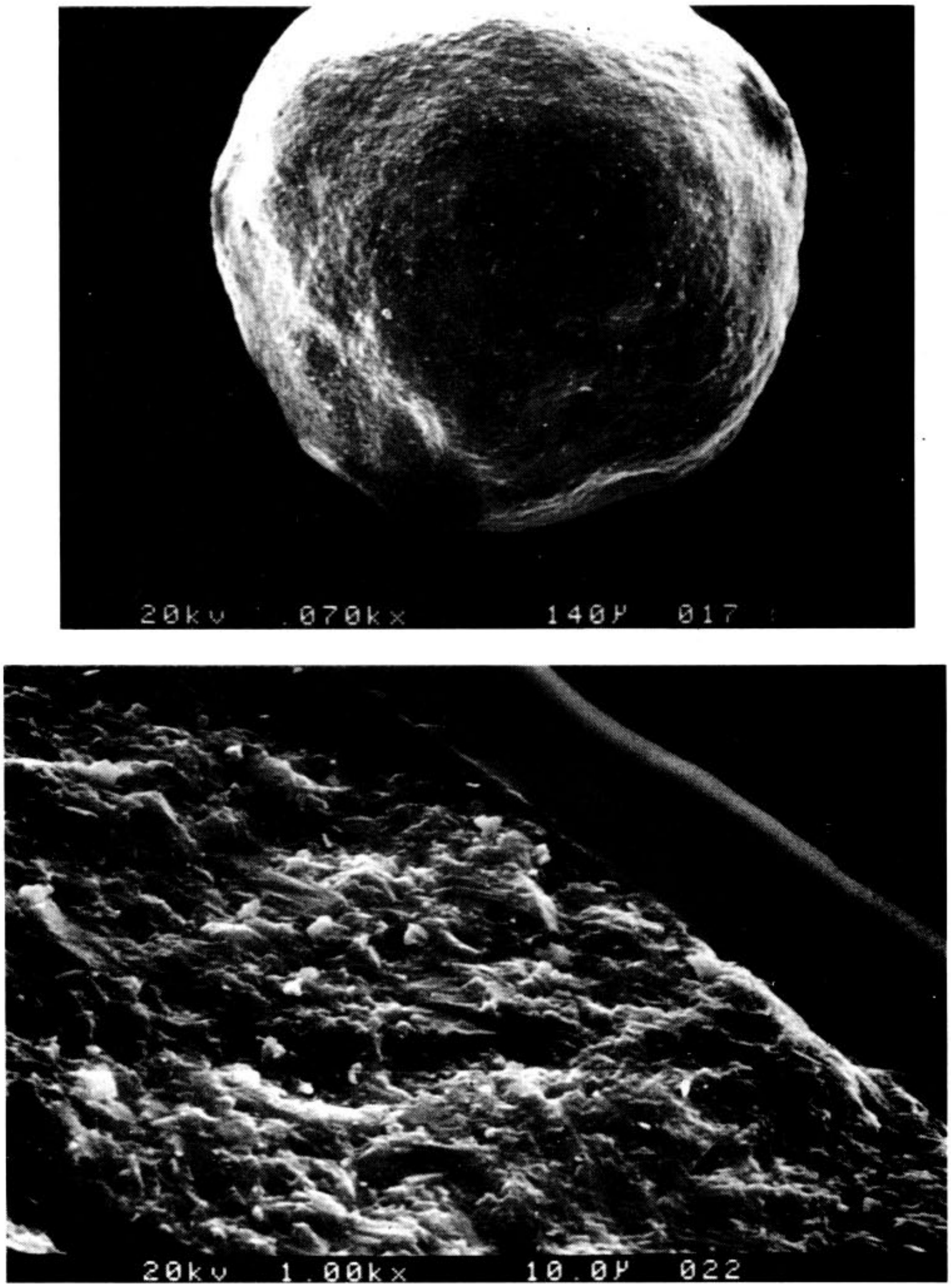

**FIG. 18.** Caffeine pellets coated to 5% w/w using an aqueous system (Eudragit L30D) and the top spray method: (*A*) magnification 70×; (*B*) cross-section magnification 1000×.

## Wurster Bottom Spray Coating

The Wurster bottom spray system has also been used successfully to coat particles as small as 100 $\mu$m. Coating of smaller particles is subject to the same difficulties as discussed in the previous section. Batch capacities range from a few hundred grams to approximately 600 kg. Laboratory and pilot scale equipment (up to 24-in diame-

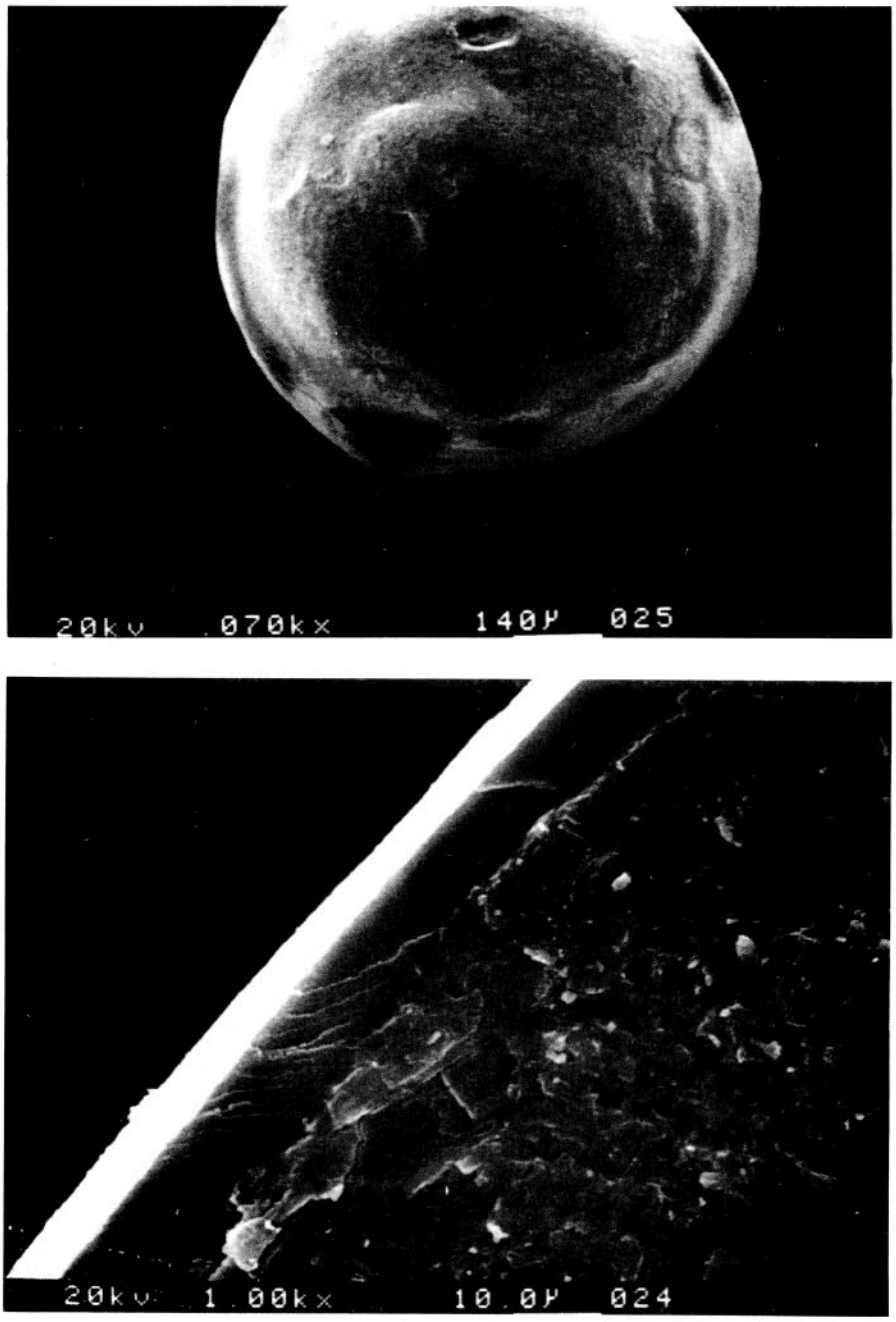

**FIG. 18. a** Caffeine pellets coated to 5% w/w using an aqueous system (Eudragit L30D) and the bottom spray method: (*C*) magnification 70x; (*D*) cross-section magnification 1000x.

ter) use a single partition and nozzle, and production equipment may contain three (32-in Wurster) or seven (46-in Wurster) partitions and nozzles of the same size and configuration found in the 18-in Wurster. Fluidization is affected by batch size, and at least 50% of the volume outside of the partition should be occupied by the

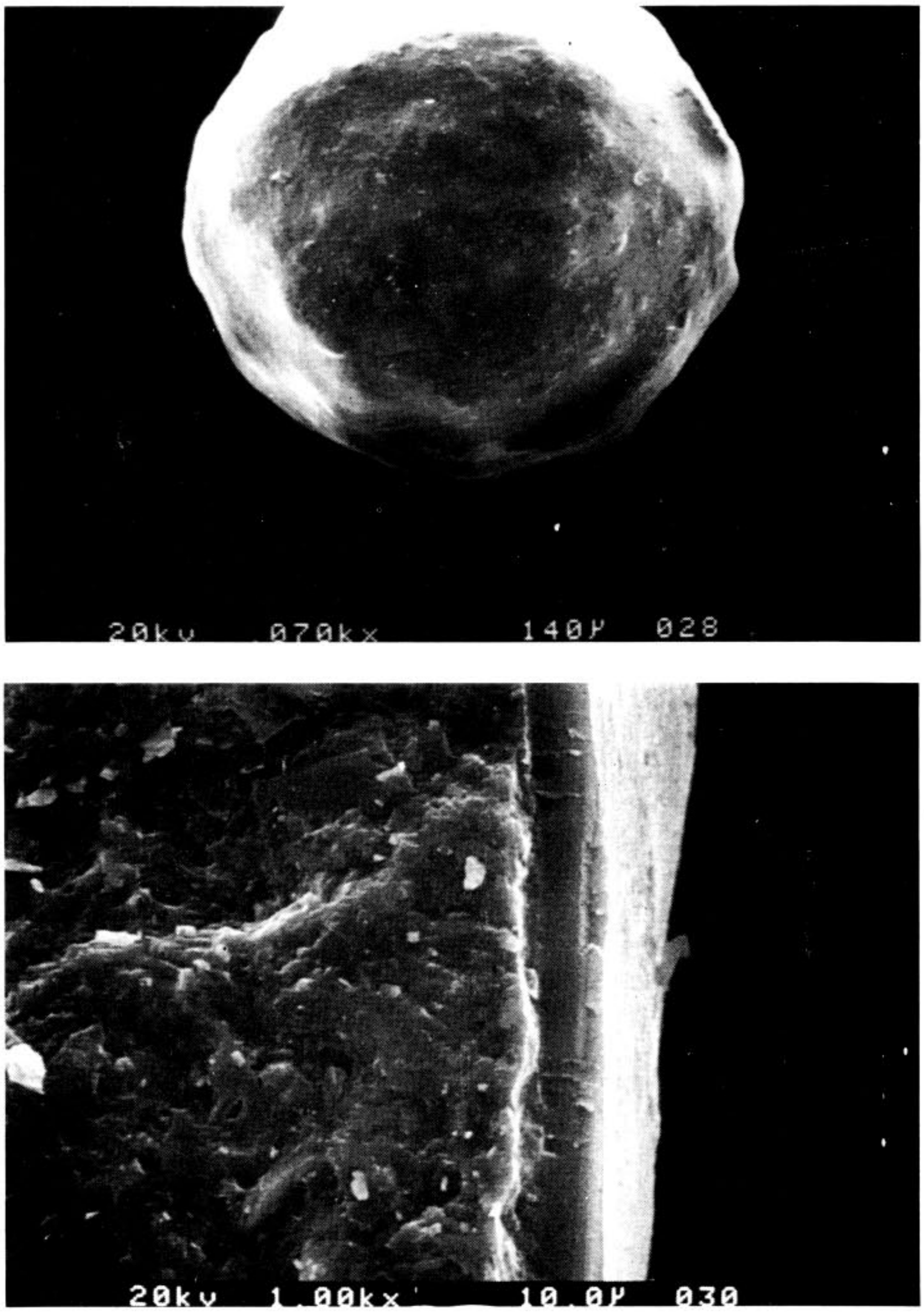

**FIG. 18. b** Caffeine pellets coated to 5% w/w using an aqueous system (Eudragit L30D) and the tangential spray method: (*E*) magnification 70x; (*F*) cross-section magnification 1000 x.

uncoated product (this requirement decreases somewhat as the coating chamber increases in size as it is dependent on length of the partition and downbed depth). Finished product batch size (for fine and intermediate particles) can be determined by the following equation:

$$B = \frac{[\pi r_1^2 L - 1/2 n \pi r_2^2 L]D}{1000}$$

B = finished product batch size in kg

$r_1$ = radius of Wurster chamber in cm

$r_2$ = radius of partition in cm

n = number of partitions

L = partition length in cm

D = finished product bulk density g/cc

*Note*: Minimum batch size before coating of small particles can be determined by multiplying B by 0.4 (or approximately 40% of finished product capacity). The batch capacity for coating of tablets is approximately 90% of $(\pi r_1^2 L/1000)D$ for coatings of up to 10% w/w.

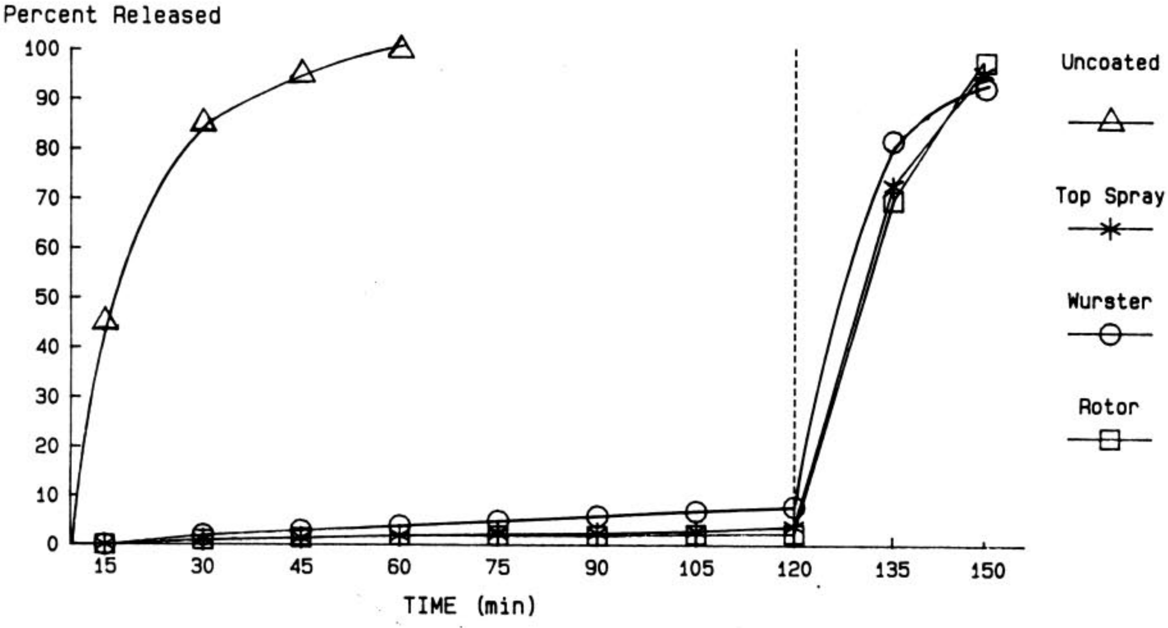

**FIG. 19.** Dissolution profiles of caffeine pellets coated to a level of 5% w/w using an aqueous system (Eudragit L30D). For 0 min to 120 min, pH = 1.2; for 120 min to 150 min, pH = 6.8.

If the coating and core bulk densities are smaller, coatings of 100 to 150% (based on starting weight) may be applied. Fluidization is also affected by the air distribution plate configuration and the partition height. The finer are the particles to be coated, the smaller the open area in the downbed section of the orifice plate and the tighter the gap between partition and orifice plate.

The Wurster system has the widest application range of both water and organic solvents; only coating with hot melts is discouraged. Organized particle flow and the immersed-nozzle, concurrent-spray system appear to offer superior film forming capabilities as seen in Figs. 16 and 18. The primary disadvantages of this system are that it is somewhat complex, it is the tallest of the three types, and the nozzles are inaccessible during the processing.

## Tangential Spray Coating

The rotary or tangential spray system, also an immersed-nozzle, concurrent-spray technique, appears to offer film characteristics similar to the Wurster system, as seen in Figs. 16, 17 and 18. It has been used successfully to coat particles as small as 250 μm using organic solvents and water-based coatings. The process is more susceptible to adhesion of particles to the upper wall of the product container (Fig. 7) owing to static electricity; hence, coating of smaller and lighter particles is difficult, especially with organic solvents. Batch capacities range from approximately 1 kg to 500 kg. Laboratory equipment (up to 500-mm disc diameter) typically uses a single nozzle, and pilot to production scale rotors (up to 2000-mm disc diameter) use from 2 to 6 nozzles. Fluidization is not affected by batch size as significantly as in the other process techniques. Working capacity is approximately 50% of total bowl volume, and the minimum batch size is that which is necessary to cause the nozzle to be fully immersed such that the coating liquid is not sprayed through the bed. This volume is typically about 15 to 20% of the working capacity. If the bulk densities of the core and coating material are similar, coatings of 400 to 500% (based on starting weight) may be applied. This process excels in producing high dose pellets using three techniques for applying drug to a small seed material: spraying a water or solvent solution of drug and binder; spraying a water or solvent suspension of drug (with a dissolved binder); or spraying a water or solvent binder solution and dosing the drug powder onto the damp seed material. The choice of technique depends on several factors, including solubility and stability of the drug. Additionally, for suspension layering and powder dosing, it is almost mandatory that the drug be micronized (less than 10 μm) to maximize drug yield and provide a smooth surface for subsequent overcoating (Fig. 20). The resulting pellets will also be very uniform in particle size distribution because of the narrow size distribution of the starting seed material, typically a nonpareil sugar seed or regular shaped crystal.

The process variables unique to the rotor system primarily involve disc slit width, disc configuration, and rotation speed. The velocity of the fluidization air through the slit controls the rate at which the bed tumbles or spirals. Typically, this velocity is as high as possible without seriously distorting the fluidization pattern and resulting in a bursting or bubbling bed. In solution or suspension layering, the slit is usually

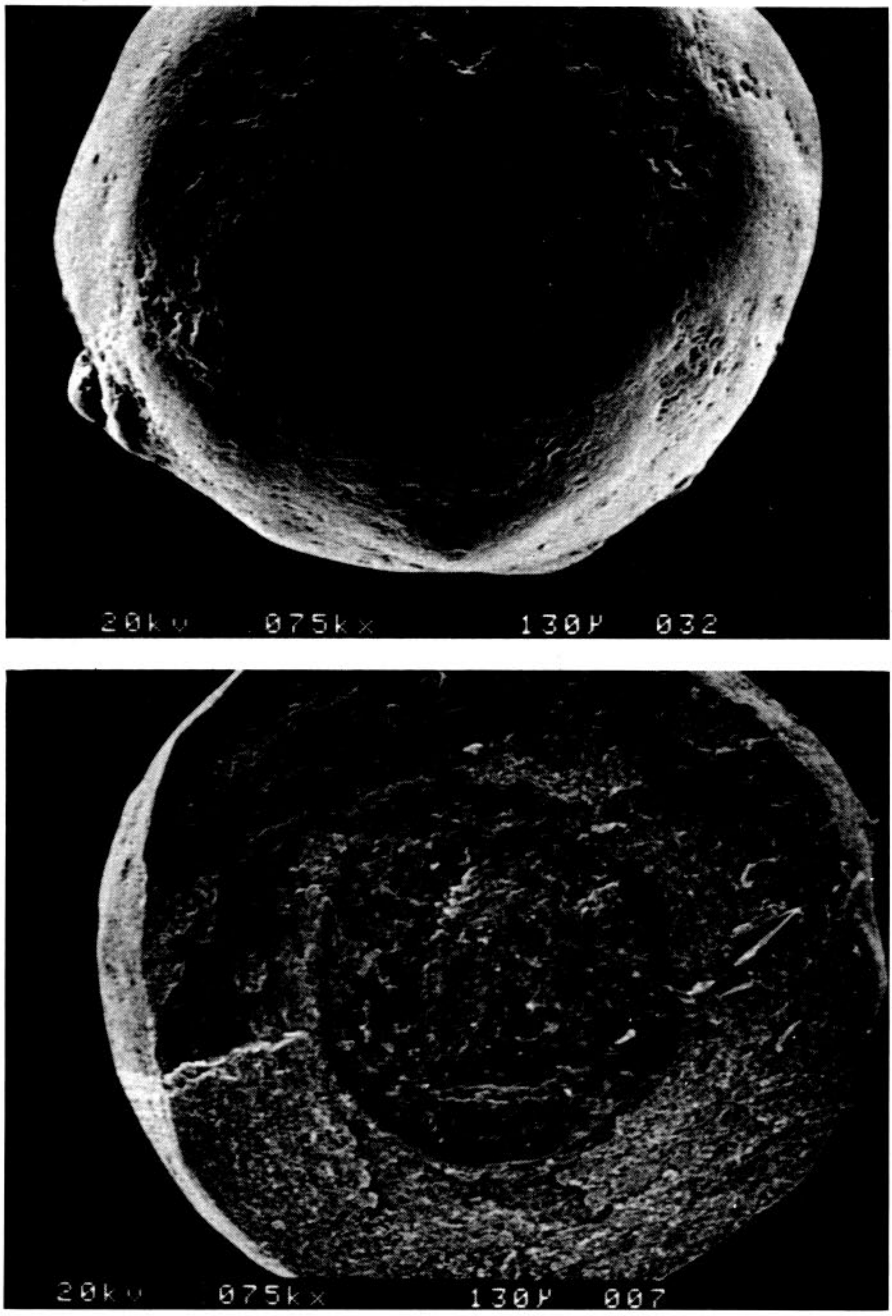

**FIG. 20.** (*A*) Layered pellet with micronized drug suspended in binder solution (magnification 75×); (*B*) layered pellet with micronized drug suspended in binder solution (cross-section magnification 75×).

wide; velocity is achieved by using a high air volume to maximize drying capacity and, to an extent, spray application rate. When spraying a binder solution and dosing powder, the slit is usually narrow and the air volume and temperature much lower. In this manner, the binder solvent assists in immobilizing the applied powder on the substrate surface. If the evaporation rate is high, as is the case when layering with a solution or suspension, excessive quantities of liquid may needlessly be applied.

As mentioned previously, the rotary or tangential spray system was conceived as a higher intensity granulator than the conventional fluidized bed. The disc, which may be configured with a variety of surfaces from simple antislide baffles to a multipyramid type of waffle plate, and high rotational speed impart an increased mechanical force on the substrate. The resulting granulation can be up to 50% denser than that produced by the conventional fluidized bed granulator.

This is not the case when layering or coating. The disc should be smooth and a rotational speed selected (less than half the speed used when granulating) such that particle motion is rapid but uniform. There is a large velocity gradient from the disc surface through the particle bed, and any type of baffle may cause fracture of the pellets, especially as the layer becomes thicker.

In addition to enhancing particle motion, the disc speed may affect the spray application rate. As is true of the other fluidized bed techniques, spray rate is limited by the tackiness of the coating material and can be elevated by increasing the velocity of the particles through the coating zone. Again, caution must be exercised to avoid excessive radial velocity, which may result in core fracture. The velocity is determined empirically and will vary with different formulations.

The rotary tangential spraying system has a relatively wide application range, is the shortest machine in height of the three, and allows nozzle access during processing. It has the ability to produce high dose pellets as well as to allow subsequent overcoating (for all types of release). Its primary disadvantage is that it exerts the greatest mechanical stress of the three methods and, thus, is discouraged for use with friable substrates.

## Scale-Up

The successful scale-up of any coating process to pilot or production equipment depends heavily on an effective development program in the laboratory. The influence of all the major product and process variables should be well known so that the list of unknowns can be minimized. Essentially, the only major unknown factor is the effect that the larger mass of material will have on itself. Product problems such as friability will be magnified by scale-up. Additionally, if the release profile of the coated product is very susceptible to minor changes in processing conditions, scale-up will be a challenge. For these reasons, a product and process must be robust on the lab scale.

Each fluidized bed technique has unique scale-up considerations. The conventional top spray method is the easiest to scale, probably partly because the most difficult coating objective, sustained release, is discouraged from being conducted with this technique. Scale-up of spray rate is generally calculated according to the increase in fluidizing air volume used, not the increase in batch size. The bed depth is not a constant in scale-up; therefore, the amount of air required to provide adequate fluidization is proportionately less. This is a common technique for determining spray rate in scale-up of the fluidized bed granulation process, where the rate-limiting factor is generally the fluidizing air's capacity for water. However, in fluidized bed coating, the more critical factor is the inherent tackiness of the coating material being applied. As mentioned previously, this property determines the maximum delivery rate through a single-headed nozzle or coating zone. For this reason, as batch sizes increase, the number of nozzles (or zones) increases, typically to 3 or 6 heads, although, in an extreme case, as many as 42 nozzle heads have been used in a particular top spray application.

When scaling a Wurster process, the most challenging step is from laboratory to pilot scale. The 6-in, 7-in, 9-in, and 12-in Wursters all employ the same size nozzle, which uses up to approximately 5 cfm of air for atomization. The 18-in, 24-in, 32-in, and 46-in Wurster systems use a larger nozzle, which may consume up to approximately 30 cfm to accommodate higher spray rates. The large difference in air volumes used by these nozzles may have an effect on the evaporation rate of coating media during atomization of the liquid. Additionally, bed depth is usually in the range of 150 to 200 mm in laboratory scale Wursters as opposed to 400 to 500 mm or more in the 18-in and larger Wursters. As a result, mass effects may not be seen in the smaller machines.

For these two reasons, scaling from a small machine to the 18-in Wurster is the most challenging. Continuing to larger equipment such as the 32-in or 46-in Wurster, although also a task not to be underestimated, is somewhat less difficult because these units employ multiples of the partition and nozzle found in the 18-in Wurster. Three partitions and nozzles are used in the 32-in unit and seven are used in the 46-in Wurster coating chamber. Spray rate in each partition of the 32-in or 46-in coating chamber will be the same as that used in the 18-in Wurster. For example, when scaling up to a 7-partition 46-in Wurster, if the spray rate in the 18-in Wurster was 400 g/min, overall spray rate in the production machine would be 2800 g/min, or 400 g/min per partition. The partition's height above the orifice plate may be the same in pilot and production equipment, which will keep particle density inside the coating zone similar. Also, the total fluidization air volume, which is controlled by orifice plate configuration, should be a multiple of that necessary in the 18-in Wurster. For example, if 500 cfm was required for adequate fluidization in the 18-in unit, 1500 cfm would be the target air volume in a 32-in coating chamber, or 3500 cfm in a 46-in machine. In this manner, evaporative conditions will be similar, as will particle velocity, a key to minimizing the mechanical stress to which the product is exposed.

Of the three fluidized bed techniques, the rotary or tangential spray system exerts the most mechanical force on any given product. Rotational speed is a key variable and should be kept constant when scaling to larger equipment. The radial velocity used in the lab machine can be calculated by using the formula:

$$V_r = (\pi d)\frac{N}{60}$$

$V_r$ = radial velocity in m/sec
$d$ = diameter of disc in m
$N$ = number of revolutions per minute the disc is traveling

Knowing the diameter of the disc in the production machine and keeping the radial velocity $V_r$ constant, one can solve the equation for N, the number of revolutions per minute the disc in the larger machine must travel such that $V_r$ is the same in both small and larger equipment.

As in the section discussing scale-up of the top spray process, the scale-up factor for determining coating liquid application rate is usually based on the increase in fluidization air volume. However, spray rate is typically more a function of the properties of the coating material, as described previously, and this scale-up factor should be used only as a base line or starting point. Optimization must be done during the first scale-up batches. Multiple nozzles (from 3 to 6) and powder dosers, where applicable, are typically used to increase the overall application rate.

## Summary

The evaporative efficiency of fluidized bed equipment and the ability to apply a film to particles discretely suspended in an airstream have resulted in widespread use of this technique for coating products ranging from 100-$\mu$m particles to tablets.

The three fluidized bed techniques, all of which are used commercially for film coating, offer a variety of applications. These methods have some common features and process variables, but each has unique advantages and limitations. In the development of a product with commercialization as the ultimate goal, criteria such as economics, product and process variables, and dosages form performance must be considered.

In recent years, there have been significant improvements in instrumentation and control for the many variables encountered in fluidized bed processing. Further equipment evolution may result in either the improvement of the limitations of a given technique or the development of an entirely new method.

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