

New Air Suspension Apparatus for Coating Discrete Solids

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A patent for the apparatus and method for coating discrete solids by means of air suspension and a modification of the basic Wurster design has recently been issued. Experience with this new apparatus and its differences from previously reported air suspension coating equipment are discussed.

SINCE WURSTER'S original patents on means for applying coating to tablets or the like (1, 2), several reports have appeared (3-12) on the use of an air suspension coating (ASC) apparatus patterned after his inventions. The Wurster apparatus comprises in combination a vertical coating chamber, a screen means extending transversely across the chamber at its lower end, and an air source and conduct means for directing an air stream through the chamber in a vertical direction in order to support the materials to be suspended in the lower part of the coating chamber. An expanded part at the top of the coating chamber is provided to reduce the air velocity and thereby prevent pneumatic transport of the particles being coated. Figure 1 is a schematic diagram of such an apparatus.

The process consists simply of supporting particles in the vertical column with an upwardly moving air stream, during which time a coating solution is atomized onto the suspended particles. The velocity of the air stream is adjusted so that the suspended particles are maintained in a region of the column relatively confined.

An experimental study by Wilhelm and Valentine (13) has disclosed the sequence of the relationships between the various phenomena that comprise the entire fluidized state spectrum. The Wilhelm and Valentine apparatus, the elements of which are shown in Fig. 2, was essentially a vertical glass tube of 4-in. diameter, fitted on its side with ports for addition of solids and admission of air. The tube was unobstructed over its entire length. For its operation spheres of 0.02 to 0.03 in. in diameter were introduced while air entered simultaneously. The number of particles and air rates could be varied over wide ranges, and it was possible to observe the behavior of the particles directly.

The results of these experiments indicated that with the proper adjustment of solids and air flows

virtually all phenomena of the fluidized state, extending from the dense-phase bed all the way through the dispersed phase into pneumatic transport, could be produced. The diagrams of Fig. 3, suggested by Wilhelm and Valentine, will

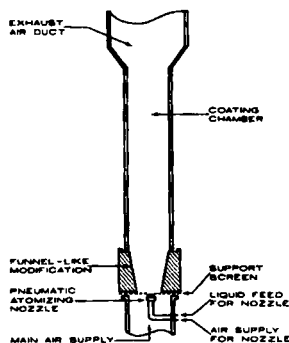


Fig. 1.—Schematic diagram of Wurster air-suspension coater as reported by Singiser and Lowenthal (5).

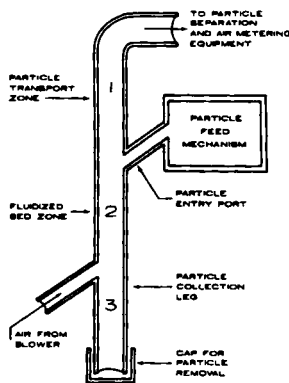


Fig. 2.—Elements of Wilhelm and Valentine apparatus (13).

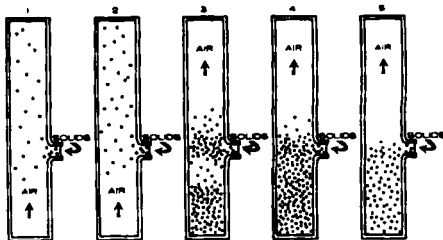


Fig. 3.—Pictorial representation of transition from concurrent to countercurrent flow of particles in rising gas stream in Wilhelm and Valentine apparatus (13).

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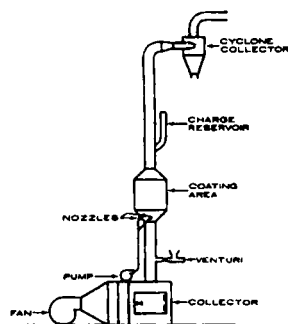


Fig. 4.—Schematic diagram of the Mesnard-Rosen-Scott air-suspension apparatus (14).

be helpful in establishing the relationship among solids, air rate, and resulting bed density. The drawings in Fig. 3 represent the upper two sections of the apparatus. Given a fixed-solids feed rate, the air rate is gradually reduced from its original high value in 1. Owing to this high air velocity in 1, the particles will be blown out of the apparatus. As the air rate is reduced as shown in 2, the particle population increases as the void space decreases slightly. However, the pellets still move concurrently upward with the air. For another small reduction in air rate, 3, solids will tend to crowd together, and violent slugging will occur with the solids moving downward. The void space decreases sharply. A condition of minimum voidage is observed near 4, and the solids now have a well-defined upper boundary. With a further reduction, the solids in the bed decrease to reach a limiting value.

In our laboratories air suspension coating apparatuses of the Wurster design operated under conditions described by Fig. 3, 4, and 5. It was possible to operate under these conditions of relatively dense bed as long as the coating materials applied were nontacky and not of great quantity—about 10% of the starting charge. However, under conditions of general operation the regions 3, 4, and 5 were relatively unstable and sufficiently sensitive to air flow rate to make frequent adjustments necessary during application of significant (over 10% of starting charge weight) quantities of coating.

To overcome this problem and provide maximum flexibility of the apparatus a series of experiments was undertaken to modify the design. Since the area of highly dispersed phase was far less sensitive to variations in air flow rate, special attention was given to this spectrum of the fluidized state.

EXPERIMENTAL

Although the area of pneumatic transport provided a starting point for experimentation, it was not a satisfactory condition in a vertical system since there was not sufficient time for particle build-up during passage of a particle through the spray pattern of a single nozzle. However, when a horizontal or air slide arrangement with a plurality of spraying nozzles was used, encouraging results were obtained.

After considerable experimentation with vertical apparatuses, a device schematically described in Fig. 4 was evolved (14).

This apparatus differs from the Wurster design primarily in that materials to be coated are truly air suspended and do not need support for screens or other air-regulating devices (such as vanes) in a highly dispersed state approaching that of pneumatic transport, in an expanded chamber situated at the top of a vertical column providing a laminar cushion of air. Also the materials to be applied are delivered out of the main suspending air stream in a direction opposite or countercurrent to the direction of the movement of the particles to be coated. This construction makes possible the application of significant quantities of coating materials and those of a tacky nature without regulating the rate of air flow to keep the solids in suspension as their weight increases incident to the application of the coating material. Furthermore, this construction makes possible the use of a single apparatus to coat charges of particles of widely varying magnitude in the same apparatus.

The expanded chamber used for coating is constructed to provide a dense zone of particles falling countercurrent to the spray pattern in the immediate area of the nozzle. This permits the most economical utilization of the coating material since there is a minimum mean free path for coating material to be entrained out of the chamber without contacting a particle to be coated. Second, the truncated cone construction permits pellets or tablets to roll down the sides, thereby achieving some of the smoothing effect of rolling before falling into the central air stream, a zone of maximum shear and disengagement. The highly dispersed state reached in the upper chamber insures complete drying of the separated particles before they again fall into the coating zone.

Equipment.—(a) A Zenith laboratory metering unit type QE equipped with a Graham variability speed transmission model 45 R2.8 with infinite variable speed motor from 0 to 200 r.p.m. and $\frac{1}{4}$ hp. master electric explosion-proof motor were used to supply fluids to atomizing nozzles. Pumps with 0.58 ml./rev. (size 1), 1.168 ml./rev. (size 2), and 2.920 ml./rev. (size 5) were used in these studies. Curves for each of these pumps were drawn to indicate the relationship of transmission setting to grams of coating pumped per minute. (b) New York blower No. 14 General Industrial fan arrangement No. 1, which has a capacity of 1400 C.F.M. at 12-in. static pressure at 3710 r.p.m., was driven by a 5 hp., 440 v., 1750 r.p.m., three-phase motor (Crocker Wheeler Electric Manufacturing Co.). Air flow rate was set by a variable-speed drive on the fan or by a restriction of the air at the fan intake port. (c) Internal and external mixing spraying systems pneumatic atomizing nozzles were used for most of these studies. Internal mixing nozzle setup No. 26 and external mixing nozzle setup No. 4 were satisfactory for most spraying needs. (d) A cyclone powder collector was fabricated to our specifications by the E. D. Menold Co., Philadelphia, Pa. The cyclone was designed to recover 95% of all powders. (e) A venturi tube was fabricated of glass in our laboratories. Powder was introduced into this venturi with a model F-00 Syntron equipped with a controller. Special tubular and flat pan troughs were used to convey the powder.

Since it was desirable to spray coatings that melt

TABLE I.—APPLICATION OF POWDERS TO PELLETS

No.	Pellet Charge, Kg.	Powder Charge, Kg.	Coating Time, Min.	% Powder Charge Applied
1	10.0	4.90 ^a	5	48
2	10.0	5 ^a	6	63
3	10.0	5 ^a	6	57
4	10.0	5 ^a	6	62
5	10.0	5 ^a	7	66
6	10.0	5 ^b	7	64
7	10.0	5 ^b	7	60
8	17.9	7.3 ^c	9	82
9	30.0	4.3 ^d	10	77
10	25.0	4.3 ^d	11	49

^a Starch:sugar (1:1). ^b Calcium sulfate, dihydrate.
^c Powdered sugar. ^d Dextro-amphetamine sulfate coating powder containing 82.5% active drug.

at about room temperature, the liquid reservoir, fluid lines, and nozzles were heated (electrically or with steam) to avoid congealing in the system. Also, since heated air was needed for some experiments, a series of steam-heated pipes was installed in the air ducts between the fan and the coating zone. The temperature was regulated to $\pm 1^\circ$ using a series of steam reducer valves.

Charge Magnitude and Operation.—The following procedure is employed during a typical coating operation. The blower is turned on and the particles to be coated are permitted to fall from a reservoir into the coating chamber. The coatings are then applied *via* the nozzle assembly and/or venturi. When all of the coating agents have been applied, the blower is turned off, and the particles are permitted to fall into an appropriate container.

Using the apparatus described in Fig. 4, it is possible to suspend a minimum charge of 1 Kg. and a maximum charge of 40 Kg. of sugar pellets ranging in size from 40–16 mesh with negligible loss through entrainment. The optimal charge range for this equipment is 10–25 Kg.

Powder Coating onto Sugar Pellets.—Conventional pan-coating procedures for application of powder onto sugar pellets are lengthy since several coats are required (15). Thus, it was of interest to determine if coating time could be reduced in the ASC device. A variety of powders were applied onto 20–25-mesh sugar pellets with an adhesive consist-

ing of 10% acidified gelatin in a hydroalcoholic solvent. The adhesive solution was sprayed through the nozzle assembly while the powder was applied simultaneously through the venturi tube. Results of 10 representative experiments are reported in Table I.

The cyclone collector was used to collect coating powder that did not adhere to the pellets on the first pass. Although the collected powder was suitable for subsequent recycling, the figures for per cent powder applied refer to the quantity that adhered on the first pass since the process was not set up for recycling of powder.

Lipid Coating of Pellets.—The classical method of preparing sustained-release pellets involves spraying of a wax and/or a fat on medicated pellets in a coating pan as described by the MacDonnell (15) and Blythe (16) patents. This pan-coating operation requires a number of separate applications to permit solvent evaporation between coats. Therefore, pan coating of sustained-release pellets is long and relatively expensive due to the costs of labor and solvent involved.

In contrast, a batch of sustained-release pellets can be prepared by the ASC procedure in a fraction of the time required for pan coating. Furthermore, the use of the ASC apparatus permits the application of waxes and fats as melts rather than as solutions in organic solvents. For example, the authors have successfully sprayed melted polyethylene, microcrystalline wax, glyceryl monostearate, glyceryl distearate, beeswax, and 12-hydroxystearyl alcohol, etc.

Data on nine batches of sustained-release pellets using 12-hydroxystearyl alcohol and glyceryl di- and monostearate-white wax as the coating agents are reported in Table II. The criteria for comparing the various sustained-release groups are the *in vitro* release profiles obtained by the method of Souder and Ellenbogen (17). The pellets coated in this case were from the same batch of *D*-amphetamine sulfate pellets. In all cases the lipid was sprayed as a melt.

The amount of coating on the pellets in Table II definitely influences the *in vitro* release of the drug; as more coating is applied, the release is depressed.

TABLE II.—APPLICATION OF SUSTAINED-RELEASE COATING TO DRUG PELLETS

No.	Starting Charge, Kg.	Spraying Time, Min.	Actual % Coating on Final Product	% <i>D</i> -Amphetamine Sulfate Released at Hr. Indicated			
				0.5	2	4.5	7
1	12	16.0	9.0 ^a	45	75	87	93
2	12	22.5	12.5 ^a	20	50	67	77
3	12	28.8	16.0 ^a	7	23	44	59
4	12	35.0	19.4 ^a	3	11	25	38
5	19.2	13.4	14.2 ^b	44	67	96	99
6	21	18	18.8 ^b	29	51	79	96
7	21	46	19.3 ^b	19	43	65	93
8	20	36	25.6 ^b	16	32	77	98
9	21	29.5	27.4 ^b	10	16	51	92

^a 12-Hydroxystearyl alcohol. ^b Glyceryl monostearate, 36%; glyceryl distearate, 54%; white wax, 10%.

TABLE III.—STUDY OF COATING CONDITIONS

No.	Starting Charge, Kg.	Spraying Time, Min.	Gm. Molten Coating ^a Sprayed Per Min.	Actual % Coating on Final Product	Air Temp., °C.	% <i>D</i> -Amphetamine Sulfate Released at Hr. Indicated			
						0.5	2	4.5	7
1	10	11.7	257	21.4	40	17	28	69	94
2	10	11.7	257	21.7	30	31	44	87	99
3	20	23.4	257	21.6	30	34	45	93	99
4	10	23.4	128	21.3	45	3	25	47	81

^a Glyceryl monostearate, 36%; glyceryl distearate, 54%; white wax, 10%.

To determine the best coating conditions, some of the variables involved in the ASC of sustained-release pellets were investigated. Table III shows the results of one study which consisted of four experiments. Each experiment was run under different conditions to determine factors critical in influencing the *in vitro* release profile of the final product.

Table III shows the effect of these different conditions. Perhaps the most important discovery is that desired quantities of coating agent can be applied to pellets with a high degree of reproducibility. Compare the amount of coating on batch 1 to the other three batches. Also, a comparison of the *in vitro* disintegration profiles for batches 2 and 3 reveals that sustained-release pellets prepared at the same air temperature are indeed comparable. Note that the weight of the starting charge and coating time for batch 3 is twice that of batch 2. Thus, it appears that the weight of the starting charge is critical.

Studies with a Laboratory Model Air Suspension Apparatus.—The above studies suggested that a minimum charge of 10 Kg. was required to obtain optimal coating results. Thus, it was desirable to make a scaled-down model with a charge capacity of 1.5 Kg. for laboratory use to study the effects of a host of possible variables encountered in air coating. While the major emphasis was on studying the variables encountered in the preparation of medicated and sustained-release pellets, it was also desirable to determine if the apparatus had utility in other coating operations.

Lipid Coating of Pellets.—To exploit the potential advantages of the ASC procedure for the routine manufacture of lipid-coated pellets, it was necessary to study the effects of the possible variables encountered in their preparation.

Results of one series of experiments in which molten 12-hydroxystearyl alcohol was sprayed onto dextro-amphetamine sulfate pellets are reported in Table IV.

Perhaps the most important part of this study was

to determine if results obtained with the laboratory model could be obtained routinely with the larger device. A comparison of the *in vitro* release profiles of batch 1 with 2 and 3, and batch 4 with 5 and 6 reveals that pellets coated in either the small or large ASC device under similar conditions possess similar release profiles. Therefore, no scale-up problems are anticipated.

Another important consideration is batch-to-batch reproducibility. Note that batches 5–9, coated under similar conditions, were coated with nearly identical quantities of 12-hydroxystearyl alcohol and had similar release profiles. Of course, this illustrates that a high degree of batch-to-batch reproducibility can be expected.

Among the variables studied, the most critical was suspending air temperature. A comparison of the *in vitro* disintegration profiles for batches 9 and 10 demonstrates this. It is thought that the warm air allows the coating to be applied more efficiently.

Other variables studied that were not critical under our conditions are rate of application and use of different nozzles. For example, when the *in vitro* disintegration profiles for batch 6 are compared to batch 9, it is evident that an increase in the rate of application from 39 to 65 Gm./minute has little effect. Also a comparison of the profiles of batches 7 and 8 to batches 5, 6, and 9 reveals that changing nozzles has a minor effect.

Enteric Pellets.—The usual methods for preparing enteric-coated pharmaceutical products are laborious. Therefore, when a development project required enteric-coated pellets, it was decided to determine if the laboratory model air suspension apparatus could be used. Since supplies of the chemical in question were in short supply, a model run was conducted with dextro-amphetamine sulfate pellets. In this study an enteric coating solution consisting of ethyl acetate (38%), ethyl lactate (11%), alcohol (38%), cellulose acetate phthalate (8.5%), and glyceryl monostearate (4.5%) was sprayed in 67 minutes with a Spraying Systems pneumatic atomizing nozzle

TABLE IV.—STUDY OF COATING VARIABLES

Batch	Starting Charge, Kg.	Spraying Time, Min.	Gm. Molten Coating ^a Sprayed Per Min.	Actual % Coating on Final Product	Suspending Air Temp., °C.	Nozzle ^b	% <i>d</i> -Amphetamine Sulfate Released at Hr. Indicated			
							0.5	2	4.5	7
1	12	16.0	86	9.0	40	2	45	75	87	93
2	3	9.0	39	9.6	40	2	51	80	93	100
3	3	9.0	39	10.2	40	2	44	77	88	100
4	12	22.5	86	12.5	40	2	20	50	67	77
5	3	9.9	53	14.1	40	2	17	45	61	80
6	3	8.0	65	14.3	40	2	19	47	71	82
7	3	13.4	39	14.1	40	1	18	52	70	80
8	3	12.5	39	14.2	40	1	20	52	69	82
9	3	13.4	39	14.0	40	2	17	45	65	78
10	3	13.4	39	14.0	R.T.	1	33	58	78	87

^a 12-Hydroxystearyl alcohol. ^b Spraying systems pneumatic atomizing nozzles: 1, external mixing nozzle set-up No. 3; 2, external mixing nozzle set-up No. 4.

TABLE V.—ENTERIC CAPSULES PREPARED IN ASC DEVICE

Batch	Charge, Kg.	Capsule Size	Capsules, No.	Actual % Coating on Final Product	Spraying Time, Min.	No. of Capsules Remaining After 4 Hr. in U.S.P. GF (with Disks)
1	0.7	2	1660	5.4	10	9 of 11
2	0.7	2	1660	9.5	6	18 of 18
3	1.0	1	2200	7.6	5	18 of 18
4	1.0	1	2200	8.8	5	18 of 18
5	1.0	4	4800	7.9	7	18 of 18

TABLE VI.—ENTERIC TABLETS PREPARED IN ASC DEVICE

Batch No.	Charge, Kg.	Tablets, No.	% Enteric Coating, Wt. Gain	Coating Time, Min.	No. of Tablets Remaining After 4 Hr. in U.S.P. GF (with Disks)
1	0.6 ^a	1320	14.6	40.5	18 of 18
2	0.6 ^a	1320	7.1	7	18 of 18
3	1.5 ^a	3110	6.2	15	18 of 18
4	1.5 ^b	6500	1.9	13	18 of 18

^a Ecotrin tablets coated with acacia and coating powder (lot 2516). ^b Placebo cores.

TABLE VII.—DISINTEGRATION OF ASC ENTERIC TABLETS

Ref.	Disintegration, Min. in U.S.P. GF at 37°C. with Disks		Disintegration, 1 Hr. in U.S.P. GF with Disks, then U.S.P. IF with Disks, Min.		Hardness (Units), Electric Strong-Cobb	
	Range	Mean	Range	Mean	Range	Mean
Ecotrin Cores Lot 2516	0.5-2	1.3	8-12	10
Placebo Cores Batch No.	5-15	10	12-20	16
1	10-15	9
2	6-9	8
3	5-10	7
4	18-29	24

set up No. 5 onto 2 Kg. of pellets which was suspended in air at 45°. Duplicate release values after 1.5-hour exposure to U.S.P. gastric fluid showed that only 1 and 3% of the drug was released. In contrast, the pellets completely disintegrated in less than 30 minutes of exposure to U.S.P. intestinal fluid.

This experiment shows that the air suspension apparatus can be used to prepare enteric-coated pellets. It is likely that the spraying time could be shortened considerably with further work.

Enteric Capsules.—Although enteric capsules are not used extensively commercially, they are often used for clinical studies. These capsules are usually prepared in pans by applying numerous coats of an enteric coating solution. Since this coating process usually requires 1 day for each batch of enteric capsules, it was of interest to determine if the process could be speeded up in the ASC apparatus.

To prevent the capsules from opening in the air stream, they were sealed in a coating pan with a solution containing ethyl acetate (43%), ethyl lactate (14%), alcohol (41%), and cellulose acetate phthalate (2%). The enteric solution reported by Blythe *et al.* (18) was diluted with an equal volume of acetone: alcohol (46% acetone: 54% alcohol) and sprayed with a Spraying Systems pneumatic atomizing nozzle set up No. 5. The usual coating time was 6 minutes.

The data reported in Table V indicate that enteric capsules of various sizes can be prepared in the ASC device. This procedure requires only a fraction of the time required for pan coating. Thus the ASC device offers an excellent method for the preparation of enteric-coated capsules. It should be of particular value for the preparation of clinical supplies.

Enteric Tablets.—Singiser and Lowenthal (5) reported that the air suspension coating technique could be used to prepare enteric ammonium chloride tablets in 30 to 60 minutes. The authors have used the apparatus for this purpose also and wish to report on this phase of our ASC studies. Aspirin tablets with sealing and rounding coats as described by Blythe *et al.* (18) and uncoated compressed placebo tablets were used for these studies. The enteric solution and nozzle are the same as used for the enteric capsules. Results of four experiments are summarized in Table VI.

In Table VII original tablet disintegration and hardness data are presented which indicate that the disintegration times of the enteric tablets in intestinal fluid were within normal limits. Therefore, it appears that the ASC device also can be used for the preparation of enteric tablets.

SUMMARY

A versatile new air suspension coating apparatus has been described. This apparatus can be used in a number of pharmaceutical coating processes. For example, it has been used successfully to apply powder and lipid materials to pellets. Furthermore, it also has been used to prepare enteric-coated pellets, tablets, and capsules.

The most critical coating variable encountered in the preparation of lipid-coated pellets was the temperature of the suspending air.

A high degree of batch-to-batch reproducibility was obtained when similar conditions were used to prepare lipid-coated pellets. Reproducible results were obtained with both the large and the laboratory models. Thus, no scale-up problems were encountered.

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