A Novel Process for Coating Objects 3 to 35 mm in Diameter

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Extended Abstract

Applying very small amounts of coating material (less than 1,000 micrograms) uniformly at high speeds to objects with a major diameter 3 to 35 mm is not possible with current industrial techniques. Objects including pharmaceutical tablets and devices for human implantation are either coated non-uniformly in large vented pans or slowly and inefficiently using one-at-a-time processes. The absence of an effective coating technique for objects in this size range has prevented or limited the development of many commercial products.

A novel process for coating objects in this size range has been developed and demonstrated to accurately deposit small amounts (200 to 400 micrograms) of an Active Pharmaceutical Ingredient (API) as part of a greater total coating weight gain [1]. A Relative Standard Deviation (RSD) of 3.0% was demonstrated on an API average weight gain of 158 micrograms to objects within a single batch [1]. However, in that study the API represented 0.1 to 1.0% of the total coating material applied, and the objects coated were known to be non-uniform as they were friable pharmaceutical tablets. It is desired to determine the coating accuracy of a small total coating weight gain (100 to 500 micrograms) on a more uniform object.

Common laboratory methods of determining thickness uniformity on objects are not as accurate as either measuring weight gain using a balance or measuring an API using a tracer, since thickness is a point measurement and must be averaged over the entire object surface. Three-dimensional imaging techniques are not practical or economically feasible for small-scale studies. A method of weighing the objects, dissolving the coating off, and re-weighing them was selected for analysis because of ease of use, object traceability, and overall accuracy. The objects selected for the study are readily available industrial flat washers with a nominal major diameter of 4.83 mm (McMaster Carr part number 90965A110, M2 metric flat washer). The washers are made of 316 stainless steel and will not deteriorate or lose mass from either the coating or dissolution process. The washers were selected because of their uniformity of surface area and weight and difficulty of coating with current industrial processes. The washer dimensions and weight are located in Table 1:

Table 1: Average flat washer dimensions

Outside Diameter (mm)	**Inside Diameter** (mm)	**Thickness** (mm)	**Surface Area** (mm^2)	**Weight** (mg)
4.83	2.24	0.30	33.32	32.34

A coating formulation was developed based on the ability to form a coating that is non-tacky in the dry state that will also dissolve off completely in solvent. The coating formulation used to coat the objects is shown in Table 2:

Table 2: Coating formulation

Component	Poly(styrene-co-butadiene) 45 wt. % styrene CAS # 9003-55-8	Polystyrene standard CAS # 9003-53-6	Toluene CAS #108-88-3	Ethyl Acetate CAS #141-78-6
Mass Percentage/(%)	0.476	0.524	54.450	44.550

The coating apparatus (Figure 1) is described in US patent 6,209,479 and EP patent 1 140 366 and eqv [2,3,4]. It consists of a processing chamber that sits on top of an air distribution plate (roto-nozzle). The roto-nozzle contains gas jets designed to accelerate the object through the coating zone in a ballistic flight path. Additionally, the gas jets impart momentum such that the object is rotating as it passes through the coating zone [2,3,4]. The spray zone is created by a low-momentum two-fluid nozzle beneath the roto-nozzle that atomizes the stream of coating solution into fine droplets.

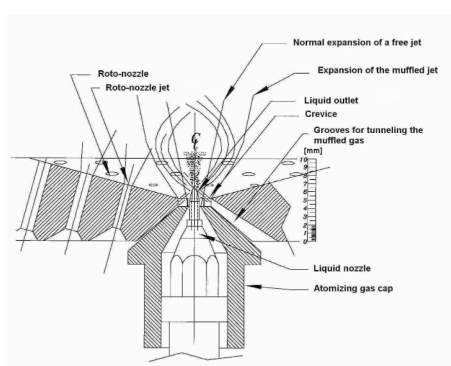

Figure 1: Cutaway of Roto-nozzle & Liquid Nozzle

Coating Apparatus Description

Tangentially located slots around the two-fluid nozzle mix the high-pressure atomizing gas with low-pressure process gas, muffling the energy from the two-fluid nozzle. The objects are loaded into the processing chamber and are coated co-currently with the drying gas.

The processing conditions were the same for all batches and are listed in Table 3:

Table 3: Processing Conditions

Drying gas rate/(kg/hr)	50		Inlet temperature/(C)	30
Inlet plenum pressure/(kPa)	4.1		Solution spray rate/(g/hr)	0.30
Atomizing gas pressure/(bar)	2.25		Number of objects/batch/(#)	100
Atomizing gas rate/(g/min)	1.8		Initial batch weight/(g)	3.23

Objects were loaded in the apparatus and coated while suspended freely in the drying gas stream. Fifty of the one hundred objects in the batch were selected at random and weighed on a Sartorius MC5 balance with an accuracy of +/- 0.006 mg. The coating was then dissolved off of the objects and they were re-weighed to determine the total weight gain. Three batches each were run at target weight gains of 100 and 500 micrograms. The results from the three 100 microgram target batches (401, 402, and 403) are located in Table 4 and Figure 2:

Table 4: Results from 100 Microgram Target Weight Gain Batches 401, 402, and 403

Batch Number	**04080401**	**04080402**	**04080403**
Number of Objects/(#)	100	100	100
Solution Delivered/(g)	5.7	5.7	5.7
Average Weight Gain/(mg)	0.123	0.121	0.123
Relative Standard Deviation/(%)	4.86	5.04	5.04
Theoretical Coating Thickness/(μm)	3.83	3.77	3.83
High Weight/(mg)	0.135	0.132	0.137
Low Weight/(mg)	0.113	0.107	0.111

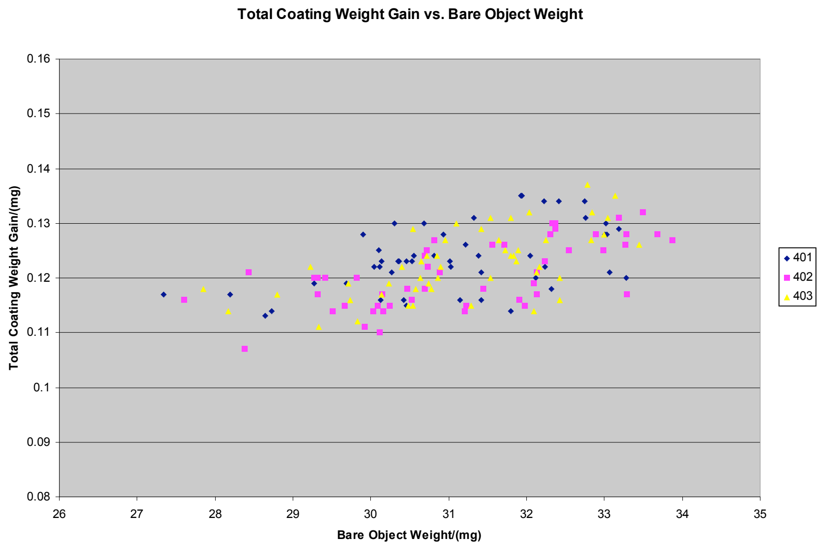

Figure 2: Total Coating Weight Gain for 100 Microgram Target Weight Gain Batches 401, 402, and 403

The average coating weight gain of the three batches was 122 micrograms, as the yield was slightly higher than predicted. The average weight gain between the batches showed good repeatability. The RSD values for the three batches were 4.86, 5.04, and 5.04%, which were satisfactory but did not meet expectations based on previous experimental results [1]. The results for the 500 microgram target weight gain batches are shown in Table 5 and Figure 3:

Table 5: Results for 500 Microgram Target Weight Gain Batches 501, 502, and 503:

Batch Number	**04080501**	**04080502**	**04080601**
Number of Objects/(#)	100	100	100
Solution Delivered/(g)	28.5	28.5	28.5
Average Weight Gain/(mg)	0.496	0.489	0.496
Relative Standard Deviation/(%)	6.66	4.37	4.68
Theoretical Coating Thickness/(μm)	15.44	15.22	15.44
High Weight/(mg)	0.553	0.555	0.539
Low Weight/(mg)	0.384	0.443	0.447

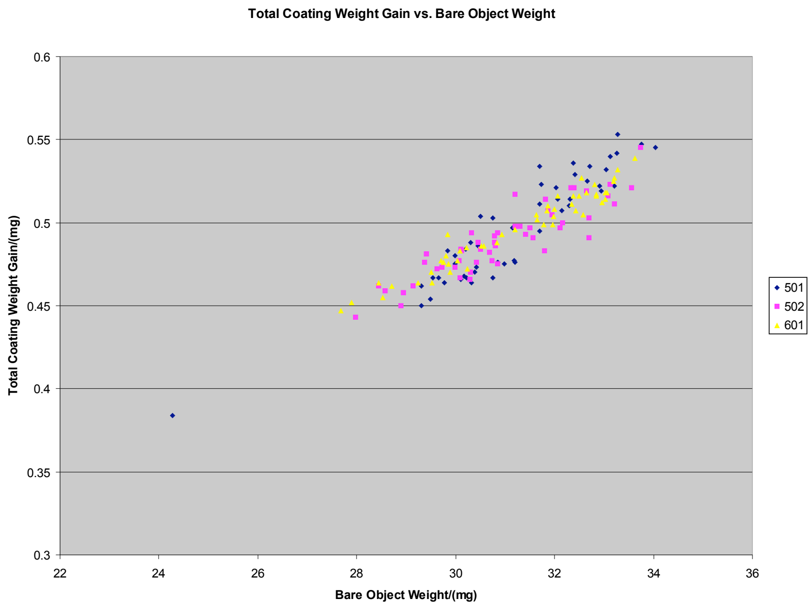

Figure 3: Total Coating Weight Gain for 100 Microgram Target Weight Gain Batches 501, 502, and 601

The average weight gain of the three batches was 0.493 mg, and the RSD values were 6.66, 4.37, and 4.68%. The 6.66 RSD for Batch 501 is high due to the presence of one washer that was much lighter than the others and the coating weight gain was much less than the average. The trend of higher weight gain for the heavier objects is much more pronounced at the higher coating weight gain. It is believed this is due to the heavier objects making more passes through the coating zone and receiving proportionately more coating. In order to achieve a more uniform coating weight gain within a batch, objects were sorted to a size range of 0.500 mg and coated. The results for these batches are located in Table 6 and Figures 4 and 5:

Table 6: Results for Weight Sorted Batches 602 and 603:

Batch Number	**04080602**	**04080603**
Number of Objects/(#)	100	100
Solution Delivered/(g)	5.7	28.5
Average Weight Gain/(mg)	0.125	0.495
Relative Standard Deviation/(%)	2.75	0.61
Theoretical Coating Thickness/(μm)	3.89	15.41
High Weight/(mg)	0.130	0.503
Low Weight/(mg)	0.119	0.489

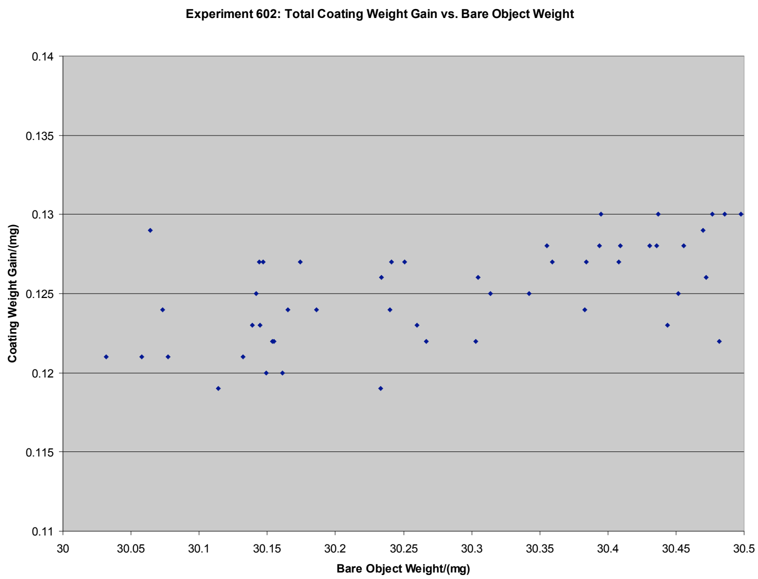

Figure 4: Total Coating Weight Gain for Sorted Batch 602

Figure 5: Total Coating Weight Gain for Sorted Batch 603

The RSD values for the sorted batches are much lower than the unsorted batches, demonstrating object weight uniformity as a significant factor in the coating weight gain per object. The weight gain range of the 100 microgram target weight gain batches was 11 micrograms (0.119 to 0.130 mg low and high), which is below the listed accuracy range of the balance of 12 micrograms.

Conclusions

A novel method of coating small objects is described which has the capability to apply total coating weight gains of 125 and 495 micrograms with RSD values of 2.75 and 0.61%, respectively. The coating process is shown to be sensitive to the object weight, and by sorting objects into batches with small weight variations the coating accuracy improved significantly. Further tests using a more accurate balance may demonstrate an improved coating accuracy, as the coating weight gain range of the 125 microgram sorted batch was below the listed accuracy of the balance. A method of measuring the uniformity of thickness on the objects should be used to determine how well the coating is distributed on each object.

References

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