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QUANTITATION OF THE AMOUNT AND UNIFORMITY OF AQUEOUS FILM COATING APPLIED TO TABLETS IN A 24" ACCELA-COTA*

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ABSTRACT

A simple technique was developed to quantify the amount of film coating applied to individual tablets. A Plackett-Burman experimental design was used to determine the processing parameters in a 24" Accela-Cota which can influence the homogeniety of film coating applied to the tablets. Tablets from various locations within the coating drum were analyzed for the amount of film coating material. The processing parameters that were found to affect the film coating were: coating drum speed; amount of aqueous film coating liquid applied; and the spray pattern. The starting location of the tablets in the tablet bed did not affect the amount of coating applied or the variability of the coating. Different size and shape tablets were found to behave similarly as to what processing parameters were significant in the amount of coating

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applied and the variability between tablets. For individual tablets, the surface coverage was found to be very uniform.

INTRODUCTION

Tablet film coating can be considered as the application of a coating material to a moving bed of tablets with a stream of heated air applied to facilitate evaporation of solvent. In the Accela-Cota tablet coater, a perforated drum is rotated on its horizantal axis with drying air directed through the tablet bed and exhausted through perforations in the drum. The distribution of the film coating on the tablets is accomplished by the rotation of the perforated drum which provides movement to the tablet bed. Baffles can be added to the drum to aid the tablet movement and provide a good distribution of tablets during the application of the coating material.

Poor tablet movement in the drum can lead to differences in the amount of film coating applied to each tablet during a coating run. This variation can result in such things as color variation, bridging of the intagliations on the film coated tablet, and variability in drug release if the film is being used as a diffusion barrier (1,2). Previous work has been done using photographic, photomultiplier, or manual counting techniques to quantify the amount of time a tablet spends with the bulk of the tablet bed and the amount of time the tablet spends on the surface of the tablet bed (2,3,4). This work involved developing a simple means to quantify the amount of film coating applied to individual

tablets. Using this technique in a 24" Accela-Cota, it could be determined which process parameters influence the homogeniety of the film coating applied to the tablets. At the beginning of the coating application, tablets were started at different locations in the tablet bed to determine if starting location would influence the amount of coating applied to the tablets. The uniformity of the film coat applied to the surface of the tablet was determined by cutting individual tablets into four sections.

EXPERIMENTAL

A combination of three hydroxypropyl methylcellulose polymers of different viscosities and hydroxypropyl cellulose were used as the basic aqueous coating liquid (Table 1). Polyethylene glycol 400 was added as a plasticizer.

FD&C Blue Dye No. 1 (Blue 1) was used in the aqueous coating liquid as a marker compound which provided a means to quantify the amount of film coating material applied to individual tablets. To verify that Blue 1 could be used to quanitate the amount of film coating material on the tablet, sprayed films were prepared in a spraybox apparatus (5) which utilizies an air atomizing spray system identical to what was used in the Accela-Cota. The aqueous film coating liquids were sprayed on 3 and one-half inch squares cut from transparency film for infrared copiers (3M Company) which allowed for easy removal of the films. The sprayed films were weighed and assayed for the amount of Blue 1 per gram of film.

TABLE 1

Formula used to prepare the basic aqueous film coating liquid.

Item	Source	Amount (%w/w)
Hydroxypropyl Methylcellulose 2910, USP, 5 CPS	Methocel E 5 Dow Chemical	2.0
Hydroxypropyl Methylcellulose 2910, USP, 15 CPS	Pharmacoat 615 Shin Etsu	2.0
Hydroxypropyl Methylcellulose 2910, USP, 50 CPS	Metolose 50 Shin Etsu	1.0
Hydroxypropyl Cellulose	Klucel LF Hercules	0.5
Polyethylene Glycol 400	Polyethylene Glycol 400 Union Carbide	1.0
FD&C Blue Dye No. 1	H. Kohnstamm	0.07
Distilled Water		93.43

The independent variables in an initial screening study using a twelve run Plackett-Burman experimental design (6) are shown in Table 2. This design was chosen to determine which processing variables affected the uniformity of the film coating applied to the tablets. As shown in Table 2, the spray pattern consisted of a "Good" or "Bad" spray pattern. The "Good" pattern used spraying variables to provide a wide uniform spray pattern and the "Bad" spray pattern provided a small spray pattern. The spray variables used are shown in Table 3. The tablets used for the study were 900 milligram ovaloid placebo tablets.

At the start of each coating run, tablets were placed in four different locations in the tablet bed. Location 1 was at the top of the tablet bed and on the surface of the tablet bed near the front

TABLE 2

Independent Variable	Low Level	High Level
1. Tablet Bed Weight (Kgs)	9	12
2. Drum Speed (rpm)	8	16
3. Baffles	Absent	Present
4. Exhaust Air Flow (scfm)	440	725
5. Spray Pattern	Bad	Good
6. Amount of Coating Applied (Liters/kg of tablets)	0.25	0.5

TABLE 3

Processing parameters used for the two different spray patterns used in the Plackett-Burman experimental design.

Parameter	Bad Spray Pattern	Good Spray Pattern
Spray Distance	6 "	10"
Aircap*	134255-45	134255-60
Fluid Nozzle*	35100	35100
Atomizing Air Pressure	20 psi	60 psi
Application Rate	75 mls/min	75 mls/min
Exhaust Temperature	45°C	45°C

* Spraying Systems, Inc

of the coating drum. Location 2 was at the top and on the surface of the tablet bed mid-way between the front and back of the coating drum. The top of the tablet bed is the highest point in the coating drum where the tablets stay after the tablets have been rotated in the coating drum. Location 3 was mid-way between the front and the back of the coating drum and buried halfway between the coating drum and the surface of the tablet bed. Location 4 was near the back of the coating drum and buried halfway between the coating drum and the surface of the tablet bed.

The tablets placed in each of the four different locations could be identified by unique intagliations on the tablets such

that after the coating run the starting location would be known from the intagliation. The background tablets had no intagliations. Fifty tablets were used during each coating run at each of the four tablet locations.

After each coating run, 20 tablets from each of the four locations and 20 background tablets were individually assayed for the amount of Blue 1. To assay the amount of Blue 1, the tablet was dissolved in water and the insoluble material from the tablet core was filtered off. Any soluble material from the tablets was shown to not interfere with the spectrophotometric assay for Blue 1 which was assayed on a Hewlett-Packard Spectrophotometer. The amount of film coating material per tablet was calculated based on the amount of Blue 1.

The means and standard deviations of the amount of film per tablet were calculated for each set of tablets. These means and standard deviations were analyzed for the effects of the six processing variables and location variables using an analysis of variance model. All analysis was done using the GLM procedure of statistical analysis system at the 0.05 level of significance (7).

The experimental design was repeated using 300 milligram round placebo tablets. Again, tablets identified with different intagliations were placed at four different locations in the tablet bed. The processing variables were the same as in Table 1 except the coating drum speeds were reduced to 6 and 14 rpms and the amount of film coating liquid applied was reduced to 0.2 and 0.4 liters per kilogram of tablets. After the coated tablets were assayed for the amount of Blue 1, the same statistical analysis was

TABLE 4

Comparison of the gravimetric method (GM) and Blue 1 assay method (AM) for determining the amount of film coating material. Results are expressed as milligrams of film coating material.

SAMPLE No.	AM	GM	SAMPLE NO.	AM	GM
1	532	539	5	530	537
2	528	536	6	528	536
3	536	539	7	531	538
4	543	551	8	527	537

performed on the amount of film coating per tablet and the standard deviations.

To quanitate uniformity of tablet surface coverage, tablets from 6 of the runs from each of the two Plackett-Burman studies were cut into four pieces and each section was analyzed for the amount of Blue 1. The intagliations on both sides of the tablets allowed for easy identification of the four sections from the different tablets. For the second study using round tablets, only the 6 runs using 0.4 liters of coating liquid applied per kilogram of tablets were assayed as the other tablets fell below the assay sensitivity when divided into four sections.

RESULTS AND DISCUSSION

The results of the assays for Blue 1 on films sprayed in the spraybox are shown in Table 4. The results indicate that the assay for Blue 1 can be used to calculate the amount of coating material as there is greater than 98 percent recovery based on the Blue 1 assay.

TABLE 5

Results of the 12 coating runs using the large ovaloid tablets. Amounts are expressed as the average number of milligrams of film coating applied per tablet.

	LOCATION				
Trial	1	2	3	4	Background
1	30.4 ± 1.81	31.8 ± 2.46	32.5 ± 1.11	30.1 ± 1.34	30.0 ± 2.25
2	32.5 ± 3.70	33.8 ± 7.58	38.7 ± 11.0	41.2 ± 4.70	37.7 ± 6.39
3	18.7 ± 1.86	19.6 ± 1.71	18.6 ± 2.22	19.6 ± 1.69	18.6 ± 2.41
4	16.6 ± 2.26	16.4 ± 0.66	17.4 ± 1.86	18.1 ± 2.35	16.5 ± 1.01
5	15.1 ± 1.04	15.5 ± 1.16	14.8 ± 1.77	14.2 ± 1.80	15.4 ± 1.22
6	36.6 ± 4.65	38.9 ± 4.44	32.7 ± 2.33	36.5 ± 4.28	34.8 ± 5.93
7	15.2 ± 2.21	17.5 ± 1.62	15.4 ± 0.50	17.1 ± 4.49	16.9 ± 2.73
8	31.4 ± 3.09	32.3 ± 1.71	28.4 ± 3.52	32.0 ± 1.47	30.3 ± 2.26
9	36.7 ± 2.14	34.7 ± 3.95	31.7 ± 5.13	36.3 ± 3.71	31.5 ± 3.82
10	15.8 ± 1.27	16.4 ± 2.67	13.3 ± 1.14	14.9 ± 3.57	15.5 ± 1.88
11	30.7 ± 1.87	31.3 ± 1.55	32.7 ± 2.17	33.0 ± 1.28	30.2 ± 1.70
12	17.1 ± 2.41	20.5 ± 1.93	19.8 ± 3.83	18.0 ± 2.99	17.8 ± 5.54

The results of the 12 coating runs for the ovaloid tablets are summarized in Table 5. The statistical analysis for the means of the amount of film coating per tablet and standard deviations is presented in Table 6. The mean values for the amount of coating per tablet were calculated by taking the average of the six values obtained at each variable level or the average of the 12 values for the mean value for each location. The mean standard deviations were calculated in a similar manner. The standard deviation is a measure of the variability of the amount of film coating material applied to the individual tablets.

TABLE 6

Statistical analysis for large ovaloid tablets. Results are expressed as average milligrams of film coating per tablet from six coating runs using either the high or low value of the processing variable. For the starting location, the average is for all twelve coating runs.

ANALYSIS OF MEANS

Processing Variable	DF	P-Value	Low	High
Tablet Bed Weight	1	NS	25.1	25.1
Drum Speed	1	0.0293	25.6	24.6
Baffles	1	NS	25.2	25.1
Air Flow	1	NS	24.8	25.4
Amount of Coating Applied	1	0.0001	16.9	33.4
Spray Pattern	1	0.0001	26.9	23.3
Starting Location	4	NS	24.7(1)	25.7(2)
			24.7(3)	25.9(4)
			24.6(Background)	

ANALYSIS OF STANDARD DEVIATIONS

Processing Variable	DF	P-Value	Low	High
Tablet Bed Weight	1	NS	2.58	2.99
Drum Speed	1	0.0001	3.53	2.04
Baffles	1	NS	2.82	2.75
Air Flow	1	NS	2.47	3.10
Amount of Coating Applied	1	0.0004	2.14	3.45
Spray Pattern	1	0.0001	3.62	1.96
Location	4	NS	2.36(1)	2.62(2)
			3.05(3)	2.81(4)
			3.10(Background)	

The results of the statistical analysis were quite similar for the amount of film coating per tablet and the standard deviations. The starting location in the pan was not a significant factor affecting the amount of film coating applied or its variation. Drum speed, amount of film coating liquid applied, and the spray pattern were the three significant variables affecting both the amount of film coating per tablet and the variability between tablets.

Higher drum speed provided a lower amount of film coating per tablet but the variability was not as great as with the lower drum

TABLE 7

Results of the 12 coating runs using the small round tablets. Amounts are expressed as the average number of milligrams of film coating applied per tablet.

	LOCATION				
Trial	1	2	3	4	Background
1	8.31 ± 0.82	8.20 ± 0.74	8.38 ± 0.82	8.82 ± 0.81	7.96 ± 0.72
2	9.09 ± 1.62	9.17 ± 1.96	9.79 ± 1.94	9.62 ± 1.64	9.17 ± 1.77
3	3.99 ± 0.72	4.81 ± 1.08	4.97 ± 1.05	4.70 ± 0.76	4.46 ± 1.04
4	4.86 ± 0.64	4.71 ± 0.70	5.12 ± 0.80	5.03 ± 0.57	4.69 ± 0.66
5	4.25 ± 0.44	3.92 ± 0.50	3.89 ± 0.55	4.48 ± 0.50	3.84 ± 0.33
6	10.1 ± 2.65	9.21 ± 1.97	11.0 ± 1.74	11.0 ± 2.15	9.47 ± 2.58
7	3.70 ± 0.71	3.36 ± 0.65	3.51 ± 0.61	4.25 ± 0.60	4.65 ± 0.58
8	8.92 ± 0.46	8.59 ± 1.16	8.85 ± 1.58	9.28 ± 1.28	8.34 ± 1.10
9	8.80 ± 0.89	9.21 ± 1.10	9.86 ± 1.85	9.88 ± 1.24	9.24 ± 0.68
10	4.18 ± 0.80	3.78 ± 0.64	4.55 ± 0.39	4.27 ± 0.72	4.29 ± 0.67
11	8.35 ± 0.63	7.82 ± 0.63	8.21 ± 0.66	8.98 ± 0.49	8.15 ± 0.59
12	4.43 ± 1.05	4.72 ± 1.10	4.21 ± 1.01	4.91 ± 1.35	4.28 ± 1.36

speed. As was expected, the amount of film coating material per tablet at the higher application rate was approximately twice the amount at the lower application rate. The "Good" spray pattern had less applied to the tablets but the variability was approximately 50% less than tablets produced with the "Bad" spray pattern.

The results of the 12 coating runs for the round tablets are summarized in Table 7. The statistical analysis for the means of

TABLE 8

Statistical analysis for small round tablets. Results are expressed as average milligrams of film coating per tablet from six coating runs using either the low or high value of the processing variable. For the starting location, the average is for all twelve coating runs.

ANALYSIS OF MEANS

Processing Variable	DF	P-Value	Low	High
Tablet Bed Weight	1	0.0144	6.58	6.84
Drum Speed	1	0.0303	6.82	6.60
Baffles	1	NS	6.73	6.69
Air Flow	1	NS	6.79	6.63
Amount of Coating Applied	1	0.0001	4.36	9.06
Spray Pattern	1	0.0001	7.15	6.26
Starting Location	4	0.0009*	6.58(1)	6.86(3)
			6.46(2)	7.10(4)
			6.55(Background)	

* Location 4 is significantly greater than other locations

ANALYSIS OF STANDARD DEVIATIONS

Processing Variable	DF	P-Value	Low	High
Tablet Bed Weight	1	0.0264	0.934	1.09
Drum Speed	1	0.0001	1.26	0.767
Baffles	1	NS	0.958	1.07
Air Flow	1	NS	1.040	0.987
Amount of Coating Applied	1	0.0001	0.753	1.28
Spray Pattern	1	0.0001	1.32	0.706
Location	4	NS	0.953(1)	1.08(3)
			1.02(2)	1.01(4)
			1.01(Background)	

the amount of film coating per tablet and the means of the standard deviations are presented in Table 8. As in the previous study, neither the starting location of the tablets, baffles, nor the air flow had significant impact on the amount of coating material applied or its variation. The tablets from location 4 were coated significantly more than the other 3 locations or background tablets. The amount of film coating applied, tablet bed weight, drum speed, and the spray pattern were the significant variables

affecting both the amount of film coating per tablet and the variability between tablets.

As expected, the amount applied is approximately twice as much at the higher application rate which corresponds to two times as much film coating liquid being applied. As was demonstrated in the previous study, the variability between tablets increased as more film coating material was applied. The higher drum speed provided less variability between tablets.

The "Bad" spray pattern had more film coating applied to the tablets. The "Good" spray pattern provided for tablets that had less variability.

The results of the two Plackett-Burman studies are quite consistent. It is not clear as to why in both studies that a higher drum speed would cause less film coating to be applied to the tablets. There are several possible explanations for this behavior, such as the increased tablet to tablet friction, but further work would be necessary to determine the exact cause. The fact that the higher pan speed provides a more uniform coverage between tablets agrees with other techniques of measuring coating processes (2).

The "Good" spray pattern did have some spray drying which would explain why there was less coating applied to the tablets as compared to the "Bad" spray pattern. However, as expected, the broader more uniform spray pattern ("Good" spray pattern) provided less variability in the amount of coating applied to the individual tablets. Applying more aqueous film coating did not improve the coating variability between tablets. In fact, it was

TABLE 9

Results for the tablets which were cut into four sections and analyzed for the milligrams of film coating material per section of tablet.

Trial	Section 1	2	3	4
OVALOID TABLETS				
2	9.10 ± 1.29	8.80 ± 1.39	9.19 ± 1.16	9.03 ± 1.22
7	4.36 ± 0.48	4.01 ± 0.49	4.32 ± 0.43	4.38 ± 0.33
8	7.32 ± 0.57	7.25 ± 0.50	7.58 ± 0.66	7.59 ± 0.59
9	8.64 ± 1.44	8.16 ± 1.28	8.87 ± 0.91	8.31 ± 1.02
10	4.15 ± 0.42	4.14 ± 0.36	4.20 ± 0.24	4.25 ± 0.34
12	4.55 ± 0.75	4.67 ± 0.74	4.67 ± 0.92	4.73 ± 1.00
ROUND TABLETS				
1	2.04 ± 0.25	2.12 ± 0.28	2.06 ± 0.28	1.82 ± 0.22
2	2.23 ± 0.29	2.13 ± 0.064	2.21 ± 0.21	2.19 ± 0.32
6	2.82 ± 0.65	2.88 ± 0.67	2.95 ± 0.74	2.87 ± 0.85
8	2.22 ± 0.29	2.22 ± 0.36	2.14 ± 0.24	1.97 ± 0.34
10	2.21 ± 0.24	1.96 ± 0.38	2.04 ± 0.23	2.12 ± 0.15
11	2.34 ± 0.14	2.19 ± 0.18	2.11 ± 0.19	2.21 ± 0.18

quite the opposite as the variability increased as more film coating material was applied to the tablets.

The results of the milligrams of film per section of tablet, for the tablets that were cut into four sections, are shown in Table 9. The data for both the small round tablets and the large ovaloid tablets shows that the surface coverage for individual tablets is homogeneous.

CONCLUSIONS

The simple experimental technique of using Blue 1 to measure the amount of film coating material per tablet has been applied to tablets that were coated in the 24" Accela-Cota. It has been shown that for the two different tablets that were studied, the starting

location in the tablet bed has little affect on the amount of film coating applied. Increased coating drum speed will decrease the variability of coating between tablets.

Applying more film coating liquid will only increase the variability between tablets. Thus one cannot eliminate the differences between tablets by applying more coating liquid to the tablets. A broad uniform spray pattern will coat tablets with less variability. The two different shaped tablets behaved similarly as to what processing parameters were important during the film coating except the tablet bed weight was significant for the smaller tablets. A surprising finding in both studies was that the presence of baffles was not a significant factor in the amount of film coating applied to the tablets or the variability between the tablets. In both cases, the coverage of film coating material over the surface of the tablet is remarkably uniform.

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