Physical Factors Affecting the Subcoating of Compressed Tablets II

Preliminary Screening of Some Variables

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A series of preliminary experiments was performed to screen several physical factors that might affect the subcoating process. On the basis of this preliminary screening, three variables were selected for further study: tablet density, pan speed, and pan load. The effect of each of these variables on the "roughness index" was studied. All three strongly influenced the roughness index value of the subcoated tablets. Two equations were developed—one showing the relationship between pan load and roughness index and the other showing the relationship between tablet density and roughness index.

THE NUMBER of physical factors that could possibly have an effect on the quality of subcoating is great. They include such variables as tablet weight, size, surface characteristics, and geometry; batch size, pan dimensions, volume, and speed; physical properties of the subcoating fluid and its constituents; physical properties of the subcoating powder; amount and frequency of addition of the fluid and the powder; temperatures involved in the process; and many others.

Obviously, it would be difficult to study such a large number of variables in a single series of experiments. Hence, the following limited number of factors were selected for the first preliminary screening: (*a*) tablet weight, (*b*) tablet diameter, (*c*) tablet thickness, (*d*) pan depth, (*e*) pan diameter, (*f*) pan volume, (*g*) rotational speed, (*h*) volume of fluid per application, (*i*) number of fluid applications, (*j*) time between applications, (*k*) weight of subcoating powder, and (*l*) pan load.

Actually (*a*), (*b*), and (*c*) vary as a single group when tablets of different sizes are used. Similarly, (*d*), (*e*), and (*f*) vary as a group with a change in pan size. Other factors (*e.g.*, temperature, viscosity and density of coating syrup, temperature of drying air, etc.) were held constant in these experiments.

The procedure of this investigation involved the following steps: (*a*) the subcoating of a number of batches of tablets under strictly controlled conditions, with the quantitative level of one or two of the physical factors sharply varied in each batch (two quantitative levels were used for each of the factors), (*b*) quantitative evaluation of the subcoating for each batch, and (*c*) further studies using the roughness recorder (1) developed for this study to establish the exact quantitative affect of the physical conditions or factors which affect the operation significantly.

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EXPERIMENTAL

Materials

Subcoating Syrup.—The heavy gelatin syrup recommended by Clarkson (2) was used.

Subcoating Powder.—The subcoating powder used was the subcoating dusting powder recommended by Clarkson (2).

Tablets.—Three kinds of tablets were used in this study: (*a*) lactose tablets, (*b*) sodium bicarbonate tablets, and (*c*) zinc oxide-lactose tablets.

Lactose Tablets.—Lactose was moistened with sufficient 20% w/v acacia solution, wet granulated through a 10-mesh screen, dried, and passed through a 16-mesh screen. The granules were then lubricated with 0.75% magnesium stearate and 2% talc and compressed into 0.300-Gm. tablets on a Stokes B2 rotary machine using $^3/_8$-in. deep concave punches. The tablets had a hardness of 6 as measured with a Strong-Cobb hardness tester and a thickness of 0.435 cm.

Sodium Bicarbonate Tablets.—Sodium bicarbonate was wet granulated with 20% w/v acacia solution, dried, and passed through a 16-mesh screen. The granules were lubricated with 0.75% magnesium stearate and 2% talc and compressed into 0.600-Gm. tablets on a Stokes B2 rotary machine using $^7/_{16}$-in. deep concave punches. The tablets had a hardness of 6 as measured on a Strong-Cobb hardness tester and a thickness of 0.445 cm.

Zinc Oxide-Lactose Tablets.—Zinc oxide was wet granulated with 20% w/v acacia solution, dried, and passed through a 16-mesh screen. The granules were lubricated with 0.75% magnesium stearate.

Batches of zinc oxide-lactose tablets having different densities were made by mixing varying proportions of lubricated zinc oxide granulation and lubricated lactose granulation (similar to that used for the lactose tablets) and compressing the mixed granulation on a Stokes B2 rotary machine using $^3/_8$-in. deep concave punches. The thickness of the tablets was maintained at 0.435 cm. The actual density of each batch of tablets was determined by dividing the mass of a tablet by the volume of liquid (liquid petrolatum) displaced by it.

Equipment and Methods

Coating Pan.—Two pear-shaped copper pans of 39.3 and 30.7 cm. maximum diameter were used. They were equipped with variable speed drives and suction and hot air ducts; the temperature of the hot air was regulated with a rheostat.

Subcoating Procedure.—Powder-free tablets were placed in the pan and preheated with hot air at 55° for 30 minutes. The pan was rotated at a predetermined rate. The hot air was turned off, and hot subcoating solution (50°) was poured over the tumbling tablets in a thin stream directed back and forth across the surface of the tablets. The tablets were immediately raked twice by hand to distribute the syrup and allowed to roll for 2 minutes (at the faster pan speeds, the time was shortened to 1 minute) before the subcoating powder was sprinkled over the tablets. The tablets were then raked again by hand and allowed to roll for 5 minutes before the hot air (55°) and suction was turned on. The tablets were allowed to roll under these conditions until a total of 20 minutes had elapsed from the time the subcoating solution was added. At the end of this period, the suction and the hot air were turned off, and the next addition of syrup was commenced. This process was repeated until the desired increase in weight was achieved. All the tablets used were subcoated until they reached a specific weight. This final weight for the subcoated tablets was 0.430 Gm. for the $^3/_8$-in. lactose tablets and 0.760 Gm. for the $^7/_{16}$-in. sodium bicarbonate tablets.

RESULTS AND DISCUSSION

Over 50 batches needed to be subcoated to complete the preliminary screening of the factors under study. The data are presented only in those instances where the factor or factors had a significant influence in the roughness index. Where the roughness index was not significantly affected by the variations of a physical factor, the negative data have not been included in the report. Wherever necessary, the results were statistically analyzed using the Student t values to test for statistical significance. In the presentation of the data, the physical factors not specifically mentioned were held to a constant value. In the interests of brevity, certain terms are used in the following statements. These terms and their meanings are:

Small Tablet—0.300 Gm. lactose tablets, 0.952 cm. diameter, 0.435 cm. thick, having a density of 1.463 Gm./cm.^{3}.

Large Tablets—0.600 Gm. sodium bicarbonate tablets, 1.111 cm. diameter, 0.445 cm. thick, having a density of 2.000 Gm./cm.^{3}.

Small Pan—pear-shaped copper coating pan, 30.7 cm. maximum diameter, 24.5 cm. deep, having a capacity of 13.7 L.

Large Pan—pear-shaped copper coating pan, 39.3 cm. maximum diameter, 30.2 cm. deep, having a capacity of 28.8 L.

Slow Pan Speed—29 r.p.m.

Fast Pan Speed—47 r.p.m.

Pan Load—unless specified, the pan load for the small pans was maintained at 3 lb. of tablets and for large pans, at 6 lb. of tablets.

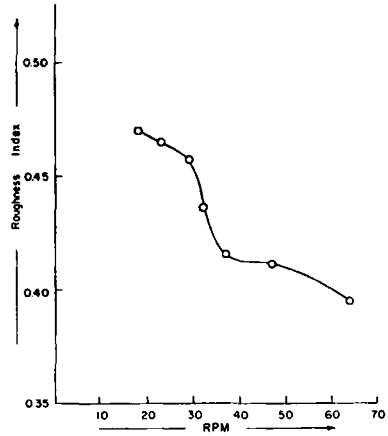

Fig. 1.—Influence of pan speed on the roughness index.

Amount of Subcoating Solution per Addition.—The optimum amount of subcoating solution used per addition was determined empirically. The amount used was just sufficient to wet the entire surface of the tablets. When a smaller amount was employed, relatively rougher tablets were obtained. The increase in the roughness index as the amount of subcoating solution is decreased is predictable since the smaller amount of syrup used failed to wet the entire tablet surface and caused the subcoating powder to adhere in patches. Also, because the tablets were not completely wetted under these conditions, grooves on the edges of the tablets were observed. Therefore, this variable has an effect on

TABLE I.—INFLUENCE OF PAN SPEED ON THE ROUGHNESS INDEX OF SMALL TABLETS[a]

Pan Size	Pan Speed	Roughness Index
Small	Slow	0.4574
Small	Fast	0.4112
Large	Slow	0.4456
Large	Fast	0.3808

[a] Subcoated in small and large pans at slow and fast pan speeds.

TABLE II.—INFLUENCE OF PAN SPEED ON THE ROUGHNESS INDEX OF LARGE TABLETS[a]

Pan Size	Pan Speed	Roughness Index
Small	Slow	0.4668
Small	Fast	0.4656
Large	Slow	0.4488
Large	Fast	0.4422

[a] Subcoated in small and large pans at slow and fast pan speeds.

TABLE III.—INFLUENCE OF PAN SPEED ON THE ROUGHNESS INDEX[a]

Pan Speed, r.p.m.	Roughness Index
18	0.4706
23	0.4652
29	0.4574
32	0.4365
37	0.4158
47	0.4112
64	0.3951

[a] Small tablets and small pan.

TABLE IV.—INFLUENCE OF PAN LOAD ON THE ROUGHNESS INDEX[a]

Pan Load, lb.	Roughness Index
1.0	0.3670
1.5	0.3833
2.0	0.4083
3.0	0.4574
4.0	0.4669
4.5	0.5221
5.0	0.5343
6.0	0.5397

[a] Small tablets, small pan, slow speed.

the roughness index. However, this appears to be an easily controlled variable since it is relatively simple to arrive at the amount of subcoating solution that is just sufficient to wet the entire surface of the tablets. For this reason this factor was not selected for further study.

Amount of Subcoating Powder per Addition.—The optimum amount of subcoating powder used was determined empirically. After allowing the wetted tablets to roll until tacky, just sufficient subcoating powder was added to cause the tablets to roll smoothly again without adhering to each other or to the sides of the pan. An increase in the amount of subcoating powder per addition caused a decrease in the number of additions necessary to add on the desired weight of subcoat, but had little influence on the roughness index of the subcoated tablet. (The excess of subcoating powder often accumulated at the back of the pan and formed small granules on the next addition of syrup. The granules attached themselves to the tablets which increased the number of rejects by creating tablets which had adhering particles.)

Time Between Additions.—The time between additions of subcoating solution had little influence on the roughness index of the subcoated tablet as long as there was sufficient time to dry the previous coat. With the temperature of the hot air blast at 55°, 20 minutes between additions insured complete drying. When the time between additions was reduced to 15 minutes, the roughness index of the

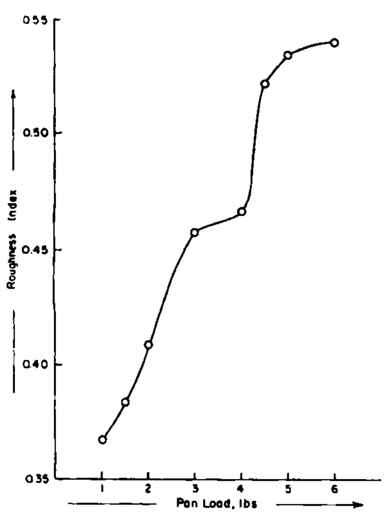

Fig. 2.—Influence of pan load on the roughness index.

TABLE V.—INFLUENCE OF TABLET SIZE ON THE ROUGHNESS INDEX OF TABLETS[a]

Tablet Size	Pan Size	Roughness Index
Small	Small	0.4574
Small	Large	0.4456
Large	Small	0.4668
Large	Large	0.4488

[a] Subcoated in small and large pans at the slow pan speed.

TABLE VI.—INFLUENCE OF TABLET SIZE ON THE ROUGHNESS INDEX OF TABLETS[a]

Tablet Size	Pan Size	Roughness Index
Small	Small	0.4112
Small	Large	0.3804
Large	Small	0.4656
Large	Large	0.4422

[a] Subcoated in small and large pans at the fast pan speed.

tablets was affected little; however, the previous coat did not dry completely and could easily be scraped off. This could create serious problems in the completely coated tablets as the trapped moisture would cause the coating to crack and peel.

Pan Size.—Changing the pan size with proportional changes in pan load had no significant effect statistically on the roughness index of the coated tablet. Slightly smoother tablets were consistently obtained with the large pan compared to the smaller pan. However, this difference was not statistically significant.

Speed of Rotation.—The preliminary data on the influence of pan speed on the roughness of subcoated tablets are shown in Tables I, II, and Fig. 1. Pan speed had a considerable influence on the roughness index of the small tablets (Table I), but had little influence on the large tablets (Table II). The differences in the results for small tablets were statistically significant ($p < 0.05$); this factor was selected for further study. The effect of pan speed on small tablets in small pans is shown in Table III.

An increase in the speed of rotation caused a decrease in the roughness index of the subcoated tablets. As the speed was increased from 18 r.p.m. through 29 r.p.m., the decrease in the roughness index was relatively small. A further increase in the speed of rotation caused a sharper decrease in the roughness index until a speed of 37 r.p.m. was reached. Then as the speed of rotation was increased further, the drop in the roughness index tended to level off. This effect of pan speed on the roughness index appeared to be related to the influence of pan speed on the visually observed roll characteristics of the tablets being coated. An increase in the speed enhanced the tumbling of the tablets, causing them to roll better. The effect was more gradual until a pan speed of 29 r.p.m. was reached. Further increases in the pan speed caused a marked improvement in the roll characteristics until a speed of 37 r.p.m. was reached. An additional increase in the pan speed did not markedly change the roll characteristics.

Pan Load.—In the preliminary screening, pan load (batch size) affected the roughness index, with the smaller pan loads producing a lower roughness index. Hence, this factor was selected for further study. The results of this study are shown in Table IV. The study was made using the small tablets in the small pan at the slow speed.

TABLE VII.—INFLUENCE OF TABLET DENSITY ON THE ROUGHNESS INDEX

Density, Gm./cm.³	Roughness Index
1.463	0.4112
1.756	0.4229
2.049	0.4319
2.439	0.4597
2.927	0.4683
3.658	0.4986

A pan load of 6 lb. of tablets was used as the upper limit since this was the maximum load the pan could hold without an overflow. A pan load of 1 lb. of tablets was chosen as the lower limit because a 0.5 lb. load failed to tumble properly.

An increase in the pan load while keeping all the other factors constant resulted in an increase in rough tablets. In the case of the tablets used there was almost a linear increase in the roughness index as the pan load was increased from 1 to 3 lb. of tablets. The effect started to level off in the 3 to 4-lb. pan load range before it again increased sharply in the 4 to 5-lb. pan load range, and finally leveled off again at pan loads of 5 lb. or more.

The influence of pan load on the roughness index also appeared to correlate with the visually observed roll characteristics of the tablets. It is likely that as the pan load is increased, the number of times a tablet would tumble would be decreased. This hindrance in tumbling might be responsible for the increase in the roughness index with the increase in pan loads. There was not much difference in the visually observed roll characteristics of the tablets at pan loads of 5 and 6 lb., which accounted for the leveling off of the roughness index at these loads. To establish an approximate relationship between pan load and the roughness index, the over-all slope of the curve (Fig. 2) was determined by drawing a line between the 1 and 5-lb. values on the curve. This line corresponds to the over-all linearity of the curve, except at the 4 and 6-lb. levels, at which this linearity does not exist, and gives the following approximate relationship between roughness index and pan load.

$$\text{Roughness Index} = 0.0418 \times \text{Pan Load (lb.)} + 0.3245$$

where 0.0418 is the slope, and 0.3245 is the roughness index intercept. It would be interesting to determine if this relationship holds true for tablets of other size and geometry.

Tablet Size.—There appeared to be little influence of tablet size on the roughness index of tablets at the slow speed. (See Table V.) The roughness indices of similar batches of tablets coated at the fast speed are given in Table VI. At the higher pan speed, the roughness index of the small tablet was reduced, but there was little influence on the roughness index of the large tablet. It was considered likely that tablet density rather than tablet size was the controlling factor in determining the roughness of the subcoated tablets. From the data accumulated, there was no way of determining whether tablet density or tablet size was the main controlling factor; tablet density was arbitrarily chosen for further study.

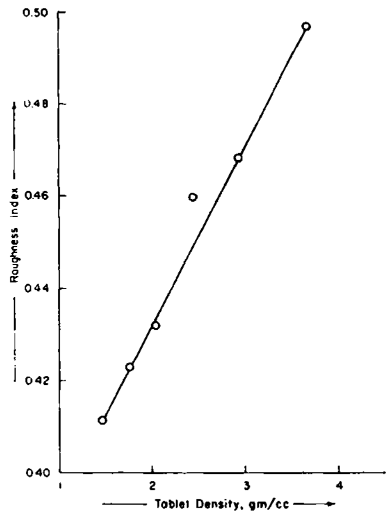

Fig. 3.—Influence of tablet density on the roughness index.

The influence of tablet density on the roughness index of subcoated tablets is shown in Table VII and Fig. 3. The study was made using 3-lb. batches of zinc oxide-lactose tablets of varying density and weight but having the same diameter, thickness, and geometry. The small pan was used at the fast speed. The fast speed was used because in the preliminary studies a greater effect was observed at this speed.

An increase in the tablet density while keeping the other factors constant resulted in an increase in rough tablets. This observation also appeared to correlate with the visually observed change in the roll characteristics of the tablets. The roll characteristics showed a progressive deterioration with increasing tablet density. A linear relationship existed between the roughness index and the tablet density under the above experimental conditions. This relationship was:

$$\text{Roughness Index} = 0.039 \times \text{Tablet Density (Gm./cm.}^3\text{)} + 0.3935$$

where 0.039 is the slope, and 0.3935 is the roughness index intercept. Additional study would be necessary to see if this relationship between the roughness index and the tablet density would hold for tablets of other size and geometry.

SUMMARY

A preliminary study of 12 factors that might affect subcoating has been carried out.

The effects of three factors—pan speed, pan load, and tablet density, which had significant effect on smoothness of the subcoating—have been studied further.

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(2) Clarkson, R., "Tablet Coating," Drug and Cosmetic Industry, New York, N. Y., 1951.