Effect of Glidants in Tableting

By LARRY L. AUGSBURGER and RALPH F. SHANGRAW

A method of measuring the fluidity of semifluid powders is described and used to investigate the role of various silica-type glidants in the direct compression of microcrystalline cellulose and a spray-dried lactose/microcrystalline cellulose blend on 2 different tablet presses. All silica-type glidants were found to improve the flow properties of microcrystalline cellulose as reflected in increased tablet weights and decreased weight variations, whereas a reversal of these effects was noted when the filler was the spray-dried lactose blend. While flow enhancement was attributed to a coating of the filler particles by the glidant, the reverse effect noted in the latter case was attributed in large measure to an increase in the bulk volume of the blend. No difference between the 2 tablet presses was found when the coefficients of variation were tested statistically. A pyrogenic silica and a silico-aluminate were found to be the most effective glidants in terms of over-all performance. These glidants were found effective in concentrations as low as 0.1 per cent by weight when added to microcrystalline cellulose and showed an optimum glidant activity at a concentration of about 0.5 per cent by weight.

THE FLOW of particulate solids is involved in many pharmaceutical operations such as tableting, encapsulation, solid-solid blending, tumbling, or fluidized bed drying. However, in none of these operations is flow any more critical, both in terms of product quality and production economics, than in the transport of solids from the hopper of tablet machines to and into the die cavities of a tablet press.

The limiting factor in the tableting of powders is often the flow properties of the material to be tableted. Uniform tablet weights and uniform doses of active ingredients, as well as production rate, are dependent on the ability of particulate matter to feed into the dies in a reproducible manner. In the past, poor flow properties have been overcome by granulating the powder or blend to be compressed. Unfortunately, granulation involves a series of steps which consumes a great deal of time and utilizes additional men, materials, and equipment. Recent advances in pharmaceutical technology and engineering have eliminated the need for granulation in many cases by making direct compression possible. Direct compression has been made commercially feasible with the advent of induced die feeding units which force-feed the die cavities, and the production of more fluid fillers by means of such engineering processes as spray-drying, instantizing, and controlled crystallization. The use of glidants has also been advocated for improving the flow properties of divided solids (1).

Glidants are defined as substances which improve granulation flow in the hopper or into the die cavity. The study of the usefulness of adjuvants in improving the flow properties of materials to be tableted has been largely confined to substances more properly defined as "lubricants" (2–4). The only "glidant" studies that have been reported in the pharmaceutical literature have been concerned with talc. Interest has developed recently, however, in the use of certain synthetic colloidal silicas to improve the fluidity of particulate solids. For example, a pyrogenic silica and a silico-aluminate were examined for their ability to improve the flow properties of spray-dried egg yolk (5). In general, the colloidal silicas consist principally of silicon dioxide and are characterized by low bulk density and very fine particle size.

Although glidants are apparently used in pharmaceutical operations, a survey of the literature has revealed the lack of any definitive study demonstrating the usefulness of glidants in tableting. Furthermore, there are no reports of a critical evaluation of the newer, silica-type flow conditioners. Consequently, a study of glidants in tableting, with particular emphasis on these silica-type flow conditioners appeared to be justified. Since tablet production of the future may well depend to a large extent upon direct compression, this study was designed, in

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particular, to establish the usefulness of glidants in direct compression.

EXPERIMENTAL

Before an investigation of glidants could commence, it was necessary to establish an experimental procedure which would truly measure increases in fluidity and, preferably, have practical industrial significance. Although angle of repose measurements and flow rate through orifices give results relatable to fluidity, reproducibility is relatively poor. It was felt that the simple measurement of tablet weight, which is a reflection of the ability of a powder or granulation to flow into a die cavity, would not only give comparable fluidity values, but would also have practical importance from a production standpoint.

Intuitively, it may be predicted that the addition of a glidant will, by enhancing fluidity, result in the more efficient filling of a die cavity. This more efficient die fill should then be reflected in increased tablet weights and decreased weight variation for the same size die and fill volume. Preliminary experimentation proved this premise to be true and glidants were evaluated using tablet weight as the measured parameter.

Materials.—Relatively free-flowing powders, microcrystalline cellulose[1] and spray-dried lactose,[2] were used as fillers, thereby eliminating the need for granulation. Microcrystalline cellulose possesses many unique advantages which make it an ideal filler to be used for such a study (6). In the first place, microcrystalline cellulose is fluid enough so that it will flow sufficiently well by itself to allow for production of uniform tablets at relatively high tablet machine speeds. At the same time, measurable effects can still be attained when glidants are added. Furthermore, because it is an "anti-adherent," it can be directly compressed without the need for a lubricant to aid ejection of the tablets from the die. As will be seen later, this is an extremely important quality, as it eliminates the need for lubricants which will cloud the action of glidants, making it impossible to separate individual effects. Microcrystalline cellulose also gives a very hard tablet at low pressures, minimizing tablet press vibration and decreasing the chances of erosion or chipping of tablets causing weight variation not attributable to die fill.

The glidants studied and their suppliers appear in Table I.

Preparation of Powders.—Uniform treatment of the powders to be evaluated was extremely important since reproducibility and meaningful results can only be obtained from this type of experiment if the history of each batch is carefully duplicated.

All powders were weighed and placed in a Patterson Kelly V-mixer model LB331 with no agitation bar. Mixing time was carefully controlled at 15 min. In order to promote good blending and uniform dispersion, all glidants or lubricants (which were needed with high concentrations of spray-dried lactose) were passed through a 100-mesh screen before blending with fillers. The importance of screening such additives, particularly when experimental batches are small, was stressed by Marlowe (7). The powders were removed from the blender and compressed immediately whenever possible to eliminate possible aggregation effects, which may result on standing. All blending and compression, except for the runs on the Stokes machine, were carried out in semi air-conditioned laboratories where relative humidity remains constant.

Compression.—Tablets were compressed on either a Stokes model B-2 or a Colton model 216 rotary tablet machine. Once the experiment commenced, the die fill adjustment was locked so that it remained constant throughout the course of the investigation. Occasionally, it was necessary to adjust compression pressure as glidants and fillers were changed in order to allow for production of tablets which were hard enough to withstand handling. Feed frames were adjusted close to the die table during direct compression to minimize leakage of powders. The same $^{7}/_{16}$ in. concave punches and dies were used in all experiments. Hopper filling was accomplished by placing a polyethylene bag full of the powder or granulation into the hopper and gently pulling the bag out from around the particulate mass.

Sampling.—The tablet press was allowed to run for approximately 1 min. before collecting tablets. One hundred tablet samples were drawn from the collected tablets by a "grab sample" method without replacement. Each tablet in the sample was weighed on a Mettler balance accurate to 0.1 mg. The weight of each tablet was recorded to the nearest milligram. The statistics determined were mean tablet weight, standard deviation, and coefficient of variation. The percentage change in mean tablet weight between the test tablets and control tablets was also calculated.

Experiment 1.—This experiment was carried out using microcrystalline cellulose and a blend consisting of 70 parts spray-dried lactose and 30 parts microcrystalline cellulose on a weight to weight basis.

The object of the experiment was twofold: (*a*) to compare the relative efficiency of various selected glidants when added to the 2 different tablet fillers;

TABLE I.—PROPERTIES[a] AND SOURCES OF THE GLIDANTS TESTED

Glidant[b]	Chemical Type	Ultimate Particle Size, mμ	Bulk Density, lb./cu. ft.
A	Pyrogenic silica	15	2.2[c]
B	Hydrated sodium silico-aluminate	22[d]	3[f], 18–20[e]
C	Amorphous non-gelled precipitated silica	12[d]	10[e]
D	...	13	4[e]
E	Silica hydrogel	10×10^3	15–20[e]
F	Silica hydrogel exhibiting aerogel type structure	3.3×10^3	4–5[e]

[a] Adapted from *References 11, 13–16.* [b] *A*, Cab-O-Sil, Cabot Corp., Boston, Mass.; *B*, Zeolex, type 7, J. M. Huber Corp., New York, N. Y.; *C*, Quso, type F-20 and D, Quso, type G-32, Philadelphia Quartz Co., Philadelphia, Pa.; E, Syloid, type 63 and F, Syloid, type 244, Grace Davison Chemical Co., Baltimore, Md. [c] Pour density. [d] Effective glidant particle size increased due to densification prior to shipping. [e] As packaged. [f] Aerated bulk density.

[1] Marketed as Avicel by American Viscose Corp., Marcus Hook, Pa.
[2] Western Condensing Co., Appleton, Wis.

TABLE II.—THE EFFECT OF SILICA-TYPE GLIDANTS ON WEIGHT AND WEIGHT VARIATION OF MICROCRYSTALLINE CELLULOSE TABLETS COLTON MODEL 216[a]

Glidant, 1% Concn.	Av. Wt., mg.	Change in Wt., %	S.D., mg.	Coefficient of Variation, %
Control	256.5	...	4.55	1.77
A	313.2	+22.11	2.66	0.84
B	314.8	+22.73	2.85	0.91
C	305.3	+19.03	4.75	1.56
D	306.7	+19.57	4.04	1.32
E	273.8	+ 6.74	4.21	1.54
F	303.2	+18.21	4.55	1.50
Calcium acetate	256.5	...	8.49	3.31

[a] Press speed: 800 tablets/min.

TABLE III.—THE EFFECT OF SILICA-TYPE GLIDANTS ON WEIGHT AND WEIGHT VARIATION OF MICROCRYSTALLINE CELLULOSE TABLETS STOKES MODEL B-2[a]

Glidant, 1% Concn.	Av. Wt., mg.	Change in Wt., mg.	S.D., mg.	Coefficient of Variation, %
Control	260.3	...	5.81	2.23
A	320.2	+23.01	2.81	0.88
B	324.2	+24.55	2.75	0.85
C	320.8	+23.24	3.43	1.07
D	313.2	+20.32	2.77	0.88
E	273.3	+ 4.99	4.69	1.72
F	310.5	+19.29	2.57	0.83
Calcium acetate	262.8	+ 0.96	2.58	0.98

[a] Press speed: 800 tablets/min.

(*b*) to compare these effects on 2 different rotary tablet machines to determine whether there was any significant between-machine effects. The same tooling was used on both machines. For the purposes of comparison, an attempt was made to adjust the initial fill on both machines so that identical average weights of the control batches (plain filler) were obtained.

The glidants were tested at a concentration of 1% by weight. In addition, magnesium stearate, at a concentration of 0.5% by weight, was added as a lubricant to the filler containing spray-dried lactose. Initially, the additives were preblended with about one-third, by volume, of the respective fillers. After about 30 sec. of shaking in a polyethylene bag, the preblend was added to the remaining two-thirds of the batch in the V-blender. Each batch of 1500 Gm. was then divided into 2 series, one of which was run on the Colton press and the other on the Stokes press at an average speed of 800 tablets/min. (Tables II–V.)

Experiment 2.—In view of the suggestion in the literature that fines (8) or talc (9) concentration is critical for effective fluidity, this experiment was undertaken to determine the role that glidant concentration plays in over-all powder flow. Glidants *A* and *B* were studied since they represent glidant types. Batches of 500 Gm. each, containing 0.1, 0.25, 0.5, 0.75, 1.0, and 2.0% by weight of glidant were prepared by simple blending according to the previously described procedures. Tablets were compressed on the Colton press at its maximum output of 1200 tablets/min. (Table VI).

Experiment 3.—The object of this experiment was to investigate the effect of press speed upon glidant efficiency. It was hoped that this experiment would affirm the present method of evaluation as a measure of powder fluidity. Glidants *A* and *B* in concentrations of 0.5% by weight were used as the previous experiment had shown that 0.5% was an optimum glidant concentration. The tablets were prepared on the Colton press at outputs of 480, 800, and 1200 tablets/min. (Table VII.)

RESULTS

As anticipated, experiment *1* showed a general increase in tablet weight and decrease in coefficients of variation for tablets compressed from microcrystalline cellulose when glidants are added. Surprisingly enough, the microcrystalline cellulose/spray-dried lactose blend showed results apparently reverse from those obtained with the plain microcrystalline cellulose. While it would appear that the standard deviations of the Stokes series were less than that obtained from tablets prepared on the Colton press, statistical analysis showed that there was no significant difference between the 2 series at the 95% confidence level. Similarly, statistical

TABLE IV.—THE EFFECT OF SILICA-TYPE GLIDANTS ON WEIGHT AND WEIGHT VARIATION OF SPRAY-DRIED LACTOSE/MICROCRYSTALLINE CELLULOSE BLEND (70:30) TABLETS COLTON MODEL 216[a]

Glidant,[b] 1% Concn.	Av. Wt., mg.	Change in Wt., %	S.D., mg.	Coefficient of Variation, %
Control	540.4	...	1.68	0.31
A	468.3	−13.34	2.55	0.54
B	515.9	− 4.53	1.94	0.38
C	485.5	−10.16	2.21	0.46
D	491.2	− 9.10	2.37	0.48
E	521.3	− 3.53	3.43	0.66
F	482.5	−10.17	1.90	0.39
Calcium acetate	541.2	+ 0.15	1.48	0.27

[a] Press speed: 800 tablets/min. [b] 0.5% magnesium stearate added to each batch.

TABLE V.—THE EFFECT OF SILICA-TYPE GLIDANTS ON WEIGHT AND WEIGHT VARIATION OF SPRAY-DRIED LACTOSE/MICROCRYSTALLINE CELLULOSE BLEND (70:30) TABLETS STOKES MODEL B-2[a]

Glidant,[b] 1% Concn.	Av. Wt., mg.	Change in Wt., %	S.D., mg.	Coefficient of Variation, %
Control	553.3	...	3.39	0.61
A	486.3	−12.11	2.23	0.46
B	530.0	− 2.40	3.15	0.59
C	510.1	− 7.81	4.45	0.87
D	505.7	− 8.60	2.49	0.49
E	534.8	− 3.34	3.14	0.59
F	508.5	− 8.10	2.38	0.47
Calcium acetate	554.8	+ 0.27	2.63	0.47

[a] Press speed: 800 tablets/min. [b] 0.5% magnesium stearate added to each batch.

testing of the difference in variation between the spray-dried lactose blend tablets produced on the 2 machines revealed no significant differences at the 95% confidence level.

Experiment 2 showed that tablet weights increased, with little or no improvement in weight variation, up to a concentration of about 0.5%. As glidant concentration was increased beyond this point, tablet weights decreased, showing, for the most part, little or no change in weight variation.

Although the glidants were quite effective at each production rate in experiment *3*, it was apparent that as press speed increased, powder fluidity became more critical, as evidenced by decreased mean tablet weights and a tendency toward an increase in coefficient of variation.

DISCUSSION

The physical and chemical properties of the silica-type glidants used in these experiments are listed in Table I. Glidant *B* is unique in that it is a silicoaluminate while the other glidants are colloidal silicas consisting primarily of silicon dioxide. Although glidant *B* has an ultimate particle size on the same order of magnitude as glidants *A* and *D* (10–20 mμ), it exhibits a mean effective particle size of 0.5–1 μ as a result of the manufacturer's "densification treatment" for increasing the bulk density (5). Glidant *C* has also been "densified" and exhibits a larger mean agglomerate size than does glidant *D*.

Glidants *A* and *B* appeared to be the most effective of the glidants in terms of over-all performance. In general, the glidants with the smaller particle sizes tended to be the most effective ones, although glidant *B*, with its larger effective particle size, proved surprisingly effective.

The weight increases observed in these experiments cannot be explained by the filling of void spaces with glidant alone (10). The true density of microcrystalline cellulose is about 1.54 Gm./cm.^{3}, and its bulk density is about 0.29 Gm./cm.^{3}. From these data it can be shown that about 81% of the total volume occupied by the powder is void space. On the other hand, the true density and bulk density of glidant *A* is 2.2 Gm./cm.^{3} and 0.039 Gm./cm.^{3}, respectively (11). In a similar manner, it can be shown that about 98% of the volume occupied by this glidant is void space. Thus, if the void space of microcrystalline cellulose was filled by glidant *A*, there would be an increase in weight of only 11%. Since glidant *A* in concentration of 1% (by weight) was able to increase tablet weights by as much as 24%, it is quite obvious that some function other than the filling of void spaces must be involved. Presumably, this function is the coating of particles (5, 10), resulting in an increased fluidity which manifests itself by allowing the particles to fill the die cavity in a more efficient manner. Furthermore, this process of coating the microcrystalline cellulose particles, instead of merely filling in the voids, would actually increase the bulk volume of the powder blend, thereby making any increase in weight of the final tablet even more significant than was demonstrated, since any weight increase must in part be negated by an increase in bulk volume.

The results with the spray-dried lactose/microcrystalline cellulose blend were not anticipated. In this series, the glidants which were the most effective in causing weight increases with microcrystalline cellulose were the most effective in causing weight decreases in this test, but not necessarily in the same order. Rather, there was a general agreement with bulk density in that the glidants exhibiting the lowest bulk density, disregarding particle size, elicited the greatest loss in mean weight. This pattern suggests that the decrease in tablet weights is a result of an increase in the bulk volume of the total blend, due to the addition of the extremely high bulk volume silicas. This suggestion follows since the bulk of the spray-dried lactose blend, being of considerably larger particle size than the microcrystalline cellulose, presents a smaller total surface area to which the glidant particles can become attached. In addition, the spray-dried lactose blend offers a smaller void space and less chance for the glidant to simply fill in between the particles. It is also quite possible that this blend may already have possessed maximum fluidity, owing to the free flowing properties of spray-dried lactose itself, and the addition of glidant actually hindered flow by acting as excess fines. No doubt, some clouding of glidant activity could have also resulted from the inclusion of magnesium stearate, which was necessary to allow for tablet ejection from the dies.

Because of these many factors, it was impossible to determine whether any useful purpose had been accomplished by adding glidants to the spray-dried lactose blend. However, the fact that coefficients of variation tended to increase and not decrease would seem to indicate that the glidants actually hindered fluidity in this case.

The effects of glidant concentration of microcrystalline cellulose tablets proved quite interesting. Effectiveness was demonstrated with a concentration of only 0.1% by weight. The additions of glidant beyond the 0.5% level caused no further increases in tablet weight but rather resulted in a decrease. Coefficients of variation showed uniform improvement over the control at all concentrations of glidant *A* but tended to be higher than the control for batches containing glidant *B*. This difference between glidants as reflected in coefficients of variation can be accounted for on the basis of the smaller effective particle size of glidant *A*. The fact that, beyond a concentration of 0.5%, tablet weights decreased, may be due to an increase in bulk volume of the mixture. If the glidant does adhere to particle surfaces rather than fill in void spaces, as indicated, then the effect would be to increase the particle diameter and hence, to increase the bulk volume.

The effect of machine speed points out the critical nature of powder or granule fluidity in tableting. As press speed increases, dwell time decreases, and the need for fluidity becomes more apparent. This effect was reflected in a decrease in tablet weight for the same die-fill as machine speed increased. Along with this effect was a tendency toward higher coefficients of variation at higher press speeds. Although they were affected by speed, both glidant blends, *A* and *B*, showed significant glidant effects at each speed run.

The use of calcium acetate in experiment *1* was analogous to the use of acetic acid or a soluble acetate in the cement industry. According to the

TABLE VI.—THE EFFECT OF GLIDANT CONCENTRATION ON WEIGHT AND WEIGHT VARIATION OF MICROCRYSTALLINE CELLULOSE TABLETS[a]

Glidant, %	Glidant A			Glidant B		
	Av. Wt., mg.	S.D., mg.	Coefficient of Variation, %	Av. Wt., mg.	S.D., mg.	Coefficient of Variation, %
Control[b]		$\bar{x} = 253.5$	S.D. = 3.30	C.V. = 1.30		
0.1[c]	301.8	3.50	1.16	271.2	3.51	1.29
0.25	304.5	3.58	1.18	282.7	5.73	2.03
0.50	304.5	3.43	1.13	291.6	7.27	2.49
0.75	298.9	3.28	1.10	299.5	5.17	1.73
1.0	286.9	3.33	1.16	287.9	4.61	1.60
2.0	277.6	2.17	0.78	280.3	8.04	2.87

[a] Press speed: 1200 tablets/min. [b] Plain microcrystalline cellulose; mean of 4 controls. [c] Data for the 0.1% samples represent the means of replicates.

theory, fine particles of calcium acetate form on the surface of cement particles, rendering the cement free-flowing (12). These studies show that calcium acetate does not affect flow properties in the same way as the silicas. Indeed, in no case was a significant increase in mean tablet weight elicited. However, in most cases, there was a marked decrease in coefficient of variation, indicating that calcium acetate exerted some influence on flow properties. No explanation is presently obvious and more work is necessary before any conclusions can be drawn.

On the basis of the experimental results there is little question that glidants can play an important role in tablet compression, particularly in the direct compression of semifluid, nongranulated powders. The results obtained in these experiments are not only of theoretical importance, but are also of particular practical importance to tableting due to the method of evaluation employed. The experimental method employed proved to yield measures of particulate fluidity which may be more meaningful to the tableting industry than such methods as angle of repose and orifice flow since the measured parameter was actual tablet weights. However, since tablet sizes (or die-fill volume) only represent small parcels of the particulate mass, a large number of tablet weights were required in order to obtain a truly representative parameter. This aspect tended to make the method a tedious one.

On rare occasions unexplainable extreme weight variations were found, using this method of evaluation. This phenomenon occurred only twice in more than 60 runs and, in one case, involved a preliminary study. In the other cases which occurred during a regular run, the sample was repeated in replicate, and the average of the replicate was reported. This fact is noted in Table VII.

One of the problems associated with the use of glidants arises out of their very fine particle size and low bulk density. These qualitites make them very "dusty," thereby creating a problem in convenience of handling as well as posing an inhalation hazard. A second problem of more concern to industry arises out of the abrasiveness of silicas. This abrasiveness may result in wear of tooling in long-term use, necessitating replacement, and increasing production costs.

While glidants may play an important role in tableting, it may very well be that a quantitative evaluation of them will have even more significance in other pharmaceutical operations such as capsule filling or solid-solid blending.

SUMMARY AND CONCLUSIONS

1. A procedure is described, based on tablet weight and weight variation, which may be used effectively to measure the fluidity of semifluid powders and which gives results directly relatable to the tableting of such powders.

2. The technique is used to investigate the role of various silica-type glidants in direct compression on 2 different tableting machines using microcrystalline cellulose and a spray-dried lactose/microcrystalline cellulose blend as fillers.

3. All silica-type glidants were found to improve the flow properties of microcrystalline cellulose as reflected in increased tablet weights and decreased weight variations. The weight increases observed are attributed to the coating of filler particles with glidant, thereby allowing them to flow more readily and uniformly into the die cavities.

4. On the whole, glidants *A* and *B* were the most effective of the silica-type glidants when tested with microcrystalline cellulose as a filler. Glidant *E* was the least effective glidant. Glidant efficiency could generally be correlated with particle size, the smaller glidant particles effecting greater increases in tablet weight and decreases in weight variation.

TABLE VII.—THE EFFECT OF MACHINE SPEED AND GLIDANTS ON WEIGHT AND WEIGHT VARIATION OF MICROCRYSTALLINE CELLULOSE TABLETS

Glidant 0.5% Concn.	30 r.p.m. (480 Tablets/min.)			50 r.p.m. (800 Tablets/min.)			75 r.p.m. (1200 Tablets/min.)		
	Av. Wt., mg.	S.D., mg.	Coefficient of Variation, %	Av. Wt., mg.	S.D., mg.	Coefficient of Variation, %	Av. Wt., mg.	S.D., mg.	Coefficient of Variation, %
Control	262.1	2.80	1.07	259.2	3.32	1.28	253.5	3.30	1.30
A	311.1	1.55	0.50	305.7	3.19	1.04	304.5	3.43	1.13
B	306.3	2.77	0.90	302.2	3.10	1.03	291.6	7.28	2.50

5. All silica-type glidants were found to produce a decrease in mean tablet weight along with a tendency toward an increase in coefficient of variation for the same size die fill when used with the spray-dried lactose/microcrystalline cellulose blend. This phenomenon was attributed in large measure to the extremely high bulk volumes of the silica-type additives which have the effect of increasing the bulk volume of the entire powder blend, thereby decreasing effective tablet weights.

6. The statistical testing of coefficients of variation revealed no difference between the Stokes model B-2 tablet machine and the Colton model 216 tablet machine at the 95% confidence level.

7. Glidants *A* and *B* proved effective in concentrations as low as 0.1% by weight when added to plain microcrystalline cellulose. No increase in glidant activity was observed with concentrations beyond 0.5% by weight.

8. For the same die fill, tablet weights decreased and coefficients of variation tended to increase as tablet machine speeds increased when glidants *A* or *B* were added to microcrystalline cellulose. As would be expected, a powder fluidity becomes more critical when press speed is increased.

9. Although calcium acetate has proved to be an effective glidant in the cement industry, it did not increase tablet weights when added to microcrystalline cellulose or the spray-dried lactose/microcrystalline cellulose blend. It did appear to decrease coefficients of variation, but no explanation is offered.

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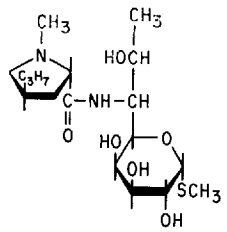
Automated Assay for the Antibiotic Lincomycin

By GEORGE C. PRESCOTT

A chemical assay for the antibiotic lincomycin has been developed which is based on the colorimetric determination of methanethiol generated from the acid hydrolysis of the methylthioglycosido group of the antibiotic. Fermentation beers and production samples as well as purified materials can be assayed by this procedure. Automation of this method increased the number of (completed) assays per man day from about 30 to about 150. Application of the assay to a series of standard solutions has given a mean recovery of 101 per cent and a standard deviation of 5.1 per cent. Analysis of a centrifuged beer containing added increments of lincomycin has given a mean recovery of 95.5 per cent and a standard deviation of 6 per cent.

LINCOMYCIN[1] is a medium spectrum antibiotic having the structure shown in I (1).

In 1962 the author developed an assay method which was based on the colorimetric determination of methanethiol generated from the acid hydrolysis of the methylthioglycosido group of the antibiotic (2). A particular advantage of this assay was that the thiol was separated from the interfering background material by distillation before it was reacted with the color reagent. Fermentation beers and production samples as well as purified products were assayed by this procedure. Early attempts to automate this assay with an automatic analyzer[2] were un-



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[1] Marketed as Lincocin by The Upjohn Co., Kalamazoo, Mich.

[2] AutoAnalyzer, Technicon Controls, Inc., Chauncey, N. Y.