Hopper Flow Electrostatics of Tableting Material II

Tablet Lubricants

By GERALD GOLD and BLAZE T. PALERMO

In an evaluation of the antistatic properties of tablet lubricants, data were obtained to indicate that magnesium stearate, polyethylene glycol 4000, sodium lauryl sulfate, and talc have the ability to lower the accumulation of static charges resulting from the flow of material through a tablet hopper. The antistatic property of these lubricants was demonstrated with different highly static materials. The antistatic effectiveness of the lubricant is decreased with lower concentrations of lubricant.

IN THE first report of this series (1) it was noted that tablet lubricants, magnesium stearate or talc, reduced the accumulation of static charges resulting from the flow of acetaminophen through a tablet hopper. This paper reports the extension of this work on the antistatic properties of tablet lubricants.

It is interesting to note that lubricating mechanisms have been proposed for both tablet lubricants and antistatic agents. In the manufacture of tablets, the primary function of lubricants is to reduce the friction between the tablet–die wall interface during tablet formation and ejection (2). This reduction in friction is generally considered to occur by the mechanism of fluid or boundary lubrication (3). In fluid lubrication, the two surfaces are separated by a finite, continuous layer of fluid lubricant. Boundary lubrication results from the adherence of polar portions of molecules with long carbon chains to the metal surfaces (3). Lubricants may also function to improve the flow characteristics of the granulation and to prevent sticking to the punch faces.

Antistatic agents function by reducing friction or by increasing conductance or by both mechanisms (4). A material added to reduce friction may not be an efficient agent for mitigating static accumulation, as the generation of static charges is thought to arise from contact rather than from friction. Surfaces may be made electrically conductive by utilizing antistatic agents which have polar or hygroscopic properties.

An attempt was made in this study to identify the lubricants which possess antistatic properties, to determine the effect of lubricant concentration, and to evaluate the antistatic characteristics of lubricants with different static materials.

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EXPERIMENTAL

The instrumentation and method for measurement have been previously described (1). In evaluating the effect of a lubricant on a static material, the unlubricated material was measured first and was followed with measurements of various lubricated samples of the same material. Each such series of measurements were repeated on 3 different days. As in the previous study, the results are expressed in arbitrary groupings as follows: 0–50, 51–175, 176–400, 401–650, 651–1050, and 1051–1800 v./cm. The range reported for each material represents in v./cm. the high limit and low limit for three consecutive readings, each made on a different day. Temperature varied from 22 to 28° and the relative humidity from 20 to 50%. The unlubricated materials were measured first as controls for daily variations in temperature and humidity and were consistently within their specified ranges. This can be attributed to the precautions taken to minimize adsorbed surface moisture, which included heating the tablet hopper and handling equipment prior to use and exposing the materials to the atmosphere for the minimum time necessary to obtain a measurement.

Materials.—Commercially available materials of either a U.S.P., N.F., or pharmaceutical grade were used. Materials used to evaluate the lubricants include acetaminophen,[1] ascorbic acid,[2] and anhydrous citric acid.[3] The lubricants studied were calcium stearate,[4] liquid petrolatum,[5] magnesium stearate,[6] polyethylene glycol 4000,[7] fumed

[1] Fine granular. Miles Chemical Co., Elkhart, Ind.
[2] Granular. Chas. Pfizer and Co., Inc., New York, N. Y.
[3] Granular. Chas. Pfizer and Co., Inc., New York, N. Y.
[4] Flexichem C. S. Swift and Co., Chicago, Ill.
[5] Drakol 19, $^{180}/_{190}$ viscosity at 100°F. Pennsylvania Refining Co., Butler, Pa.
[6] Mallinckrodt Chemical Works, St. Louis, Mo.
[7] Carbowax 4000. Carbide and Carbon Chemicals Co., New York, N. Y.

silicon dioxide,[8] sodium lauryl sulfate,[9] sodium myristate,[10] stearic acid,[11] talc,[12] and hydrogenated vegetable oil.[13] The lubricants were added to the granules as 60 mesh or finer powders. Liquid petrolatum was sprayed from laboratory prepared aerosols onto granules tumbling in a 6-in. coating pan. The lubricated samples were placed in polyethylene bags and stored in cardboard drums.

Loss on Drying.—Samples of each material were subjected to either 70° or 40° for 16 hr. Less than 0.1% weight loss was obtained for each material, with the exception of magnesium stearate (0.4%), polyethylene glycol 4000 (0.2%), and fumed silicon dioxide (0.7%).

RESULTS AND DISCUSSION

Ten tablet lubricants were evaluated for their ability, when added in 1% concentrations, to lower the hopper flow static charge of anhydrous citric acid. The results are listed in Table I. Anhydrous citric acid without the addition of a lubricant had a static charge range of 1051–1800 v./cm. The addition of magnesium stearate, polyethylene glycol 4000, sodium lauryl sulfate, or talc lowered the charge to the 0–50 range. Calcium stearate and sodium myristate lowered the ranges to 176–400 and 651–1050, respectively. The addition of liquid petrolatum (in 0.5% concentration), fumed silicon dioxide, stearic acid, or hydrogenated vegetable oil did not influence the magnitude of the charge.

The effect of lubricant concentration on the static charge was studied. The charge of ascorbic acid was determined with 0.1, 1.0, and 5.0% concentrations of magnesium stearate, polyethylene glycol 4000, and talc. Ascorbic acid without the addition of a lubricant, as listed in Table II, had a static charge range of 651–1050 v./cm. At concentrations of 5.0 and 1.0%, each of the lubricants lowered the static charge range to 0–50 v./cm. At the 0.1% level, however, the lubricants were not so effective in lowering the static charge. The values obtained for magnesium stearate, polyethylene glycol 4000, and talc in 0.1% concentrations were in the ranges of 51–175, 401–650, and 51–175, respectively. These data indicate that the concentration of lubricant influences its ability to lower the static charge and that at the same concentration different lubricants may vary in their antistatic effectiveness.

The antistatic effect of selected lubricants on different materials was then studied. Magnesium stearate, polyethylene glycol 4000, talc, and stearic acid were added in 5% concentrations to acetaminophen, ascorbic acid, and anhydrous citric acid. The results are listed in Table III. In the absence of any added lubricant, acetaminophen, ascorbic acid, and anhydrous citric acid had static charge ranges of 401–650, 651–1050, and 1051–1800 v./cm., respectively. The addition of either magnesium stearate, polyethylene glycol 4000, or talc to each of these materials lowered their static charges to the 0–50 range. The addition of stearic acid, however, did not alter the magnitude of their static charges. It, therefore, appears that the presence or absence of antistatic properties in a lubricant is independent of the material accumulating the charge.

[8] Cab-O-Sil. Godfrey L. Cabot, Inc., Boston, Mass.
[9] Duponol C. E. I. du Pont de Nemours and Co., Wilmington, Del.
[10] K and K Laboratories, Inc., Jamaica, N. Y.
[11] Emersol 132. Emery Industries, Inc., Cincinnati, Ohio.
[12] No. 1755. Whittaker, Clark and Daniels, Inc., New York, N. Y.
[13] Sterotex. The Capital City Products Co., Columbus, Ohio.

TABLE I.—HOPPER FLOW STATIC CHARGES OF ANHYDROUS CITRIC ACID WITH 1% LUBRICANT[a]

	Range[b]
Anhydrous citric acid	1051–1800
Magnesium stearate	0–50
Polyethylene glycol 4000	0–50
Sodium lauryl sulfate	0–50
Talc	0–50
Calcium stearate	176–400
Sodium myristate	651–1050
Liquid petrolatum[c]	1051–1800
Fumed silicon dioxide	1051–1800
Stearic acid	1051–1800
Hydrogenated vegetable oil	1051–1800

[a] Negative charge (v./cm.). [b] Preselected ranges to indicate high and low limit of three measurements. [c] Added in 0.5% concentration.

TABLE II.—HOPPER FLOW STATIC CHARGES OF ASCORBIC ACID WITH VARIOUS CONCENTRATIONS OF SELECTED LUBRICANTS[a]

% Lubricant	Magnesium Stearate Range[b]	PEG 4000 Range[b]	Talc Range[b]
0	651–1050	651–1050	651–1050
0.1	51–175	401–650	51–175
1.0	0–50	0–50	0–50
5.0	0–50	0–50	0–50

[a] Negative charge (v./cm.). [b] Preselected ranges to indicate high and low limit of three measurements.

TABLE III.—HOPPER FLOW STATIC CHARGES OF ACETAMINOPHEN, ASCORBIC ACID, AND ANHYDROUS CITRIC ACID WITH 5% SELECTED LUBRICANTS[a]

	Acetaminophen Range[b]	Ascorbic Acid Range[b]	Anhydrous Citric Acid Range[b]
No lubricant	401–650	651–1050	1051–1800
Magnesium stearate	0–50	0–50	0–50
PEG 4000	0–50	0–50	0–50
Stearic acid	401–650	651–1050	1051–1800
Talc	0–50	0–50	0–50

[a] Negative charge (v./cm.). [b] Preselected ranges to indicate high and low limit of three measurements.

SUMMARY AND CONCLUSIONS

The objective of this study was to investigate the antistatic properties of tablet lubricants as they relate to the flow of granules through a tablet hopper. Ten tablet lubricants were investigated for their ability, when added in 1% concentrations, to lower the static charge of anhydrous citric acid. Magnesium stearate, polyethylene glycol 4000, sodium lauryl sulfate, and talc significantly lowered the static charge. Calcium stearate and sodium myristate had slight antistatic properties, and liquid petrolatum (in 0.5% concentration), fumed silicon dioxide, stearic acid, and hydrogenated vegetable oil had no antistatic properties.

The antistatic effectiveness of the lubricant is decreased with less than 1% concentration of lu-

bricant. Concentrations of 1% or more of magnesium stearate, polyethylene glycol 4000, or talc were effective in lowering the accumulation of static charge by ascorbic acid to the lowest range while concentrations of 0.1% gave only partial reduction.

The antistatic properties of the lubricant were not altered by the materials to which they were added. The addition of magnesium stearate, polyethylene glycol 4000, or talc in 5.0% concentrations to either acetaminophen, ascorbic acid, or anhydrous citric acid resulted in a significantly lower static charge, whereas the addition of 5% stearic acid to the same materials did not alter the magnitude of their charge.

REFERENCES

(1) Gold, G., and Palermo, B. T., *J. Pharm. Sci.*, **54**, 310(1965).
(2) Nelson, E., *et al.*, *J. Am. Pharm. Assoc., Sci. Ed.*, **43**, 596(1954).
(3) Strickland, W. A., Jr., Higuchi, T., and Busse, L. W., *ibid.*, **49**, 35(1960).
(4) "Encyclopedia of Chemical Technology," 2nd ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 654

Physical and Chemical Stability Testing of Tablet Dosage Forms

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The influence of excipients and lubricants on the chemical and physical stability of tablets is demonstrated. Tablet color stability and its measurement is reviewed. The applicability of chemical kinetic principles and the Arrhenius relationship to stability data for tablet systems is illustrated. The importance of the package to product stability is shown. The utility of exaggerated temperature, light, and humidity conditions in the stability testing of tablet dosage forms is demonstrated. The importance and significance of a well-organized stability testing program for evaluating the physical and chemical stability of solid dosage forms are discussed.

FOR MOST pharmaceutical manufacturers, the tablet dosage form accounts for a major portion of their product line. This dosage form is well accepted in the United States by both patient and physician for use in the oral administration of drugs.

Generally, in solid heterogeneous systems, the active ingredient tends to decompose at a slower rate than in liquid heterogeneous or homogeneous systems. However, this does not mean that it can be assumed that a drug in a tablet dosage will not exhibit stability problems. In fact, it is possible to encounter considerable instability of the drug in the tablet, as well as change in the physical properties of the tablet form.

In the subsequent sections of this paper, the factors contributing to the chemical and physical instability of tablet dosage forms, the feasibility of employing chemical kinetic principles to predict stability at shelf conditions from accelerated data, the influence of the package on product stability, and the significance and importance of a well-organized stability testing program for evaluating the physical and chemical stability of tablet dosage forms will be reviewed.

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CHEMICAL AND PHYSICAL STABILITY

Influence of Inert Ingredients.—It is only within recent years that considerably more attention has been paid to the influence that tablet diluents, lubricants, and granulating systems have on the stability of the active ingredient in the tablet and on the physical properties of the tablet dosage form. These materials, once regarded as inert fillers, have been found to potentiate the chemical degradation of the active ingredient, cause the disintegration time and dissolution rate of tablets to change with storage, influence the therapeutic effectiveness of the medicament in the tablet by modifying its absorption characteristics, cause changes in the color of the tablet, and affect other physical properties, such as friability and hardness.

In a recent study (1), a number of common tablet diluents were evaluated as to their influence on the stability of vitamins A and B_1 and ascorbic acid. One-gram disks were compressed of the diluent, vitamin, and 0.5% magnesium stearate to simulate conditions of storage for a tablet dosage form of the vitamins. The disks of the various diluents and vitamins were stored in amber bottles at room temperature and 45°, assayed at intervals for residual vitamin content, and observed for changes in physical appearance.

The data in Table I show that vitamin A is most stable in the presence of mannitol and lactose, while in the presence of diluents containing high initial moisture, the worst stability is obtained.

The data in Table II show that vitamin B_1 exhibits excellent stability in the presence of mannitol, sucrose, lactose, and kaolin. However, as