Effect of Concentration and Size of Lubricant on Flow Rate of Granules

F. Q. DANISH* and E. L. PARROTT

Abstract ☐ The flow rates of lactose granulations containing 50% of phenobarbital, sulfadiazine, and sodium salicylate were compared to the flow rate of the basic lactose granulation. Hydrogenated castor oil, glyceryl monostearate, polyethylene glycol 4000, and stearic acid were investigated as lubricants by means of a flowometer. For each lubricant, there was an optimum concentration, not exceeding 1%, which produced a maximum flow rate of the sodium chloride and the lactose granulation. For a constant concentration of lubricant, the flow rate was increased to a maximum rate as the size of the lubricant was reduced to 0.0213 cm. A further reduction in size of the lubricant slowed the flow rate.

Keyphrases ☐ Granule flow rates—lubricant size, concentration effects ☐ Lubricant size, concentration effects—granule flow rates ☐ Flow rates, granules—optimum lubricant size, concentration ☐ Fines concentration in granules—flow effect

The flow of particulate solids is involved in many pharmaceutical operations such as blending, encapsulation, tableting, and the packaging of powders and granules. The flow properties of a formulation may be improved by operational procedures such as granulation or spray drying. If modification of the particles is not feasible, the flow properties may be improved by the addition of a lubricant.

The flow of particles *per se* is the primary consideration in the formulation of particulate solids. Any friction or adhesion between the material and the equipment is of secondary concern, although it cannot be ignored in tableting. Münzel and Kägi (1) classified lubricants used in the preparation of compressed tablets as: (*a*) true lubricants (die eigentlichen Gleitmittel), which improve the flow properties of the granules and do not deform significantly under compressional pressures; (*b*) antiadhesive agents (die Antiadhäsionsmittel), which prevent the adhesion of the tablet to the punches and die and easily deform under pressure; and (*c*) substances and mixtures that are concomitantly lubricants and antiadhesive agents. Inherent in this classification is the recognition that lubricants, *e.g.*, calcium stearate and magnesium stearate, often perform more than a single function and are not so precisely classified in reality. Thus, in this report on the flowability of granules, a lubricant is defined as any other substance added in small amounts to improve the flow of a particular solid. Selection of a lubricant is often on a trial-and-error basis because no single method has been widely accepted as suitable for the evaluation of lubricants (1–5). The flowometer offers a simple and objective method to evaluate the effectiveness of lubricants under dynamic conditions (6, 7).

Table I—Flow Rate of a 16/20-Mesh Size Fraction of a Lactose Granulation and of a Granulation Containing Equal Quantities of Drug and Lactose

Orifice Diameter, cm.	Flow Rate, g./sec. Lactose Granulation	Lactose and Drug (1:1) Granulation	Percent Change
	Phenobarbital		
1.428	16.4	15.8	−3.6
0.925	4.3	4.0	−7.2
	Sulfadiazine		
1.428	16.4	15.5	−5.3
0.925	4.3	4.0	−7.2
	Sodium Salicylate		
1.428	16.4	18.0	9.8
0.925	4.5	4.6	9.1

Lubricants are generally recommended to be used in concentrations up to 5% and as very fine powder (8–11). This investigation was conducted to determine the effect of size and concentration of the lubricant on the flow rate of sodium chloride and lactose granulations. The effect on flow rate of the incorporation of several drugs into the lactose granulation was examined.

EXPERIMENTAL

Preparation of Particles—The method of preparation and separation of size fractions of sodium chloride and lactose particles has been described (7). Lactose granulations containing 50% of a drug were prepared by a wet granulation method. All materials were USP grade. The drugs were phenobarbital, sulfadiazine, and sodium salicylate. Equal weights of lactose and the drug were mixed in a V-blender for 1 hr. The mixture was transferred to a Hobart mixer, and portions of a 10% starch paste were added until a total of 3% starch had been added. The water solubility of sodium salicylate necessitated the use of a 20% starch paste. The wet mass was passed manually through a 6-mesh screen. The wet granulation was collected on trays lined with paper and dried in an oven at 38° for 17 hr. The dried granulation was milled through a No. 4 circular screen in a FitzMill, with the blunt edges forward while operating at low speed. The 16/20-mesh size fraction was separated by a Tyler sieve shaker using U. S. standard sieves. The granulation was treated with compressed air to remove fine particles.

The lubricants were melted on a water bath and then allowed to solidify at room temperature. The lubricants were milled in a FitzMill with the aid of dry ice. To prepare large particles, a No. 10 screen was used with the mill operating at slow speed and the blunt edge forward. To prepare small particles, a No. 40 screen was used with the mill operating at fast speed. A Tyler sieve shaker was used to collect the 16/20- and 30/40-mesh size fractions. The 60/80-, 100/140-, and 140/230-mesh size fractions were separated by using a 10-g. sample in an Allen-Bradley sonic sifter for 3 min. at an amplitude of 10.

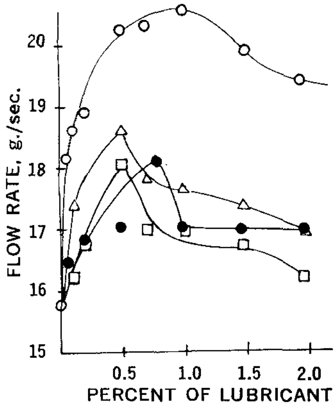

Figure 1—*Influence of concentration of 100/140-mesh size fraction of lubricants on flow rate through a 1.428-cm. circular orifice of a 16/20-mesh size fraction of lactose granulation. Key:* ○, *stearic acid:* ●, *hydrogenated castor oil;* □, *polyethylene glycol 4000; and* △, *glyceryl monostearate.*

The materials studied as potential lubricants were purified glyceryl monostearate[1], hydrogenated castor oil[2], polyethylene glycol 4000[3], and stearic acid USP. The lubricants were added in increasing proportions to 500 g. of the 16/20-mesh size fraction of sodium chloride and lactose granulations and mixed for 5 min. in a V-blender with a 2-qt. shell.

Measurement of Flow Rate—Flow rates through orifice diameters of 0.925 and 1.428 cm. were determined with a flowometer described in a previous report (7). The flow rate, expressed in grams per second, represents the average of five measurements.

RESULTS AND DISCUSSION

Influence of Drug on Flow Rate—Granulations containing equal quantities of lactose and a drug were used to determine the effect of a drug on the flow rate. The density of lactose is 1.59 g./ml. Since flow rate is a function of the density of the material (12), drugs were selected that had approximately the same density as lactose. Phenobarbital, sulfadiazine, and sodium salicylate were chosen because their densities are 1.30, 1.50, and 1.50 g./ml., respectively.

In the powdered form, the drugs flowed poorly. It was somewhat surprising that the flow rates of the granulations containing a drug did not change more than 10% from that of the lactose granulation. As shown in Table I, with sodium salicylate the flow rate was increased; and with sulfadiazine and phenobarbital the flow rate was decreased. It appears that these drugs do not greatly alter the flow rate of a basic lactose granulation. The granulation operation *per se* is important in the preparation of flowing particulate solids.

Influence of Concentration and Size of Lubricant—The influence of the concentration of a lubricant of a given size on the flow rate was determined by the addition of a 100/140-mesh size fraction of the lubricant to a 16/20-mesh size fraction of sodium chloride and lactose granulations. The effect on the flow rate of the lactose granulation upon the addition of various percentages of glyceryl monostearate, hydrogenated castor oil, polyethylene glycol 4000, and stearic acid is shown in Fig. 1. A maximum flow rate was obtained

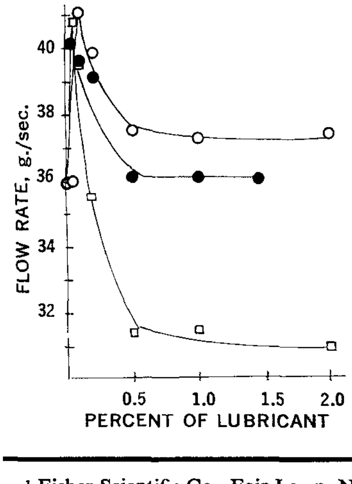

Figure 2—*Influence of concentration of 100/140-mesh size fraction of lubricants on flow rate through a 1.428-cm. circular orifice of a 16/20-mesh size fraction of sodium chloride granules. Key:* ○, *hydrogenated castor oil;* ●, *polyethylene glycol 4000; and* □, *glyceryl monostearate.*

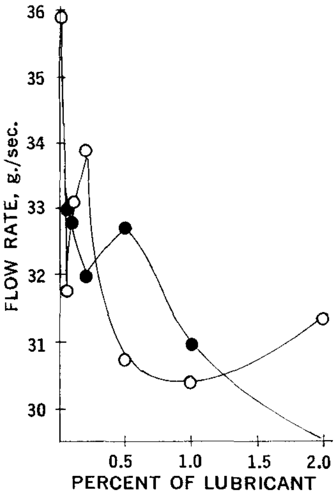

Figure 3—*Influence of concentration of 100/140-mesh size fraction of stearic acid on flow rate through a 1.428-cm. circular orifice of sodium chloride granules. Key:* ○, *100/140-mesh size fraction; and* ●, *30/40-mesh size fraction of sodium chloride.*

at 1% stearic acid, 0.7% hydrogenated castor oil, 0.5% polyethylene glycol 4000, and 0.5% glyceryl monostearate. A similar effect was demonstrated upon the addition of lubricants to sodium chloride particles. As shown in Fig. 2, a maximum flow rate was obtained at 0.1% hydrogenated castor oil, 0.05% polyethylene glycol 4000, and 0.05% glyceryl monostearate.

Münzel and Kägi (1) reported that the addition of 5 and 10% stearic acid and polyethylene glycol 6000 impaired the flow rate of sodium chloride and increased the flow rate of other substances. They did not investigate the influence of the lubricant at concentrations less than 1%. The present report demonstrates that the flow rate is increased by a small quantity of lubricant and that the maximum flow rate is usually attained with less than 1% lubricant.

The variation of behavior upon the addition of stearic acid to the sodium chloride particles is shown in Fig. 3. The addition of 0.05% stearic acid decreased the flow rate, and the addition of a greater concentration of stearic acid increased the flow to a maximum rate at 0.2% stearic acid. The variation was verified by adding stearic acid to a 30/40-mesh size fraction of sodium chloride particles. Again the flow rate was decreased as the concentration of the stearic acid was increased to 0.2%; as the concentration was increased to 0.5% stearic acid, the maximum flow rate was attained. An electrostatic effect was observed on the stearic acid particles and was assumed to be responsible for this variation (13).

The action of lubricants has been studied from the viewpoint of concentration, but apparently no research has been reported concerning the influence of size of the lubricant on flowability. It is usually assumed that particles of a lubricant have a diameter less than 0.015 cm., *i.e.*, 100 mesh (8).

In this investigation of the effect of size of a lubricant on flow rate, a constant concentration of lubricant was selected for which a 100/140-mesh size fraction of lubricant had produced a maximum

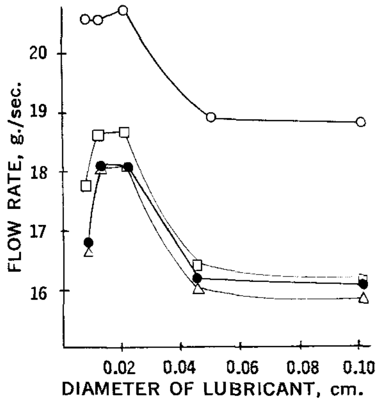

Figure 4—*Influence of various sizes of lubricant maintained at a constant concentration on the flow rate through a 1.428-cm. circular orifice of a 16/20-mesh size fraction of lactose granulation. Key:* ○, *1% stearic acid;* ●, *0.7% hydrogenated castor oil;* △, *0.05% polyethylene glycol 4000; and* □, *0.05% glyceryl monostearate.*

[1] Fisher Scientific Co., Fair Lawn, N. J.
[2] The Baker Castor Oil Co., Bayonne, N. J.
[3] Union Carbide Corp., New York, N. Y.

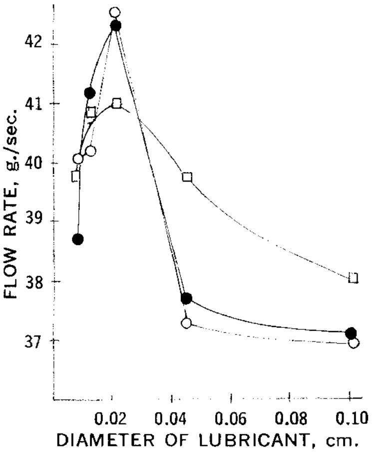

Figure 5—*Influence of various sizes of lubricant maintained at a constant concentration on the flow rate through a 1.428-cm. circular orifice of a 16/20-mesh size fraction of sodium chloride granules. Key: ●, 0.1% hydrogenated castor oil; ○, 0.05% polyethylene glycol 4000; and □, 0.05% glyceryl monostearate.*

flow rate. For example, 1% stearic acid had produced a maximum flow rate of the lactose granulation. Therefore, with the concentration of stearic acid maintained at 1%, various size fractions of stearic acid were added to a 16/20-mesh size fraction of lactose granulation, and the flow rates were measured. As shown in Fig. 4, the maximum flow rate occurred with stearic acid particles having a diameter of 0.0213 cm., *i.e.*, 60/80-mesh size fraction. Similarly, with 0.7% hydrogenated castor oil, the maximum flow rate occurred with the particles of lubricant having a diameter of 0.0213 cm. With 0.5% polyethylene glycol and 0.5% glyceryl monostearate, the maximum flow rate occurred when the lubricant had a diameter of 0.0213 cm.

As shown in Fig. 5, the maximum flow rates for the 16/20-mesh size fraction of sodium chloride particles were observed with the lubricant possessing an average diameter of 0.0213 cm. The concentrations of lubricants employed in these experiments were 0.1% hydrogenated castor oil, 0.05% polyethylene glycol 4000, and 0.05% glyceryl monostearate.

With both sodium chloride and lactose granulation, the maximum flow rate occurred when the lubricants had a diameter of 0.0213 cm. This finding suggests that there is an optimum diameter for a lubricant and that a smaller size will reduce flowability. Thus, when a lubricant is used in a formulation, there is an optimum concentration and size that should be used to obtain maximum flowability.

For a given material, the addition of fines increases the flow of a granulation to a maximum flow rate (14). As the concentration of the fines is increased and the void is progressively filled to a greater degree, the flow reaches a maximum rate. With a further increase in concentration of fines, the contact surface between the particles and the concomitant increase in interparticular friction becomes so great that the movement of the particles is less and the rate is slowed.

The smaller size of fines of the granule required a lower percent of fines to attain a maximum flow rate (7). When the concentration of fines was maintained at 10%, the flow rate was increased to a maximum value for sodium chloride and lactose granulations as the diameter of the fines was reduced to 0.009 cm., *i.e.*, 140/200-mesh size fraction. A further reduction of size of the fines produced a slower flow rate, presumably due to the larger specific surface and greater interparticular friction.

With the four lubricants used with the sodium chloride and lactose granulations, the maximum flow was attained if the diameter of the lubricant was 0.0213 cm. The difference in size of particles of lubricant and the size of fines needed to attain a maximum flow rate suggests that the mechanisms by which lubricants and fines increase flowability are different. It has been proposed for powders that lubricants act by mechanically separating the coarser particles, with a reduction in van der Waals' force (4, 15, 16). It appears that a lubricant increases flow rate of a granulation by a reduction of interparticular friction within the flowing stream of the particulate solid.

SUMMARY

1. The flow rate of a lactose granulation was not markedly affected by the addition of 50% phenobarbital, sulfadiazine, and sodium salicylate.

2. The effect of varying the concentration of lubricants—hydrogenated castor oil, glyceryl monostearate, polyethylene glycol 4000, and stearic acid—on the flow rate of sodium chloride and lactose granulations was investigated with a flowometer.

3. For the four lubricants investigated, a 1% or less concentration produced a maximum flow rate of sodium chloride and lactose granulations.

4. For a constant concentration of the four lubricants studied, a maximum flow rate was obtained when the diameter of the lubricant was 0.0213 cm.

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