

room temperature for almost 4 years did not exhibit any degradation.

Stability of Ethacrynic Acid in Solution—A solution of sodium ethacrylate (pH 6.8, 20 mg./ml.) showed no loss of intact ethacrynic acid after 3 days at room temperature. Losses were noted at elevated temperatures, however, indicating that sterile solutions of ethacrynic acid should be prepared by suitable filtration rather than by autoclaving.

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TECHNICAL ARTICLES

Effects of Moisture in Compaction of Particulate Material

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Abstract □ By using an ideal particulate system of crystalline sodium chloride and three liquids—water, decahydronaphthalene, and light liquid paraffin—the role of moisture in the compaction process was investigated. Interrelated effects of liquid at the die wall boundary and within the compact are discussed. Although differences in the behavior of the three liquids could be attributed partly to the viscosity difference, water apparently exerted a boundary lubricant effect in addition to hydrodynamic properties. Despite its lower viscosity, water was, therefore, a more effective lubricant than light liquid paraffin. In general, decahydronaphthalene adversely affected the compaction process. Cumulative changes in the difference between applied and transmitted force during consecutive compressions can be used to assess the lubricant efficiency of materials.

Keyphrases □ Compaction process—role of moisture, ideal particulate system □ Compression changes—lubricant efficiency assessment, ideal particulate system □ Water as lubricant—with sodium chloride, role in compaction process □ Die wall effects—studied using ideal particulate system of sodium chloride and water, decahydronaphthalene, or paraffin

During compaction of particulate material, the proportion of applied force transmitted to the die wall is influenced by several factors including: (a) the radial component of the applied force, and (b) the effective area of contact and coefficient of friction at the die wall. Since interparticulate lubrication increases the ratio of radial stress to axial stress (1), application of lubricant to the die is more effective than the addition of lubricant to a powder before compression (2). However, lubrication of both the die wall and interparticulate junctions produces a net decrease in the die wall reaction (1), because reducing the coefficient of interpar-

ticulate friction usually has little effect on die wall friction compared with a decrease in the coefficient of friction at the die wall.

A reduction in friction may be produced by: (a) hydrodynamic lubricants, forming a finite layer of low shear strength which prevents contact between adjacent surfaces; and (b) boundary lubricants which reduce adhesive forces between the surfaces.

The high viscosity of a boundary lubricant may produce an excessive resistance to shear (3). Therefore, a medium viscosity is often preferable, although the resistance to contact between sliding surfaces is less. Whereas values of shear strength were not directly related to lubricant efficiency, Lewis (4) found that lubricants with a lower melting point were more efficient, possibly due to the formation of a film on the die. Strickland *et al.* (5) showed that if more than 1% stearic acid was present in a sulfathiazole granulation, the semisolid material itself resisted compression. For a liquid lubricant such as mineral oil, however, increasing the concentration to 4% produced a continual decrease in the required compression force.

Numerous authors (6-8) commented on the effects of moisture during compaction. Anomalous compression results, attributed by Train (9) to electrostatic effects, were eliminated by humidifying the material. Wolff *et al.* (10) observed that a nonlubricated granulation could not be compressed when the moisture content was greater than 4%, although the results of Stephenson (11) and Shotton and Rees (8) showed that die wall friction may be reduced in the presence of moisture.

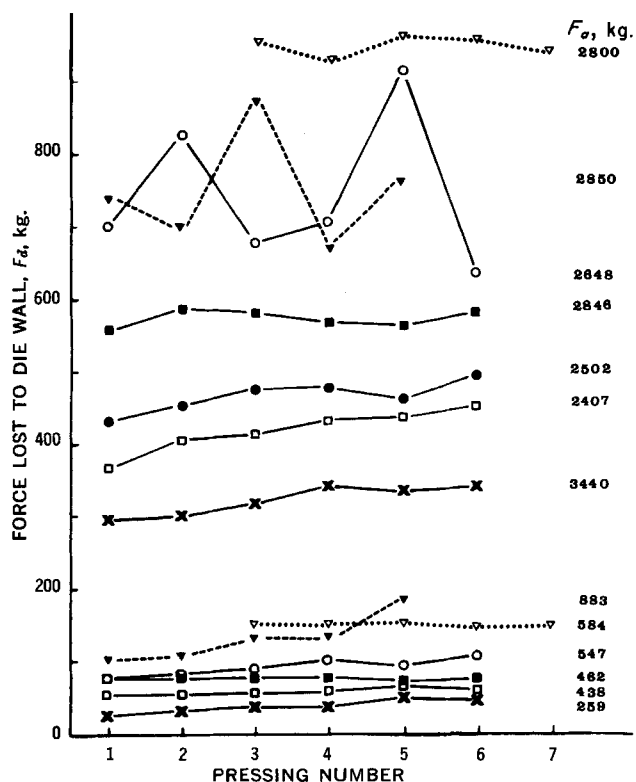


Figure 1—Effect of moisture on the changes in F_d with pressing number. Dried material: conditioned die (∇), and clean die (\blacktriangledown). Moisture content: 0.02% (O), 0.16% (■), 0.34% (●), 0.55% (□), and 10% (X).

EXPERIMENTAL

Selection and Characterization of Materials—A pharmaceutical tablet is usually a complex aggregate of particles of active substance and several excipients. The compression behavior of such a system depends on the interrelated properties of the constituents; therefore, it is preferable to use a simple system to study the compaction process.

Sodium chloride BP was selected as a crystalline material that forms a coherent compact by direct compression. The crystals were screened to obtain 30–40-, 60–80-, and 80–100-mesh fractions, corresponding to mean particle sizes of approximately 500, 220, and 160 μ . Adhering fines were then removed using an air-jet sieve¹ with a 100-mesh screen. The density (2.17 g. cm.⁻³) was determined pycnometrically, and the compression weight was then calculated as sufficient material (982 mg.) to produce a plane-faced, cylindrical compact of 1.2-cm. (about $15/32$ -in.) diameter and 0.4-cm. (about $5/32$ -in.) theoretical thickness at zero porosity.

Since the compaction behavior might be influenced by solvent properties of a liquid additive, it was decided to compare the effects of moisture and a nonsolvent. It was difficult experimentally to minimize evaporation of volatile liquids other than water. Therefore, a liquid of low volatility and high flash point, immiscible with water and a nonsolvent for sodium chloride, was required. Light liquid paraffin BPC was selected, but its viscosity (31.2 cps.) is appreciably higher than that of the moisture present as a saturated aqueous solution of sodium chloride (approximately 1.8 cps.) on the crystal surfaces. Thus, experiments were also made with decahydronaphthalene², which possesses fairly low volatility and a viscosity of 2.3 cps.

A reduction in particle size by the solvent action of water decreases the weight of solid in each compression sample. In most experiments, 30–40-mesh material was used; but to assess the

possible effects of a decrease in particle size by dissolution, 60–80- and 80–100-mesh fractions of dried material were studied. The effect of reducing the weight of 30–40-mesh material to 928 mg. also was investigated.

Addition of Moisture to Particulate Material—Exposing the material to relative humidities of 60–90% produced a suitable range of moisture contents. Individual samples of dried sodium chloride, sufficient to produce single compacts, were stored in uncapped glass vials above appropriate saturated salt solutions. When the required moisture content was reached, each vial was sealed with a polyethylene closure, and compression experiments were completed with a minimum delay.

Moisture Determination—The moisture content of representative samples was determined using the remote weighing assembly of a gram electrobalance³ installed in a vacuum chamber with an observation panel. A humidified sample was weighed and then dried for 1 hr. in an oven at 110° and 10 mm. Hg. Without cooling, the sample was replaced on the electrobalance, and the vacuum chamber was rapidly evacuated to 10 mm. Hg. After 15 min., air was allowed to enter the chamber through a drying tube before the dried sample was weighed.

Addition of Nonsolvents to Particulate Material—A uniform distribution of 0.1–10.0% decahydronaphthalene or light liquid paraffin was obtained by adding the calculated weight of liquid to a bulk quantity of sodium chloride in a cylindrical container, followed by standardized agitation. The container was shaken manually in a three-dimensional movement with simultaneous rotation about its axis⁴. Uniformity in weight of selected compacts from which the liquid was removed by chloroform extraction indicated that replicate samples of the compressed material were identical. Any loss of liquid during compaction could also be confirmed using this solvent extraction technique.

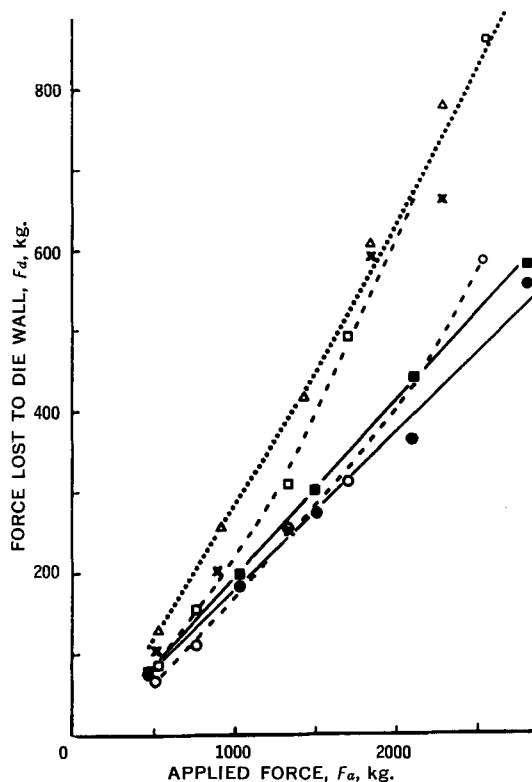


Figure 2—The relations between applied force and F_d during the first and sixth pressings in the presence of a low concentration of liquid. Liquid content: 0.16% moisture: 1st (—●—) and 6th (—■—), 0.1% light liquid paraffin: 1st (—○—) and 6th (—□—), 0.1% decahydronaphthalene: 1st (X) and 6th (Δ). Dried material in a conditioned die (...).

¹ Alpine Air Jet Sieve, model 200, Alpine, Augsburg, West Germany.
² Dekalin MAR (microanalytical reagent grade), Hopkin & Williams Ltd., Chadwell Heath, England. It consisted of 36% *trans*-isomer and 64% *cis*-isomer.

³ Cahn Instrument Co., Paramount, Calif.

⁴ As in a Turbula mixer, Willy A. Bachofen, Basle, Switzerland.

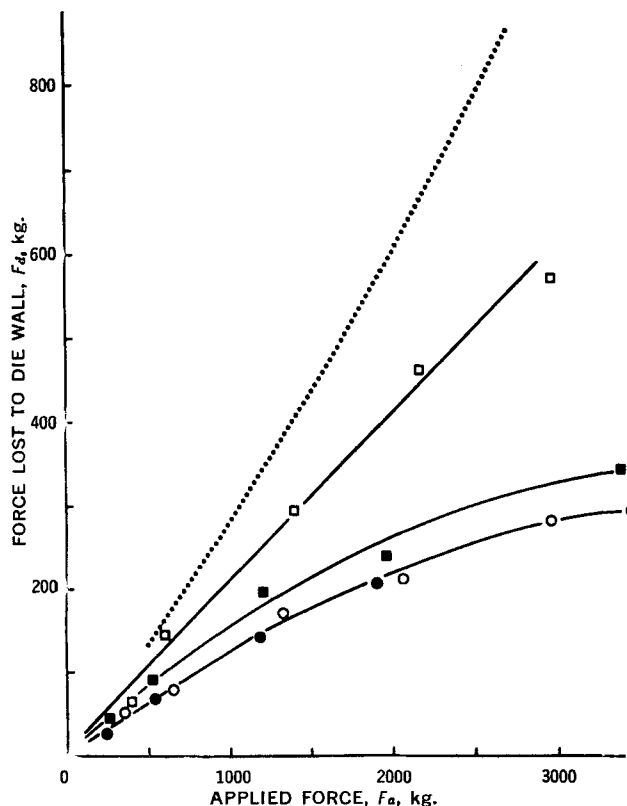


Figure 3—The relations between applied force and F_d during the first and sixth pressings in the presence of 10% moisture: 1st (●) and 6th (■), and 10% light liquid paraffin: 1st (○) and 6th (□). Dried material in a conditioned die (...).

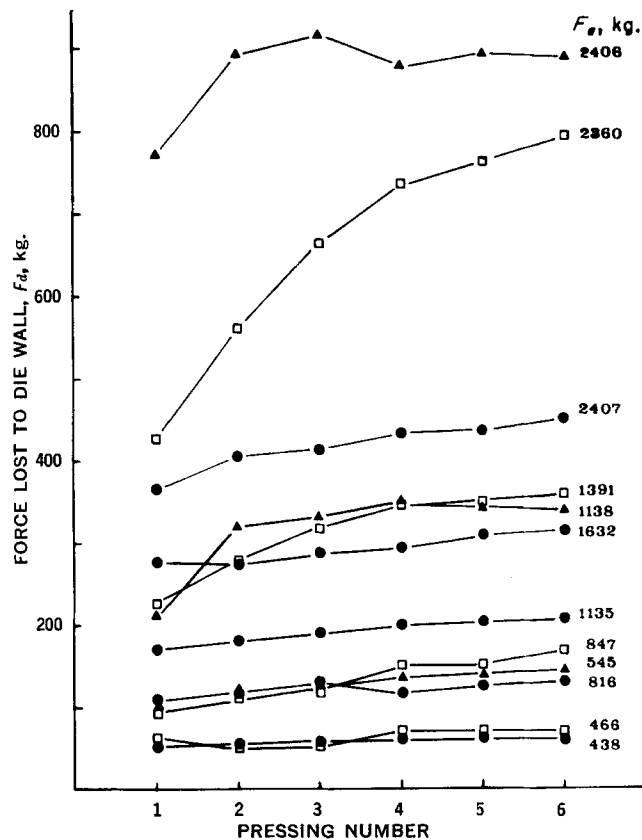


Figure 4—Dependence of F_d on the number of pressings in the presence of 0.55% moisture (●), 0.5% light liquid paraffin (□), and 0.5% decahydronaphthalene (▲).

Compression Equipment and Measurement of Compaction Forces—Plane-faced punches⁵ of 1.2-cm. (about $\frac{15}{32}$ -in.) diameter were used with a single-punch eccentric tablet press⁶. The upper punch and the lower punch holder were instrumented (12) using 0.31-cm. (0.125-in.), linear foil resistance strain gauges⁷, which were coated with a polysulfide rubber compound⁸ to protect them from atmospheric humidity. Details of the techniques for calibration of the strain gauge circuits were described elsewhere (12). The applied loads, corresponding to a 0.1% resistance change in the gauge circuits, were 1027 kg. for the upper punch and 3151 kg. for the lower punch holder.

The strain gauge circuits were connected to separate channels of a carrier amplifier⁹ and a six-channel recorder¹⁰ with pencil-type moving-coil galvanometers¹¹. Galvanometer deflections were recorded on UV-sensitive paper¹², and the measurements were converted to force data using the calibration values already quoted. The difference, F_d , between the force applied by the upper punch, F_a , and the force transmitted to the lower punch, F_b , during a compression cycle is a function of the force lost to the die wall due to friction.

Compression Technique—To prevent rapid loss of moisture from humidified sodium chloride samples, it was necessary to establish an elevated ambient relative humidity in equilibrium with the particular samples being compressed. Similarly, to avoid moisture uptake during the compression of dried sodium chloride and samples containing light liquid paraffin or decahydronaphthalene, the ambient conditions were controlled at 20% relative humidity. It was not possible to study the compression characteristics of

samples containing more than 2% decahydronaphthalene because of rapid loss by evaporation.

Six compacts were prepared at each of five compression settings of the tablet press, the punches and die being cleaned before studies at a different pressure.

For sodium chloride containing no liquid, the weighed samples were dried for 1 hr. at 110° and stored over silica gel for 24 hr. before use. Compression behavior was investigated in a clean die and in a die conditioned by the previous compaction of material (8).

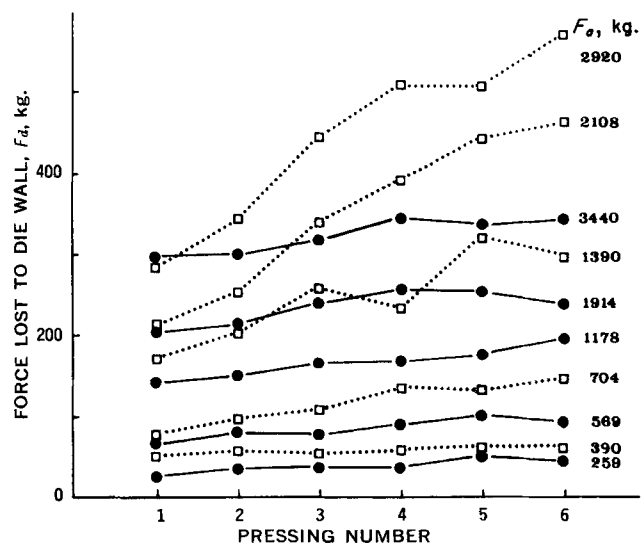


Figure 5—Dependence of F_d on the number of pressings in the presence of 10% moisture (●) and 10% light liquid paraffin (□).

⁵ Lewin Engineering, London, England.
⁶ W. Lehman & Co., London, England.
⁷ Saunders Roe, East Cowes, Isle of Wight, England.
⁸ PR 720, British Paints Ltd., London, England.
⁹ Type 1070, New Electronic Products, London, England.
¹⁰ Type 1050, New Electronic Products, London, England.
¹¹ Type BB, undamped frequency 250 c/s, New Electronic Products, London, England.
¹² Oscilloscript D, Gevaert, Mortsel, Belgium.

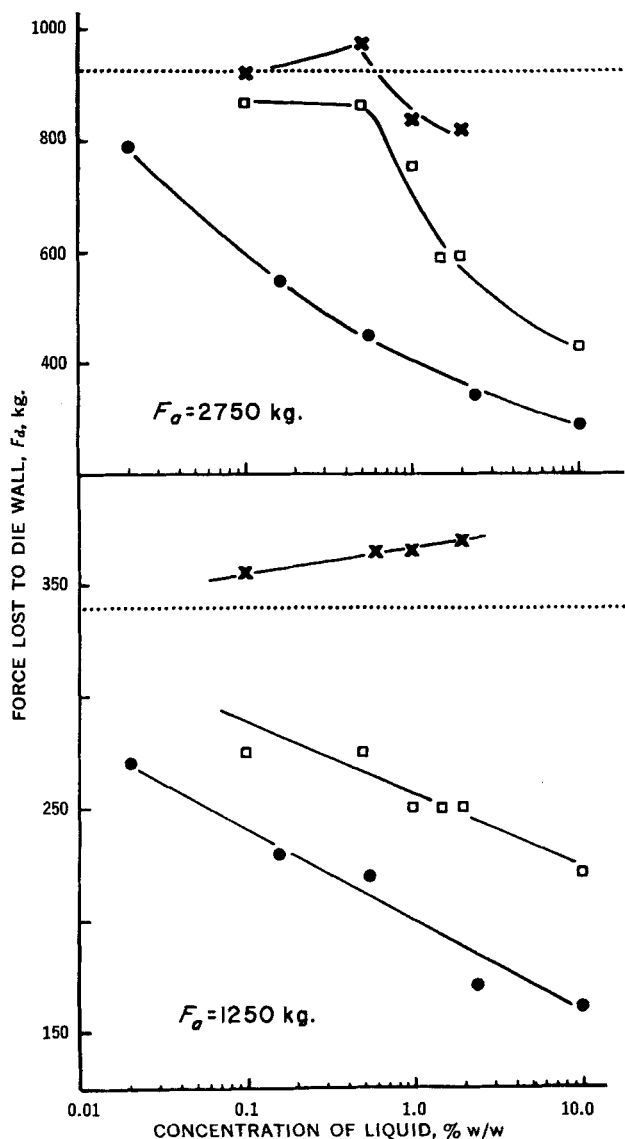


Figure 6—Effect of liquid concentration on the force lost to the die wall at high (2750 kg.) and low (1250 kg.) applied force. Liquids: moisture (●), light liquid paraffin (□), and decahydronaphthalene (×). Dotted line represents the value of F_d for dried material pressed in a conditioned die at each applied force.

Relative Volume of Compacts—Immediately after ejection, the dimensions of each compact were measured using a thickness gauge, and the weight was determined. These measurements, and the experimentally determined density of the crystalline material, were used to calculate the ratio of the observed volume of the compact to the volume of material present as a true solid.

RESULTS AND DISCUSSION

Figure 1 shows, for a series of moisture contents, the relation between the force lost to the die wall and the number of compacts pressed in a die at high and low applied force. Although 0.02% moisture reduced F_d , the fluctuating values showed that efficient lubrication could not be maintained during compaction at high pressure. Higher moisture contents further reduced F_d , and only small changes in the value of F_d occurred between the first and sixth compressions.

For material containing the same amount of water or light liquid paraffin, the values of F_d during the first compression at each pressure were almost equal (Figs. 2 and 3). However, during consecutive compressions with light liquid paraffin, the die wall force increased (Figs. 4 and 5); during the sixth compression with 0.1%

light liquid paraffin at high pressure, F_d was the same as for dried material pressed in a conditioned die (Fig. 2). There was little evidence of a die wall lubricant effect of decahydronaphthalene even during the first compression (Figs. 2 and 4).

Despite the low viscosity of moisture, there was less cumulative contamination of the die wall with compressed material than in the presence of the other liquids, as shown by the relation between F_d and the number of consecutive compressions. This finding may be attributed to a boundary lubricant effect of moisture, which supplements the hydrodynamic effect shown by light liquid paraffin and decahydronaphthalene. If the lubricant film breaks down and the shear strength of bonds between the die and the compressed material exceeds that of the material itself, contamination of the die wall occurs. A reduction in the adhesive forces at the die wall by a boundary effect of moisture reduces this effect.

Figure 6 summarizes the effect of liquid concentration. Each coordinate represents the mean value for six compressions. Although the replicate values of F_d increased to different extents (Figs. 4 and 5), the graphs clearly indicate differences in the behavior of the three liquids. In all cases, moisture produced the lowest force lost to the die wall; with an increasing moisture content, there was a continual decrease in F_d . It was suspected that the increases in F_d with decahydronaphthalene (Fig. 6) were due to interparticulate lubrication, which increased the radial component of the applied force as reported for other systems (1, 13, 14). Although this almost certainly occurred with moisture and light liquid paraffin, the values of F_d were consistently less than for dried material since these two liquids are more effective die wall lubricants than decahydronaphthalene.

At 2750 kg. of applied force, samples containing more than 0.5% light liquid paraffin or decahydronaphthalene showed a decrease in F_d (Fig. 6), which was associated with expression of liquid to the die wall. Determination of the residual liquid after compression also showed that a higher viscosity retarded the expression of liquid during consolidation. This result increases the interparticulate lubricant effect of light liquid paraffin and may contribute to the higher values of F_d than for moisture. Air enclosed by liquid in the voids increases the force transmitted radially to the die but also facilitates expression of liquid. Furthermore, liquid that occupies a large proportion of the void space offers a hydrodynamic resistance to consolidation of a compact.

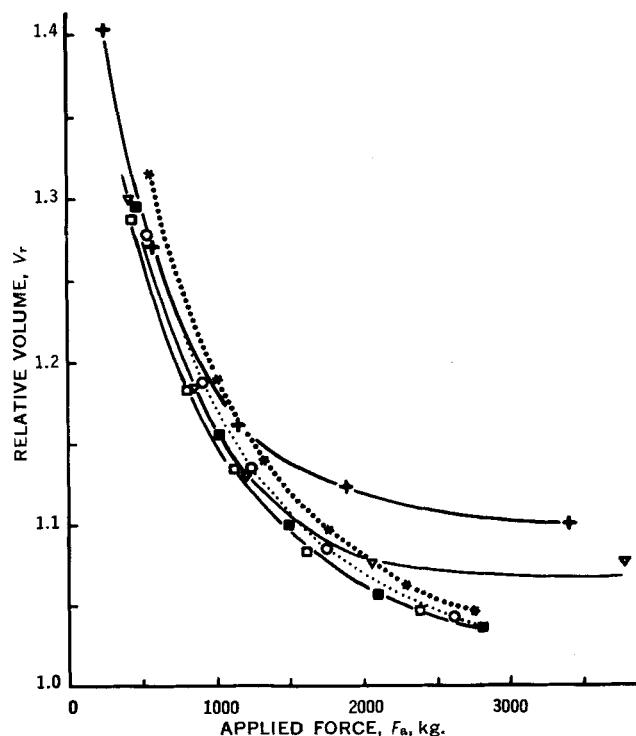


Figure 7—Effect of applied force on the consolidation of compacts containing moisture. Moisture content: 0.02% (···○···), 0.16% (■), 0.55% (□), 2.4% (▽), and 10% (+). Dried material in a conditioned die (·····).

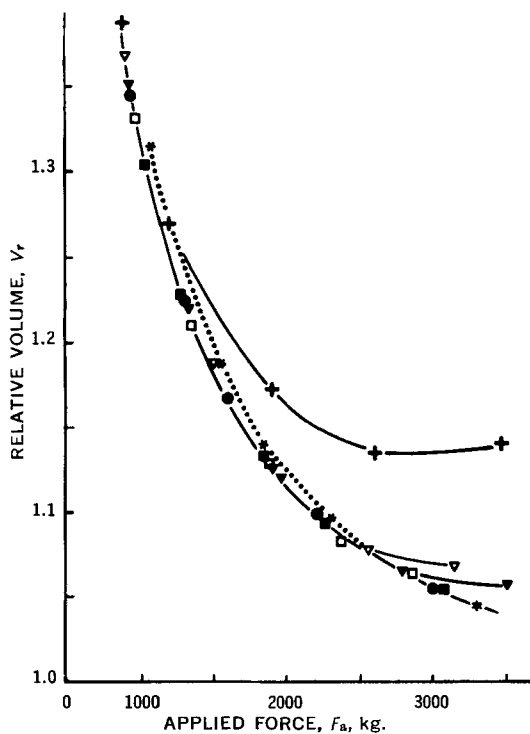


Figure 8—Effect of applied force on the consolidation of compacts containing light liquid paraffin. Liquid concentration: 0.1% (■), 0.5% (□), 1.0% (●), 1.5% (▼), 2.0% (▽), and 10% (+). Dried material in a conditioned die (·····).

Many of these conclusions are supported by the results shown in Figs. 7 and 8. Since moisture provided more effective lubrication, the results (Fig. 7) show clearly the effect of liquid concentration. Increasing the moisture content to 0.55% reduced the relative volume, but the hydrodynamic resistance to consolidation in the presence of 2.4 and 10% moisture reversed this trend, even at low applied pressure. The results for light liquid paraffin show similar effects (Fig. 8), but, in most cases, the relative volume was higher than with moisture. Negligible improvement in consolidation was observed with decahydronaphthalene at applied forces below 800 kg. At higher forces, the consolidation of material was restricted; above 2000 kg., a hydrodynamic resistance to consolidation was evident.

A small decrease in the thickness of a compact by a reduction in the compression weight from 982 to 928 mg. produced only small changes in the force lost to the die wall and the relative volume (15). Even 10% moisture dissolves less than 4% of the solid material, and lower concentrations have proportionately less effect. It was concluded that this effect of solvent action was negligible.

A reduction in particle size of about 60% from 30–40 to 60–80 mesh increased the force lost to the die wall and the relative volume of the compacts produced. However, since even with 10% moisture the reduction in mean linear dimension of particles will be only about 1%, size reduction by solvent action probably had no significant effect on the forces of compression or the relative volume of a compact.

Although moisture caused a rounding-off of many sodium chloride crystals due to preferential dissolution at the edges and corners, it is unlikely that this change in particle shape facilitated compaction. According to Lazarus and Lachman (16), rounded surfaces are characteristic of crystals of potassium chloride which cannot be readily compressed.

Huffine (17) considered that moisture increases the resistance to consolidation of particulate sodium chloride due to increases in the tensile strength and yield point of crystals when surface defects are removed by dissolution. However, there is some doubt

(18) whether this conclusion is valid, and the present results show no evidence of this effect.

SUMMARY AND CONCLUSIONS

1. Moisture, light liquid paraffin, and decahydronaphthalene produce several interrelated effects during compaction of particulate sodium chloride, including: (a) die wall lubrication, (b) interparticulate lubrication, (c) hydrodynamic resistance to consolidation, and (d) expression of interstitial liquid to the die wall.

2. Increases in force lost to the die wall, F_d , during consecutive compressions represent cumulative contamination of the die wall. This criterion may be used to assess the lubricant efficiency of materials.

3. In the presence of moisture, the force lost to the die wall and the increases in this parameter with consecutive compressions were appreciably less than with light liquid paraffin or decahydronaphthalene. It is concluded that moisture possesses boundary lubricant properties in addition to the hydrodynamic effects shown by light liquid paraffin.

4. There was no evidence of an optimum lubricant concentration of moisture or light liquid paraffin. However, concentrations of liquid exceeding 0.5% caused a hydrodynamic resistance to consolidation of compacts.

5. With more than 0.5% liquid, F_d decreased as liquid was expressed to the die wall from within a compact.

6. Decahydronaphthalene has a negligible die wall lubricant effect. High values of F_d were attributed to an increase in the radial component of applied force by interparticulate lubrication.

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