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COMPRESSIBILITY OF SALTS

Nicholas Lordi, and Prafull Shiromani*[x]

Department of Pharmaceutics
School of Pharmacy, Rutgers University
New Brunswick, New Jersey 08854

ABSTRACT

The mechanism of tablet compression of the chloride, bromide and iodide salts of sodium, potassium and ammonium was studied, by obtaining their force-displacement curves. The area under these curves, which represents the work done on the tableting mass during compaction, was calculated. The effect of duration of the compressive force, of applied pressure on tablet strength and of pressure on the relative volume for potassium bromide were also studied.

INTRODUCTION

The plotting of the displacement of the upper punch on the x-axis versus the force on the upper or lower punch on the y-axis, results in a force-displacement curve (F-D curve). Such curves have been used to illustrate the compression process qualitatively[1-4]. Compression curves of the bromide salts of sodium and potassium have been obtained[5]. It was found that pressures of 15,000 to 25,000 lbs. were necessary to form pharmaceutically acceptable tablets of these salts. A method was described for the registration and quantitative interpretation of force-displacement curves using a small digital computer[6]. Load-displacement

*Present address: Merck Sharp & Dohme, West Point, Pa. 19486

[x]To whom inquiries should be directed.

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curves for sodium chloride tablets have been obtained[7].

This report describes force-displacement curves as a tool to study the mechanism of tablet compression of directly compressible salts.

EXPERIMENTAL

Materials

Single lots of salts (Fisher Chemicals), magnesium stearate (Amend Drug) and polyethylene glycol 4000 (Ruger Chemicals) were selected for this investigation.

Incorporation of Lubricants

An approximately 250g sample of 30/40 mesh salt was dried in a hot air oven at 65°C for 24 hours. The dried salt was blended with screened lubricant. Mixing was carried out in a V-type blender (Paterson-Kelly) for fifteen minutes.

Compressibility of Salts

A 1.27 cm punch and die assembly was used to make the tablets on the hydraulic press attached to its motorized unit. This permitted the application of a consistent rate of compression and a constant maximum pressure for each salt tested. The force applied to the tablet during the test was continually monitored using a 4545 kg. load cell (Baldwin-Lima-Hamilton Corp.) attached to the upper platen of the hydraulic press. This cell was connected to a Daytronic Transducer Unit (Daytronic Corporation) which converted the mechanical output to an electrical one and was, in turn, connected to the "Y" axis input on a "X-Y" recorder (Electronic Associates, Inc.). This recorder eliminated the time or rate parameters and allowed the use of two active variables to be recorded simultaneously. The load cell was calibrated with respect to the Daytronic unit with the help of a universal testing machine. The calibration curve is presented in Figure 1. A displacement gauge (Calvin Laboratories) was used to compare the displacement of the salts during compression, and hence, to measure the

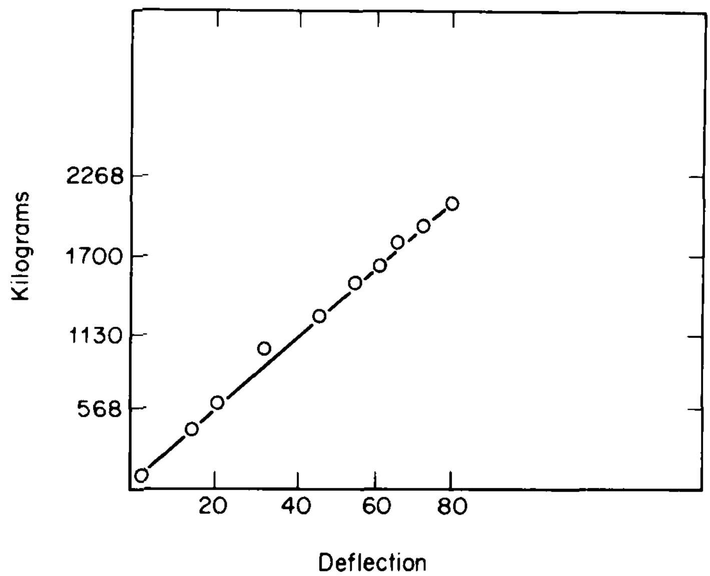

FIGURE 1

Calibration Curve for the Load Cell Range Selection of 1000 MicroInches/Inch on the Daytronic® Transducer Unit
®Daytronic Corporation, Dayton, Ohio

corresponding distance between the upper and lower platens of the hydraulic press. The displacement transducer was set so that the maximum displacement occurred when the two punches were in contact, hence zero thickness. The arrangement of the transducers is shown diagramatically in Figure 2.

The maximum pressure setting on the hydraulic pump of the hydraulic press was set at 2272 kg. The weight of each compact was kept fairly consistent. The thickness of the compact, before and after compression, was measured using a micrometer. With a constant rate of compression, constant weight of the tablet, constant maximum pressure, and constant settings on the transducer unit and recorder, all variability was eliminated.

The above experiment was repeated on the salts mixed with the lubricants, polyethylene glycol 4000 and stearic acid, respectively.

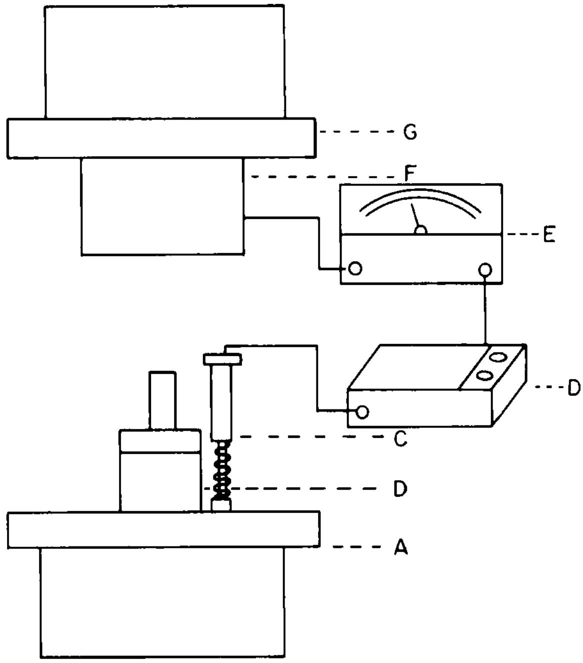

FIGURE 2

Schematic Diagram Showing Different Parts of Compression Study Equipment

Key:
A = Lower Stage of the Hydraulic Press
B = Punch and Die Assembly
C = Displacement Transducer
D = X-Y Recorder
E = Amplifier
F = Load Cell
G = Upper Stage of the Hydraulic Press

Compressibility Study of Potassium Bromide

In order to determine the effect of weight on the force-displacement (F-D) curve, the above experiment was repeated using three different weights of potassium bromide.

The above experiment set up was also employed to ascertain the effect of different compaction pressures and different dwell times within the die on the strength of potassium bromide compacts. The range of pressures employed was from 318 kg. to 4363 kg. The dwell times ranged from 1/2 minute to 30 minutes.

RESULTS AND DISCUSSION

Compressibility Studies on Salts

In order to study the compression characteristics of sodium, potassium and ammonium halides, equal weights of the salts were compressed at the same pressure on the hydraulic press. Applied force and displacement measurements were continuously monitored and have been used to generate what is referred to as F versus D curves. The area under such curves represents the work done on the tableting mass during compaction. The experimental data was normalized. For measurements whose distributions are not normal, a simple transformation of the scale may induce normality. Therefore, by normalizing the data, a single variable, viz. the response of the salts to the test, can be studied without interference from other variables.

Figure 3 shows the normalized curves plotted as force versus relative density, where relative density is apparent tablet density/material density. Studies of bonding in sodium and potassium chloride suggest that consolidation occurs primarily by plastic flow[8] with little evidence of fracture and fragmentation.

The hardness of the compacts and the area under the F-D curves is presented in Table 1. The hardness was measured after application of the maximum force. A larger area under the F-D curve implies more work to be done on the material during compaction and hence a decreased cohesiveness of the material, which should be manifested as a lower compact hardness value. This relationship is more pronounced for the sodium salt.

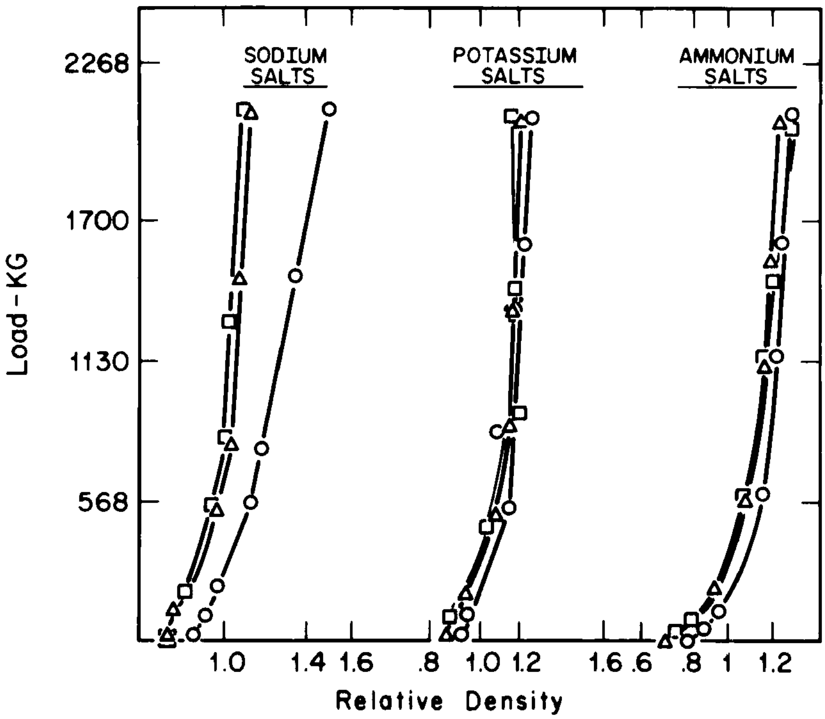

FIGURE 3

Load Versus Relative Density Curves for Pure Salts

Key: ○ - Chloride Salt

△ - Bromide Salt

□ - Iodide Salt

TABLE 1

The Hardness of Salt Compacts and the Area under the F-D Curves

Salt	Area Under the F-D Curve (cm^2)	Hardness (kg)
Sodium chloride	22.35	1.78
Sodium bromide	11.23	5.79
Sodium iodide	10.49	5.27
Potassium chloride	7.82	2.57
Potassium bromide	6.61	3.20
Potassium iodide	7.47	2.96
Ammonium chloride	9.27	7.38
Ammonium bromide	11.62	3.97
Ammonium iodide	13.59	3.89

Figures 4 and 5 represent the corresponding normalized F-D curves for the salts mixed with the lubricants polyethylene glycol and stearic acid, respectively. The area under the curve and the hardness is presented in Table 2.

Tablet lubricants act by interposing a film of low sheer strength at the interface between the die-wall and the compact, thus reducing the friction force. Accordingly, the work to be done on the tableting mass during compaction is reduced. This is specifically indicated by the lower values for the area under the curve in the case of sodium chloride blended with lubricants when compared with the corresponding area for the pure salt.

The lubricants reduce the strength of salts. This effect is more pronounced with the hydrophobic lubricant, stearic acid than with polyethylene glycol. The

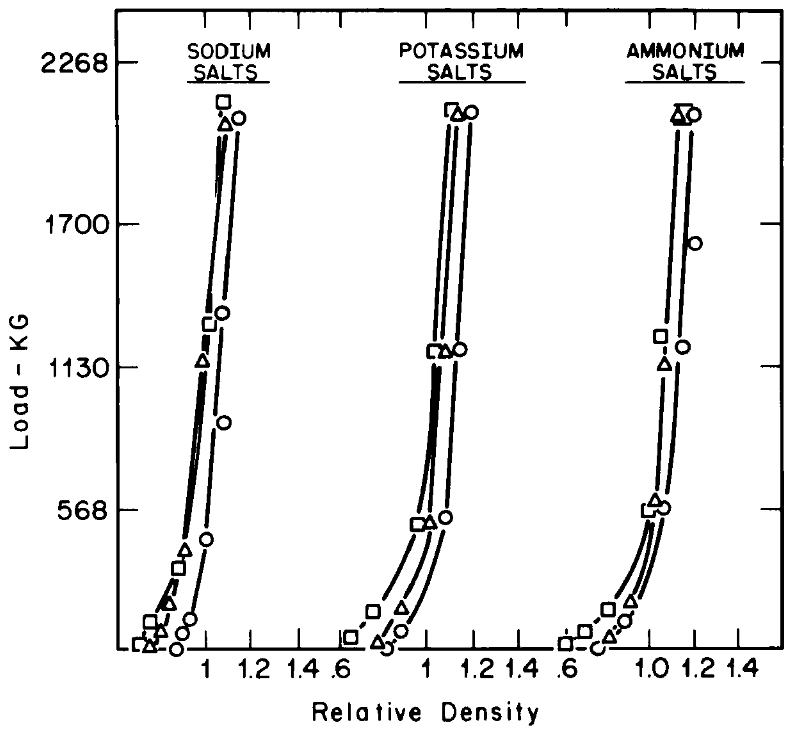

FIGURE 4

Load Versus Relative Density Curves for Salts Mixed with Polyethylene Glycol

Key: ○ - Chloride Salt

△ - Bromide Salt

□ - Iodide Salt

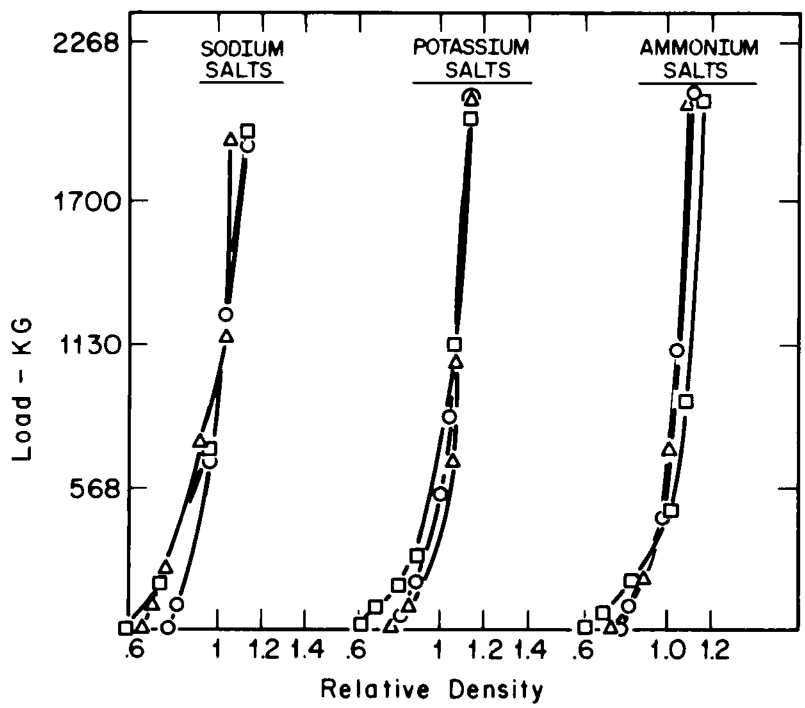

FIGURE 5

Load Versus Relative Density Curves for Salts Mixed with Stearic Acid

Key: ○ - Chloride Salt

△ - Bromide Salt

□ - Iodide Salt

TABLE 2

The Hardness of Salt Compacts Mixed with Lubricants and the Area under the F-D Curves

	0.3% Polyethylene Glycol 4000		0.3% Stearic Acid	
Salt	Area Under The Curve (cm^2)	Hardness (kg)	Area Under The Curve (cm^2)	Hardness (kg)
Sodium chloride	7.52	0.92	9.78	0.13
Sodium bromide	9.68	5.27	10.14	5.27
Sodium iodide	9.59	5.01	13.28	4.61
Potassium chloride	8.54	0.46	8.42	0.13
Potassium bromide	8.56	1.49	8.24	1.45
Potassium iodide	9.69	1.84	9.96	1.64
Ammonium chloride	8.31	5.01	7.11	3.82
Ammonium bromide	7.01	1.25	5.80	1.19
Ammonium iodide	10.64	2.88	9.70	2.89

lubricants coat the crystals and thereby increase the distance between neighboring crystals. These separations reduce the molecular forces of attraction, namely the van der Waals forces. Polyethylene glycol provides some bonding by forming a bridge between two crystals.

Compression Studies on Potassium Bromide

A. Effect of Weight

In order to evaluate the effect of weight on the F-D curve, different weights of potassium bromide were compressed at the same pressure on the hydraulic press. The F-D curves are presented in Figure 6. Within the limits of accuracy of the displacement transducer, the curves superimpose on each other. This implies that a similarity in structure exists within the different sizes of tablets. Newton and Rowley[9] arrived at the same conclusions on compacting different weights of lactose or dextrose in the same diameter die.

B. Effect of Duration of the Compressive Force

Since plastic deformation is time-dependent, one parameter in tablet compaction is the time for which the material is held under load. The more plastic the material, the more likely it is to form a compact. Figure 7 shows the effect of duration of the compressive force on strength of compacts prepared on the hydraulic press.

Increasing the duration of the maximum force resulted in greater tablet strengths. When the same material was compressed on the single punch machine where the dwell time is about one second, the initial compact hardness was found to be around 2 kg. Since plastic flow is an important factor affecting the compressibility of this salt, a prolongation of the dwell or contact time would be expected to increase the strength of these tablets, as more surface contact for interparticulate bonding would be produced through plastic flow. Sagawa et al.[10] studied the relation of dwelling time with hardness of sodium chloride

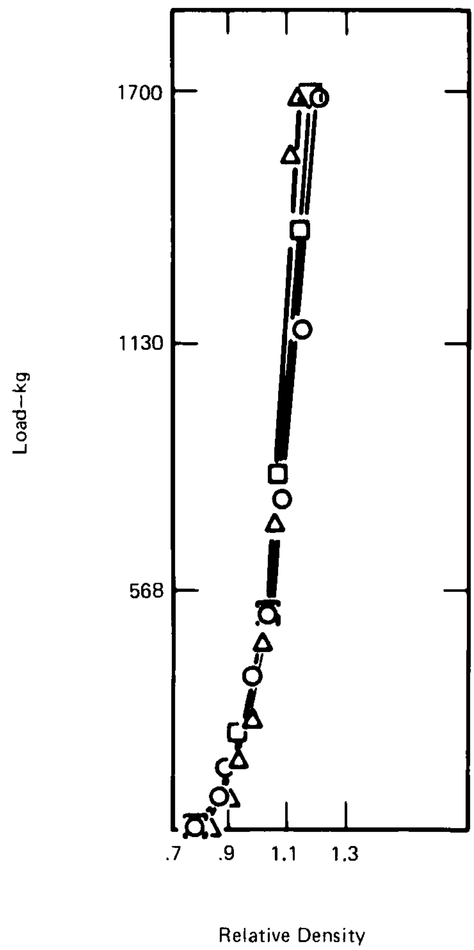

FIGURE 6

Load Versus Relative Density Curves for Different Weights of Potassium Bromide

Key: △ - 0.75 g

□ - 1.00 g

○ - 1.50 g

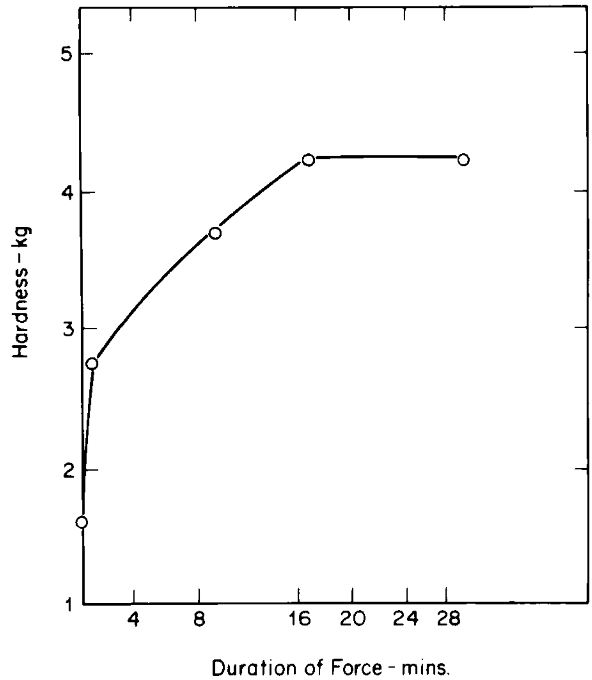

FIGURE 7

Hardness Versus Duration of Compressive Force for Potassium Bromide

tablets. They found that the hardness increased with increasing dwell times. They concluded that increasing the dwell time increased the stress relief of the compressed powder particles, decreased the strain reduction in the tablet and increased the tablet hardness.

After 15 minutes, maximum bonding and hence strength was attained.

C. Effect of Applied Pressure on Tablet Strength

The relationship between tablet tensile strength and compaction force is non-linear. The shape of the curve shown in Figure 8 is probably indicative of the different ways in which the work of compaction is utilized at various stages of tablet formation. Rees and Rue[11] obtained a similar shaped curve for sodium chloride.

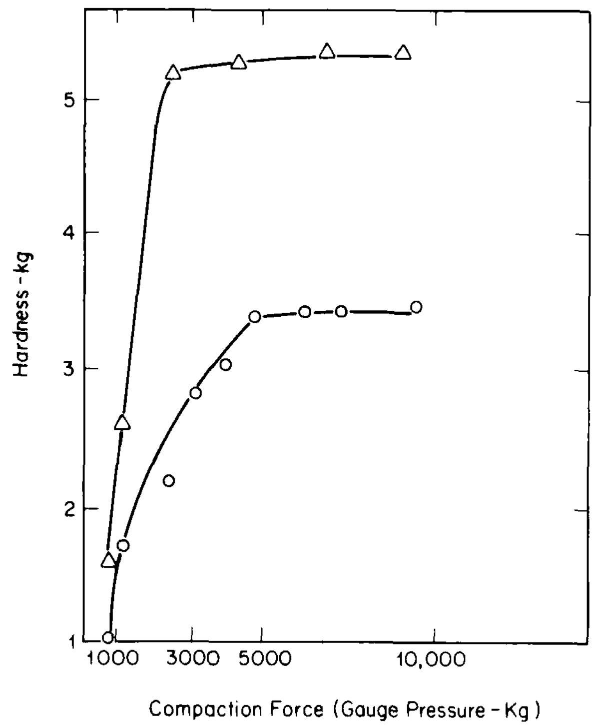

FIGURE 8

Hardness Versus Compaction Force for Potassium Bromide

Key: O - Compacts tested immediately

△ - Compacts tested after one day storage at 47% relative humidity

The first stage in the compaction process involves rearrangement and closer packing of particles, work being done to overcome particle-particle and particle-die wall friction. As compaction continues, elastic and plastic deformation of the particles takes place; this increases the area of interparticulate contact which must be associated with bond formation. The tensile strength of the material correspondingly increases, as seen in stage AB. During stage BC the slope starts to decrease, indicating that more work has to be done to produce an equivalent increase in the area of surface contact. Eventually a state of

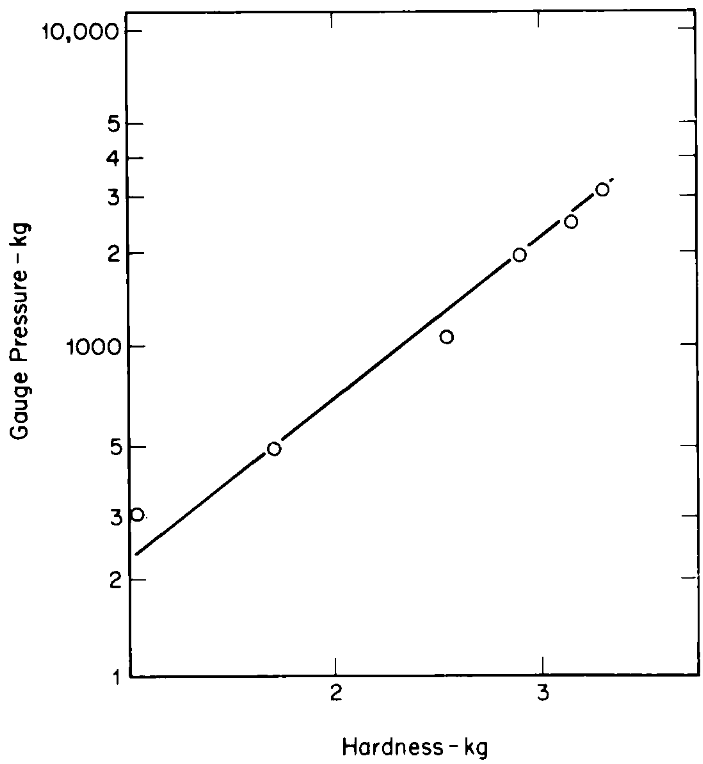

FIGURE 9

Hardness Versus Logarithm of Applied Force for Potassium Bromide

maximum consolidation is approached, represented by stage CD, where the gradient of the curve decreases more rapidly, showing a smaller rise in tensile strength with compaction force. The same trend is followed by compacts stored for one day at 47% relative humidity. The compact strength, however, has increased.

Figure 9 shows that the strength of the tablet can be directly related to the logarithm of the force applied. A linear regression analysis was carried out on the data which yielded a correlation coefficient of 0.9787, thereby confirming the validity of this relationship. Shotton and Ganderton[12] found such a relationship to hold true for sodium chloride crystals. They developed the

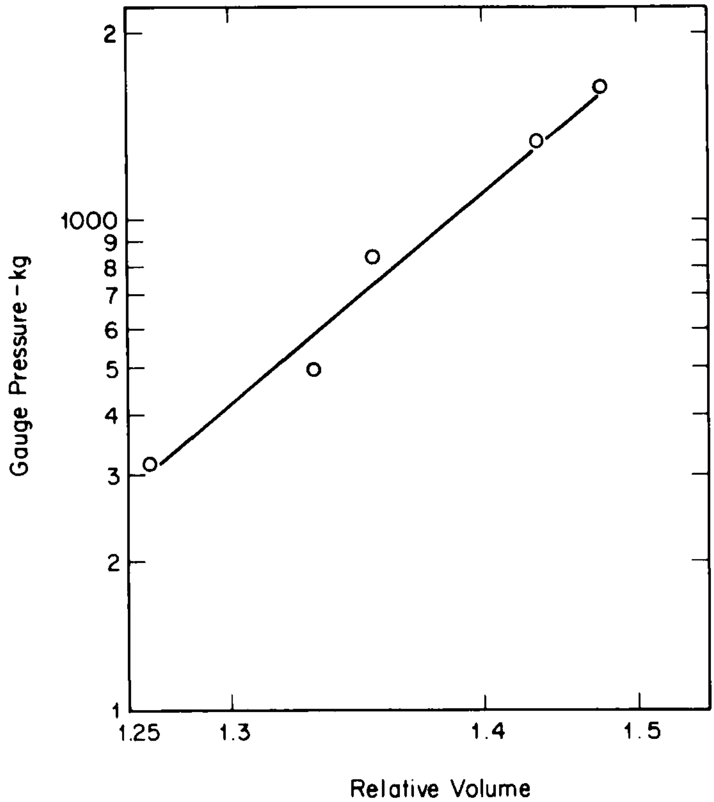

FIGURE 10

Relative Volume Versus Logarithm of Applied Force of Potassium Bromide

following equation to relate the strength of the tablet Fc to the applied force P:

$$\log P = nFc + C \qquad \text{(Eq. 1)}$$

where n and C are constants depending on the substance used. Extrapolating this plot will give a value of C, which probably represents the minimal pressure for the formation of a tablet. The value of C for potassium bromide is about 250 kg. gauge pressure.

D. Effect of Pressure on the Relative Volume

The strength of the compact depends on the area of bonding within the mass, which may be considered the effective load bearing area, and this is related to the relative volume, Vr, or the porosity, e. The relative volume of the compact is calculated from the distance the punch moves into the die at each pressure.

$$Vr = \frac{L}{Lo} \qquad \text{(Eq. 2)}$$

Where,

L = Observed length of compact

Lo = Length of compact at zero voidage

The relative volume and porosity of the compact are related as:

$$e = 1 - \frac{1}{Vr} \qquad \text{(Eq. 3)}$$

Walker[13] expressed a relationship between the relative volume and the pressure for the consolidation of sodium and ammonium chlorides.

$$Vr = C - K \log Pa \qquad \text{(Eq. 4)}$$

Where C and K are constants.

Figure 10 shows that the above relation between the relative volume and the logarithm of the applied pressure for potassium bromide is satisfied. A linear regression analysis was carried out on the data which yielded a correlation coefficient of 0.9633, thereby confirming the validity of the relationship for the compression of potassium bromide.

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