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RELATIONSHIP BETWEEN COMPRESSION PROFILE AND PHYSICAL PROPERTIES OF LITHIUM CARBONATE FORMULATION

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ABSTRACT

Relationship between the compression profile and physical properties of a directly compressed lithium carbonate tablet formulation was examined using an instrumented tablet press. The measured physical parameters included hardness, disintegration time, and dissolution. A linear correlation was observed between the compression force, 4000 to 7020 lbs. and tablet hardness, 5 to 9 Kp. The disintegration time, 80 to 100 seconds, did not significantly change with the increasing compression force. Dissolution of lithium carbonate tablets complied with the USP limits at all compression forces. A dissolution rate maximum related to compression force was

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observed. The overall results indicate that the processing parameter, compression force, affects the physical properties of the tablet formulation.

INTRODUCTION

The compression force is one of the critical physical factors which affects the dissolution and disintegration time and hardness of tablet dosage form (1-8). Several investigators (9) have examined methods to study relationship between the applied compression force and tablet properties. The purpose of this investigation was to characterize a relationship between the compression force and physical properties of a directly compressed lithium carbonate formulation. Once the correlation is established, the compression force measurement can be used to monitor the physical properties such as hardness and dissolution of the active drug.

MATERIALS

A directly compressed lithium carbonate formulation included the following ingredients: lithium carbonate USP, corn starch USP, calcium phosphate dibasic USP, polyethylene glycol USP, magnesium stearate USP, and sodium lauryl sulfate USP.

METHODS

Two kilograms of direct compressible blend was prepared by mixing 60% of the formula lithium carbonate, corn starch, calcium phosphate, dibasic; and polyethylene glycol in a laboratory V-blender for 20 minutes. A

sufficient quantity of lubricant mix containing the remaining materials was added and the mixing was continued for an additional 10 minutes.

The particle size of the blend was determined using a sieve analysis, bulk and tapped densities were measured using a JEL apparatus[1]. The blend was compressed using a rotary tablet press with a standard round tooling of 3/8 inch diameter and the compression force was measured using strain guages[2] and a high speed analog recorder[3].

The physical properties of tablets were determined as follows: tablet hardness was measured with a Schleuniger[4] hardness tester and disintegration[5] and dissolution[6] tests were performed according to the USP procedures. Lithium carbonate analysis was performed using an atomic absorption[7] spectrophotometric analysis and products complied with all USP requirements.

RESULTS AND DISCUSSION

Table 1 shows the physical properties of the major ingredients of the formulation. The percentage compressibility was computed as follows:

$$\% \text{ compressibility} = \frac{Dt - Db}{Dt}$$

where: Dt = tapped density

Db = bulk density

1 J. Engelsmann, AB., Ludwigshafen, West Germany.
2 Manesty B3B tablet press, Manesty Machine Ltd., Liverpool, England.
3 Gould 2200 Recorder, Gould Inc., Cleveland, OH USA.
4 Schleuniger Hardness Tester, Vector Corp., Marion, IA USA.
5 Tablet Disintegration Tester, Van Kel Industries, Chatham, NJ USA.
6 Dissolution Apparatus, Hanson Research Corporation, Northidge, CA USA
7 Instrumentation Laboratory AA Spectrophotometer, Instrumentation Laboratory, Inc., Lexington, MA USA.

Table 1: Physical properties of ingredients

	bulk density gm/cm^3	tapped density gm/cm^3	% compressibility
Lithium carbonate	0.53	0.80	34
Dicalcium phosphate	0.92	1.47	37
Corn starch	0.59	0.78	24
Formulation blend	0.63	0.90	30

Lithium carbonate, which showed poor flow properties represented 60% w/w of the formulation. The three ingredients listed in Table 1 accounted for more than 95% w/w of the granulation. The particle size distribution of the different ingredients used in this formulation is shown in Figure 1. Lithium carbonate exists as a very fine powder with 90% w/w less than 44 microns. The plot also shows that the final blend exhibited a poor particle size distribution with 90% w/w of the blend containing particles less than 74 microns.

A typical compression profile of the lithium carbonate formulation is shown in Figure 2. The highest peak represents the maximum compression force developed during tableting. In this study, the maximum compression force varied from 4000 to 7020 lbs. Below 4000 lbs compression force, the tablet friability exceeded a 1% limit and above 7020 lbs, tablet capping was observed.

Relationship between compression force and hardness of lithium carbonate tablets is represented in Figure 3. The results show that the compression force exhibits a linear relationship with hardness (r^2 >0.99), leading to an acceptable product in terms of compressibility. The compression force and hardness ranges are adequate for incorporating these values in scale up manufacturing of the product.

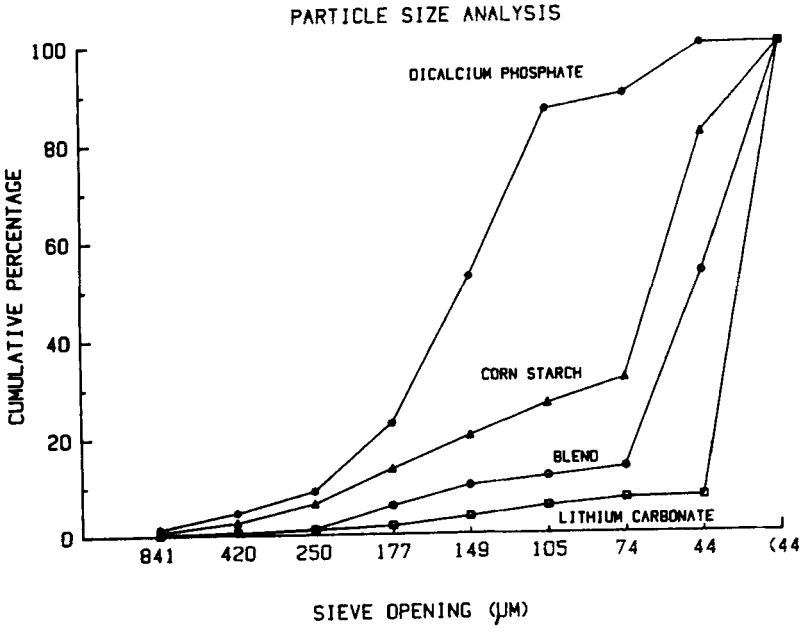

Figure 1: Particle size analysis.

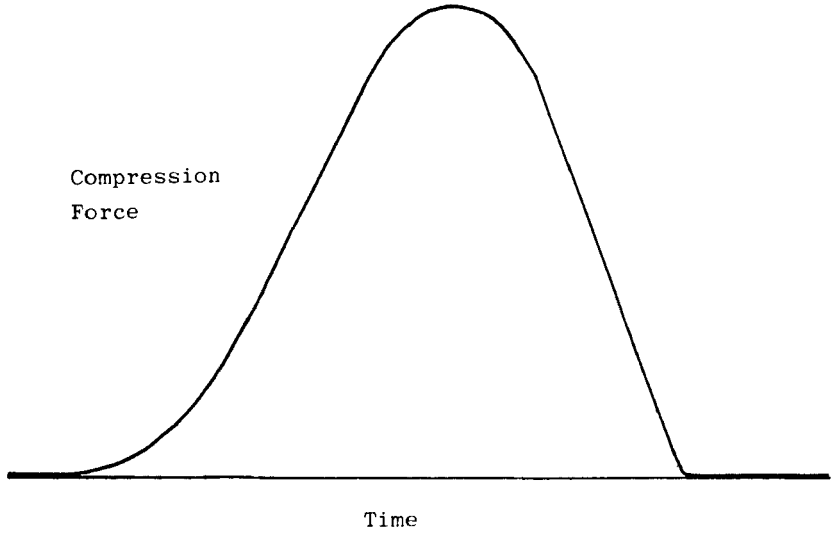

Figure 2: Analog recording from the instrumented press.

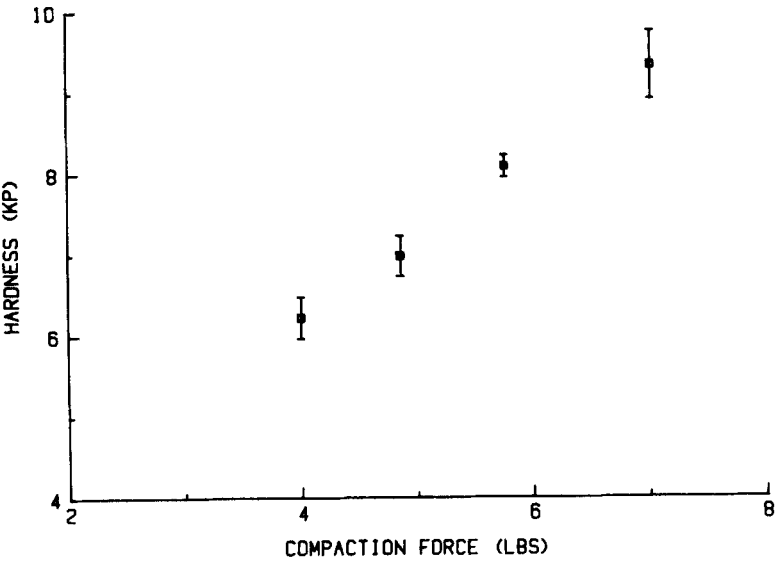

Figure 3: Relationship between and hardness of lithium carbonate tablets.

Disintegration time was measured using the USP procedure. All tablets disintegrated within a time range from 80 to 100 seconds. No significant differences were observed in the disintegration time from one compression force to another.

Dissolution of lithium carbonate tablets was examined using the USP XXI basket procedure. The dissolution profiles at different compression forces are shown in Figure 4. This formulation exhibits the dissolution compression force relationship in which the initial dissolution at 15 minutes is faster to a maximum as the compression force is increased and then further increases in the compression force slow the initial dissolution of lithium carbonate. These results correlate extremely well with those obtained by Smith et. al (6) on dissolution of tablets prepared by a wet granulation of lithium carbonate. These investigators studied the dissolution at 20 minutes and tablet hardness relationship of a lithium carbonate formulation containing lithium carbonate, lactose,

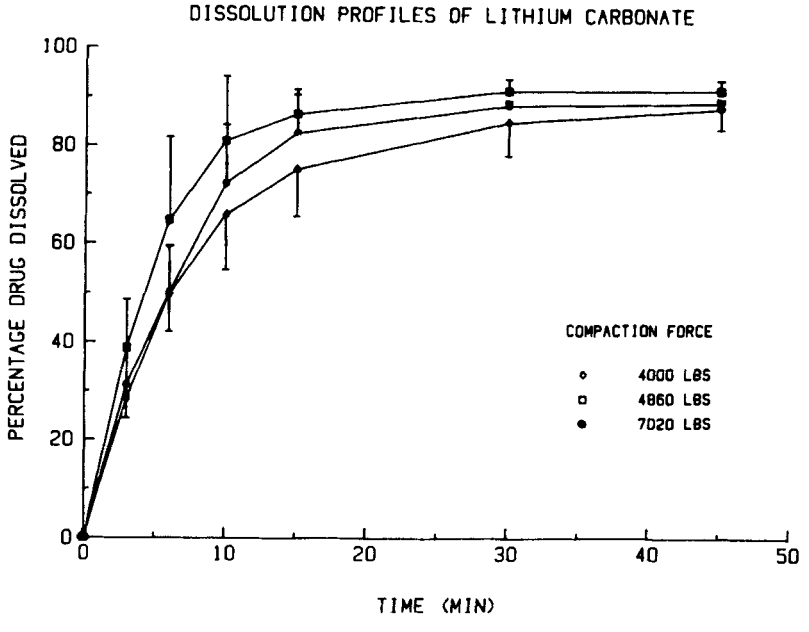

Figure 4: Dissolution profiles of lithium carbonate.

cornstarch and magnesium stearate. In their study, the tablet hardness was increased using higher compression force. The dissolution at 20 minutes showed two maxima as the hardness of the tablets were increased.

Levy et. al (5) showed that the initial dissolution rates of salicylic acid tablets increased when the tableting compression force was increased. This increase in dissolution of salicylic acid was attributed to fracturing of the drug particles at higher force yielding smaller particles with increased surface area. In case of the directly compressed lithium carbonate, initial increase in the compress force probably results to fracture of lithium carbonate and

subsequent increase in the compression force leads to bonding and or the fusion. The fracture and bonding mechanism is postulated to increase and decrease the apparent surface area of lithium carbonate. This increase or decrease, therefore, enhances or retards the initial dissolution flux of

lithium carbonate. The thermodynamic solubility governing mechanism, independent of the surface area, controls the amount of drug dissolved after 45 minutes as indicated by a constant plateau value. It is possible that such fracture and bonding of lithium carbonate can yield a dissolution rate maximum.

CONCLUSION

Results of this study show that the compression force is directly correlated to the hardness of lithium carbonate tablets. The results of initial dissolution rate show a maximum when the compression force is increased. It is suggested that the dissolution behavior is caused by the fracture and bonding of lithium carbonate. The method described in correlating the compression force with physical properties provides a process monitoring procedure for lithium carbonate tablets.

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