lowing ATCC test organisms were used to test dimethyl sulfoxide for bacterio- and fungistasis: *Bacillus subtilis* (6633), *Staphylococcus aureus* (6538), *Candida albicans* (10231), *Pseudomonas aeruginosa* (9027), *Clostridium perfringens* (11437), and *Aspergillus niger* (16404).

Six sets of four tubes each, containing 100 ml of fat emulsion[3], were prepared. Each tube was inoculated with 1 ml of a test organism suspension. Dimethyl sulfoxide (25 ml) was added to two tubes per set, and 50 ml to the remaining two tubes. All tubes were vigorously stirred for 30 sec using a vortex mixer. The mixtures were membrane-filtered using a 0.4-μm polyester membrane[2]. The membranes were washed with 200 ml of fluid A (1) and 100 ml of fluid D (1) and then cut into two sections. One section was transferred to fluid thioglycolate and the other to soybean casein digest broth. The fluid thioglycolate was incubated at 33 ± 2° and soybean casein digest broth at 23 ± 2°, both for 7 days (1).

D Value Determination—D values were determined using *B. subtilis* and *C. albicans*. *C. albicans* was used because the results of the bacteriostatic and fungistatic test showed that it was more sensitive to dimethyl sulfoxide at concentrations of 33%.

Spore stock suspensions containing ~10^9 *B. subtilis* organisms/ml of water were used for inoculum.

Cultures of *C. albicans* were grown in 13 × 100-mm trypticase soy agar slants at 37 ± 2° for 72 hr. The slants were washed with 2 ml of phosphate buffer to a final concentration of 10^9 organisms/ml.

Six 25-ml aliquots of a 10% fat emulsion were transferred to separate glass screw-capped test tubes. Three of the tubes were each inoculated with 0.1 ml of a spore stock suspension of *B. subtilis* and the other three tubes with *C. albicans*. The contents of the tubes were vigorously stirred using a vortex mixer, and 6.25 ml of dimethyl sulfoxide was added to each tube. The tubes were stirred as before, and 5-ml aliquots were taken at 0, 15, 30, 45, and 60 min. Each aliquot was filtered through a 0.4-μm polyester membrane. The membranes were washed with 100 ml of fluid A and transferred to 38 × 200-mm test tubes containing 100 ml of fluid A. The tubes were ultrasonicated for 6 min at 55 kHz and dilutions plated using trypticase soy agar. The plates were incubated at 35 ± 2° for 48 hr.

RESULTS

The results show that 20% dimethyl sulfoxide was not bacteriostatic or fungistatic to the test organisms used in this study. The growth rate of the sample was comparable to that of the control samples. A concentration of 33% dimethyl sulfoxide showed some fungistasis only against *C. albicans* after 7 days incubation at 23 ± 2°.

When 20% dimethyl sulfoxide was used, the D values of *B. subtilis* and *C. albicans* were >60 min.

The polyester membrane had good filtration rates, taking ~4 min to filter dimethyl sulfoxide and the emulsion. No problem was noted in the rinsing of the membrane with fluids A and D. Other membranes tested, such as acetate cellulose, pyroxylin, mixed esters of cellulose, and mixed cellulose acetate pyroxylin, were either dissolved by dimethyl sulfoxide or the pores were plugged by the fat emulsion.

In contrast to the direct inoculation of a product, the entire product could be analyzed in this membrane filtration method, with no problem of the media showing turbidity upon inoculation. The use of dimethyl sulfoxide as a solvent and of polyester membrane filters for the filtration of the product and rinsing fluids provided a rapid method of analysis. Since dimethyl sulfoxide showed no bacteriostasis or fungistasis and the analysis time was short, the probability of obtaining a better bacterial recovery is greatly increased by using the described method.

REFERENCES

(1) "The United States Pharmacopeia," 20th rev., U.S. Pharmacopeial Convention, Inc., Rockville, Md., 1980, pp. 873–882.

(2) L. B. Quesnel, B. L. Scott, and J. L. Taylor, in "Spore Research," J. Wolf, Ed., Academic, New York, N.Y., 1971, pp. 303–314.

(3) D. A. Cotter, J. W. Morin, and R. W. O'Connell, *Arch. Microbiol.*, **108**, 93 (1976).

(4) J. P. Widdowson, *Nature*, **214**, 812 (1967).

(5) A. W. Kotula, M. D. Pierson, B. S. Emswiler, and J. R. Guilfoyle, *Appl. Environ. Microbiol.*, **38**, 789 (1979).

(6) C. O. Yehle and R. H. Doi, *Can. J. Microbiol.*, **11**, 745 (1965).

(7) C. E. Huggins, *Transfusion*, **3**, 483 (1963).

(8) T. Nash, *Nature*, **4898**, 1113 (1963).

(9) G. S. Kalesperis, K. V. Prahlad, and D. L. Lynch, *Can. J. Microbiol.*, **21**, 213 (1975).

(10) V. L. Miller and A. C. Jerstad, *J. Med. Chem.*, **9**, 208 (1966).

(11) A. M. Kligman, *J. Am. Med. Assoc.*, **193**, 923 (1965).

(12) S. W. Jacob, M. Bischel, and R. J. Herschler, *Curr. Ther. Res.*, **6**, 134 (1964).

(13) D. C. Wood and J. Woo, *Ann. N.Y. Acad. Sci.*, **243**, 7 (1975).

(14) G. E. Pottz, J. H. Rampey, and F. J. Benjamin, *ibid.*, **141**, 261 (1967).

(15) F. B. Seibert, F. K. Farrelly, and C. C. Sheperd, *ibid.*, **141**, 175 (1967).

(16) H. Basch and H. H. Gadebusch, *Appl. Microbiol.*, **16**, 1953 (1968).

Tensile Strengths and Hardness of Tablets

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Abstract □ The axial and radial tensile strengths were compared to the hardness of compressed tablets containing various concentrations of lubricants. Since radial tensile strength measurement considers the thickness of a tablet, and only tensile stress and axial tensile strength express the strength in the direction in which capping may occur, the tensile strengths characterize the strength of a tablet more completely than hardness.

Keyphrases □ Tensile strength—axial and radial tensile strengths compared to the hardness of compressed tablets □ Tablets—axial and radial tensile strengths compared to the hardness of compressed tablets

Although the strength of pharmaceutical tablets, which must be sufficient to withstand handling and shipment, may be expressed in a variety of ways, hardness (the force which, when applied diametrically to the tablet, causes fracture) has been the most common expression of strength. Studies of various hardness testers have shown the variations in fracture strength to be due to inaccuracies of instrumental scale values, zero errors, variations in the method of application of the load, physical dimensions, and shape of the tablet (1–4).

Although hardness has been a convenient and useful parameter for in-process control and quality assurance, it

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Table I—Hardness of Dibasic Calcium Phosphate Dihydrate with Various Concentrations of Magnesium Stearate Compressed at 1134 kg

	Magnesium Stearate, %						
	0.0	0.075	0.125	0.25	0.5	1.0	2.0
F_c, kp	9.4 N[a]	9.7 T[b]	9.7 N	9.9 T	8.4 N	8.1 T	9.6 N
	8.9 N	7.0 T	7.8 T	10.4 T	8.1 N	9.4 T	10.1 N
	9.4 N	9.3 N	9.6 N	9.7 T	8.5 T	8.9 N	10.6 T
	9.8 N	8.8 T	7.7 T	9.7 N	7.4 N	9.5 N	9.7 N
	8.9 T	7.3 T	9.0 N	9.4 N	8.4 N	9.4 N	9.5 N
	8.0 T	8.8 N	9.4 N	9.4 N	8.1 N	10.6 N	10.6 N
	9.9 T	7.5 N	9.4 N	8.5 T	8.7 N	8.9 T	9.8 N
	9.7 T	9.8 T	9.3 N	9.7 N	8.4 T	9.2 N	9.5 T
	8.7 T	10.2 T	8.9 N	9.9 N	8.9 N	9.6 N	9.4 N
	9.2 N	8.0 T	8.7 N	9.9 T		8.0 T	9.7 N
$\bar{X}$, kp	9.2	8.6	8.9	9.7	8.3	9.2	9.8
s, kp	0.6	1.1	0.7	0.5	0.4	0.8	0.4
CI[c]	0.4	0.8	0.5	0.3	0.3	0.6	0.3

[a] Nontension failure. [b] Tension failure. [c] Confidence interval at 95% probability.

is an empirical property. Tensile strength is a property of the compressed material, and it is a basic parameter which maintains consistency of property if the size of the tablet is changed (5). In an earlier report (6), the values of axial and radial tensile strengths were reported to present a directional appreciation of the strength of tablets. The purpose of the present report is to suggest that the evaluation of the axial and radial tensile strengths will characterize the strength of a tablet with more validity than hardness.

EXPERIMENTAL

The preparation of tablets and the method of measurement of the axial and radical tensile strengths of tablets by a tensiometer[1] have been reported previously (6). Tablet hardness was measured by diametral compression using a motor-driven hardness tester[2]. The maximum of the scale was 20 kp. Typical data are given in Table I. The mean hardness and the standard deviations plotted in the figures represent data for 10 tablets.

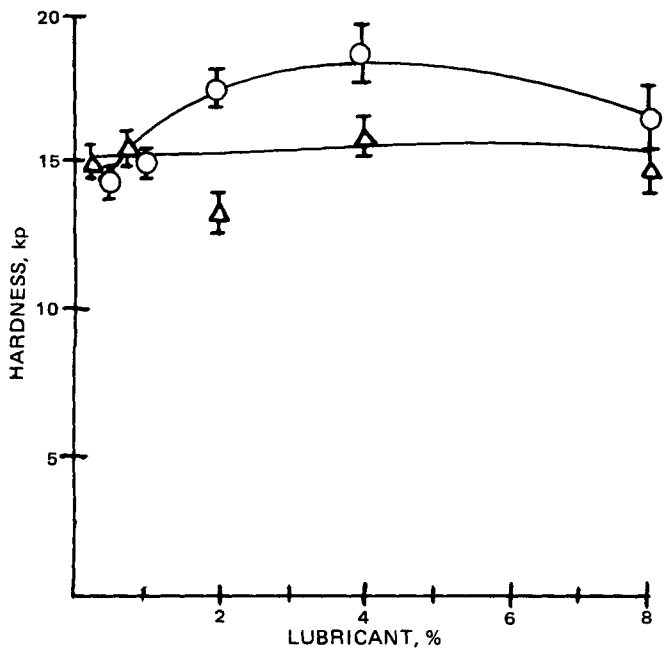

Figure 1—*The influence of the concentration of lubricant on the hardness of dibasic calcium phosphate dihydrate compressed at 2268 kg. Key: (○) hydrogenated vegetable oil; and (△) stearic acid.*

RESULTS AND DISCUSSION

Dibasic calcium phosphate dihydrate[3] and various concentrations of hydrogenated vegetable oil[4] and stearic acid were compressed at 2268 kg of force into flat-faced tablets with a 1.27-cm diameter. The hardness of the tablets was measured and plotted against the concentration of lubricant in Fig. 1. Based on the hardness values obtained by diametral compression, it is concluded that the addition of stearic acid to dibasic calcium phosphate dihydrate has no significant effect on the strength

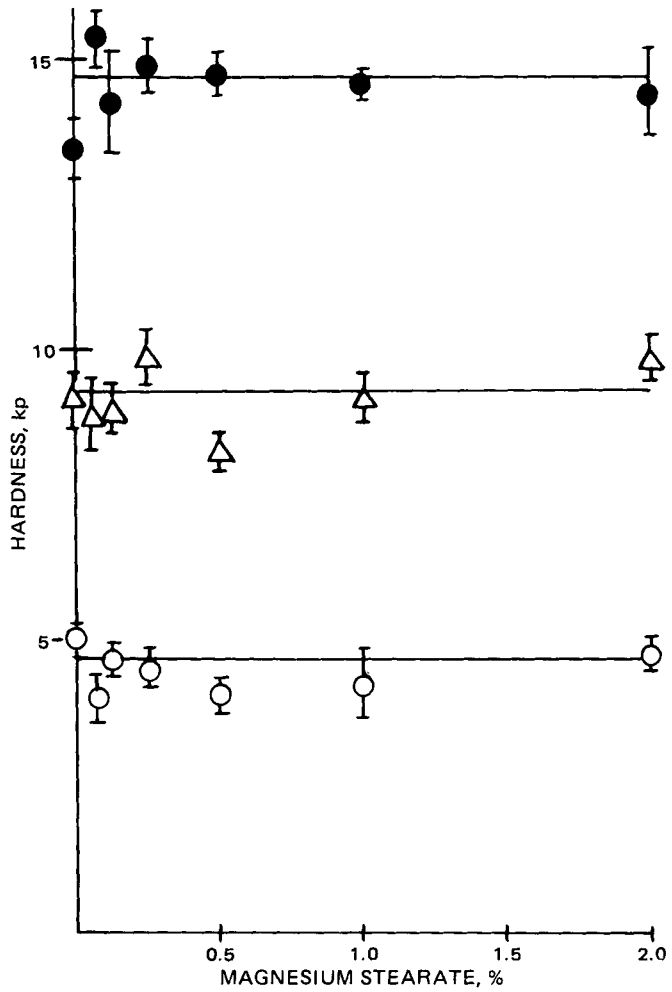

Figure 2—*The influence of the concentration of magnesium stearate on hardness of dibasic calcium phosphate dihydrate compressed at various forces. Key: (○) 454 kg; (△) 1134 kg; and (●) 2268 kg.*

[1] Hounsfield Tensiometer, Type W, Tensometer Ltd., Croydon, England.
[2] Schleuniger model 2E/205, Vector Corp., Marion, IA 52302.
[3] Encompress, Edward Mendell Co., Carmel, NY 10512.
[4] Lubritab, Edward Mendell Co., Carmel, NY 10512.

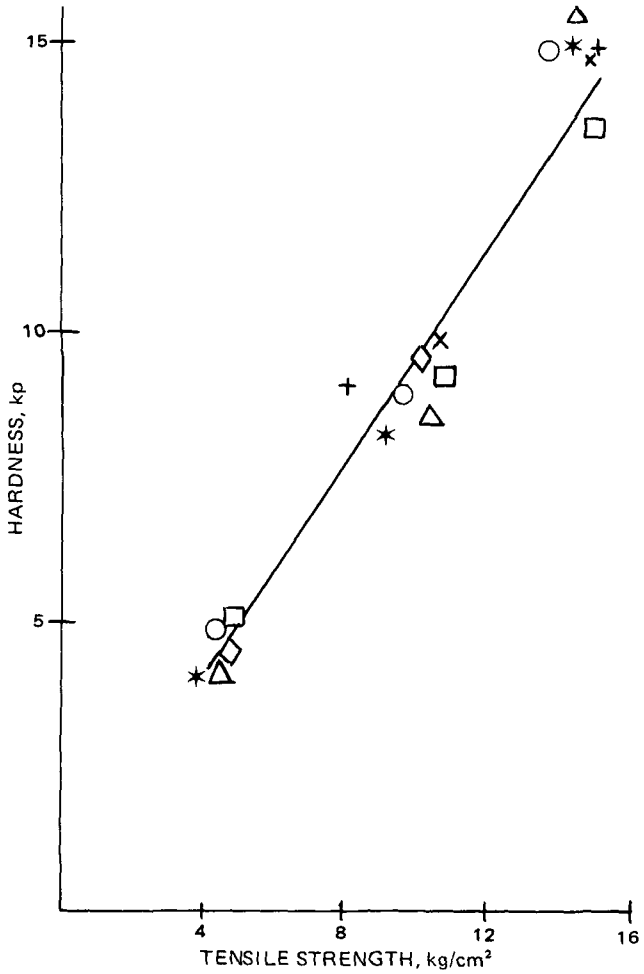

Figure 3—*The relationship of hardness and radial tensile strength for dibasic calcium phosphate dihydrate with various concentrations of magnesium stearate. Key: (□) 0%; (△) 0.075%; (○) 0.125%; (◇) 0.25%; (★) 0.5%; (+) 1.0%; and (×) 2.0%.*

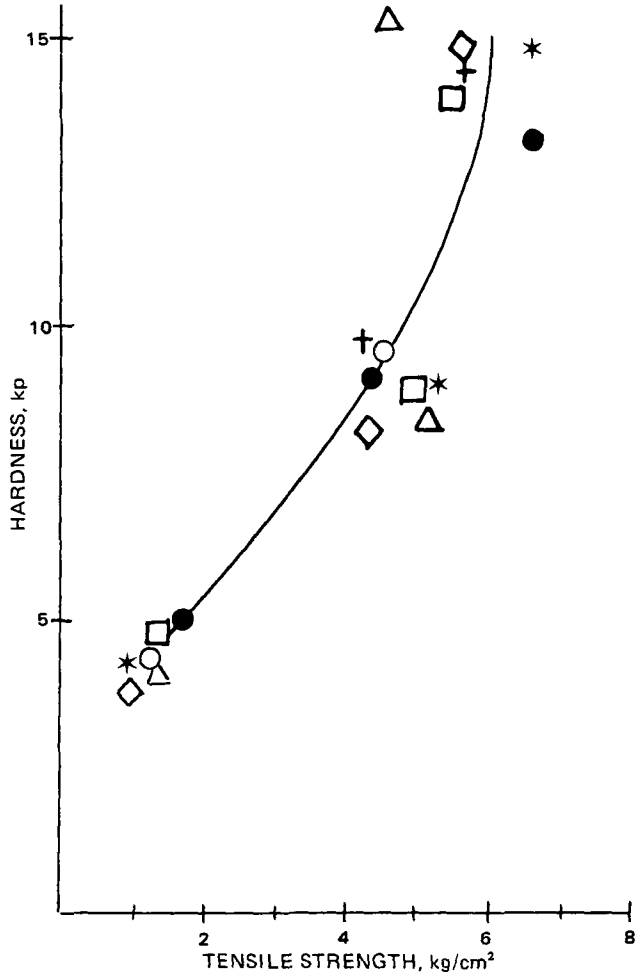

Figure 4—*The relationship of hardness and axial tensile strength for dibasic calcium phosphate dihydrate with various concentrations of magnesium stearate. Key: (●) 0%; (△) 0.075%; (□) 0.125%; (○) 0.25%; (◇) 0.5%; (★) 1.0%; and (+) 2.0%.*

of the tablet. For hydrogenated vegetable oil it appears that, as the concentration is increased to 4%, there is an increase in hardness as the concentration of lubricant is increased. A material that would lubricate and strengthen a tablet would be a useful excipient.

The wide variance in measurement may lead to erroneous conclusions. As illustrated in Fig. 1, for dibasic calcium phosphate dihydrate with hydrogenated vegetable oil, the variance in hardness may be a result of composite stresses (compressive, tensile, and shear) causing failure and minute differences in thickness of the tablets (5). In a tensile strength test, only tensile stress causes failure, and any difference in thickness is considered.

Dibasic calcium phosphate dihydrate and various concentrations of magnesium stearate were compressed at 454, 1134, and 2268 kg of force. The hardness of the tablets was measured and plotted against the concentration of lubricant in Fig. 2. Based on the hardness values obtained by diametral compression, it is concluded that the addition of magnesium stearate to dibasic calcium phosphate dihydrate has no significant effect on the strength of the tablet. As shown in Table I, the majority of the breakage was by a nontension failure. In the hardness tester, weaker tablets failed due to tensile stresses, and stronger tablets failed due to compressive stresses. For low values, the hardness is proportional to the radial tensile strength (Fig. 3).

The relationship of hardness to axial tensile strength is nonlinear as shown in Fig. 4. As the hardness is increased, at higher values of hardness, there is a progressive lessening of the rate of increase of axial tensile strength until a limiting axial tensile strength is attained. Thus, if the strength of a tablet as its hardness is considered, the axial tensile strength could be weak, and the tablet would be likely to laminate and cap under stress. If the axial tensile strength is measured, the strength in the axial direction and its implication in terms of capping are known. It appears that if both axial and radial tensile strengths are known, the strength of a tablet is basically characterized.

REFERENCES

(1) F. W. Goodhart, J. R. Draper, D. Dancz, and F. C. Ninger, *J. Pharm. Sci.*, **62**, 297 (1973).

(2) D. B. Brook and K. Marshall, *ibid.*, **57**, 481 (1968).

(3) F. W. Goodhart, J. R. Draper, M. J. Killeen, and F. C. Ninger, *ibid.*, **65**, 1072 (1976).

(4) W. A. Ritschel, F. S. Skinner, and R. Schlumpf, *Pharm. Acta Helv.*, **44**, 547 (1969).

(5) J. M. Newton, G. Rowley, J. T. Fell, D. G. Peacock, and K. Ridgway, *J. Pharm. Pharmacol.*, **23**, 195S (1971).

(6) P. J. Jarosz and E. L. Parrott, *J. Pharm. Sci.*, **71**, 607 (1982).

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