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COMPARATIVE EVALUATION OF SEVERAL DIRECT COMPRESSION SUGARS II

Clive O. Ondari*, Chester E. Kean** and C.T. Rhodes+

*Department of Pharmacy
University of Nairobi
P.O.Box 30197
Nairobi,Kenya

** California and Hawaiian Sugar Company
Crockett, CA 94525

+ Department of Pharmaceutics
University of Rhode Island
Kingston, RI 02881

ABSTRACT

The formulation efficiency of several sucrose based direct compression vehicles has been evaluated. The effect of compression force on various fundamental tablet properties has been investigated.

It has been observed that even chemically similar matrices may show differences in formulation efficiencies if there are subtile changes in the structure of the particles.

A simple method for evaluating acid neutralizing efficiency of antacid tablets, particularly when aging is concern, has been presented.

INTRODUCTION

In an earlier study (1), the utility of several sucrose-based tableting matrices manufactured by California and Hawaian Sugar Company (C & H) were comparatively evaluated against Nutab and Dipac .The study demonistrated that among the new matrices, C & H Products A,B, and C, no significant formulating

TABLE I

MATRIX	A.H VALUE Sec x 10^3	INTERCEPT,N.SEC.	R^2(Number of points)
A	54.93	-0.086	0.99(4)
B	59.04	-0.2065	0.99(4)
C	61.34	-0.2466	0.99(4)

	IPO:H VALUE (x 10^2)	INTERCEPT,N	R^2 (Number of points)
A	57.34	0.2479	0.99(4)
B	54.53	0.5057	0.99(4)
C	55.03	0.4724	0.99(4)

	S_{max}:H VALUE (Sec^{-1})	INTERCEPT,N (Sec^{-1})	R^2 (Number of points)
A	23.79	16.77	0.99(4)
B	23.46	57.13	0.99(4)
C	22.22	75.61	0.99(4)

A:H - Area to Height

IPO:H - Inflection Point Ordinate to Height

S_{max}:H - Maximum Slope to Height

R^2 - Correlation Coeffient

efficiency existed. However, it appeared that Products A and B were most promising as direct compression vehicles.

Although C & H Product A appeared to be slightly more effient than Product B, it was felt that the difference between the two matrices could be more decernable if more precise methods of evaluation were used. In order to achieve this goal, a computer -interfaced single punch tablet press,Stokes F-1, was used to obtain compression peaks to which various fundamental tablet properties were related.

Several methods of evaluating antacids have been presented (2,3,4,5). The method introduced by the Food and Drug Administration (FDA) to determine the acid neutralizing rate and acid consuming capacity of over-the-counter antacids(3),

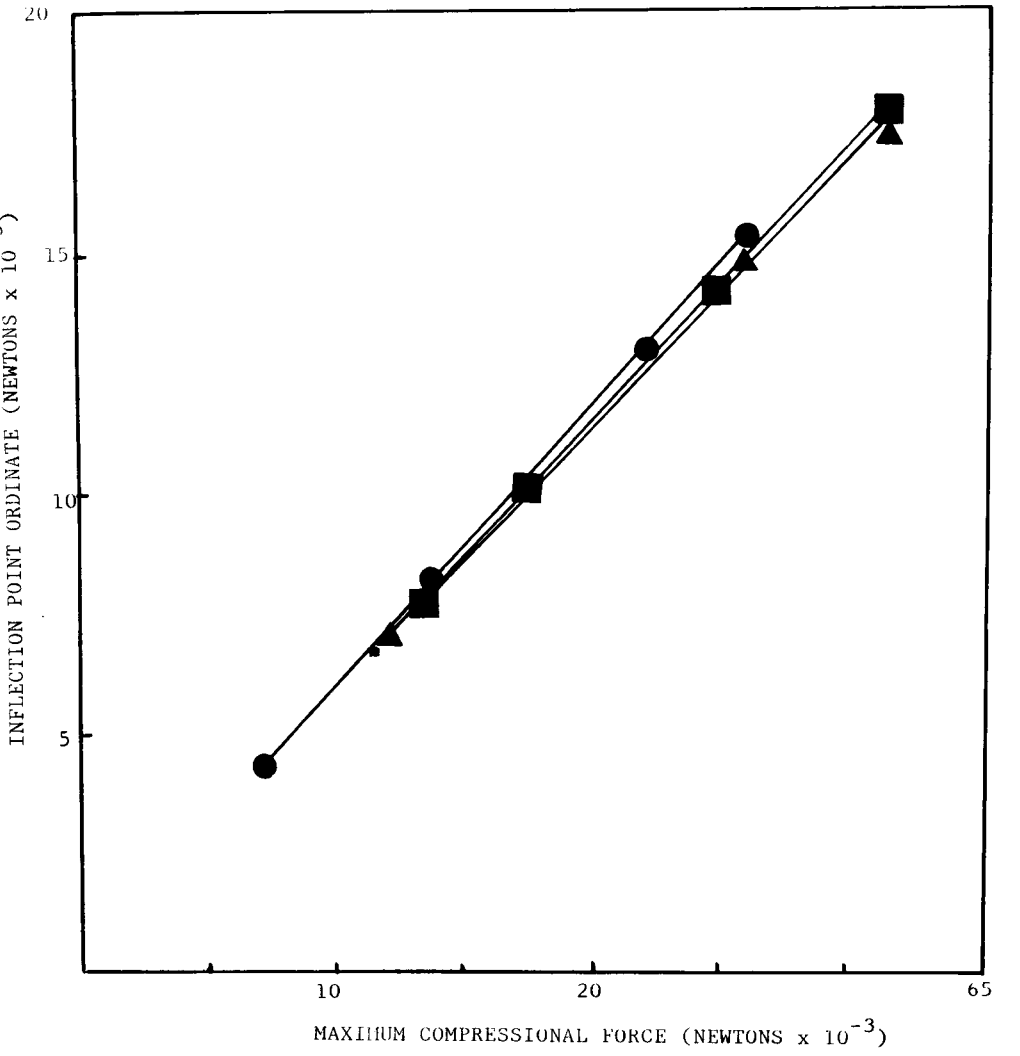

FIGURE 1

Inflection ordinate as a function of compressional force

Key: ● C & H Product A ▲ C & H Product B ■ C & H Product C

and the Dynamic testing method suggested by Brown et al, are the most realistic. Smyth et al have presented an excellent methodology for the correlation of in-vitro and in-vivo performance of antacids.

This work adapts a method similar to the FDA and Brown et al methods in an effort to evaluate the aging process in a chewable antacid tablet formulation.

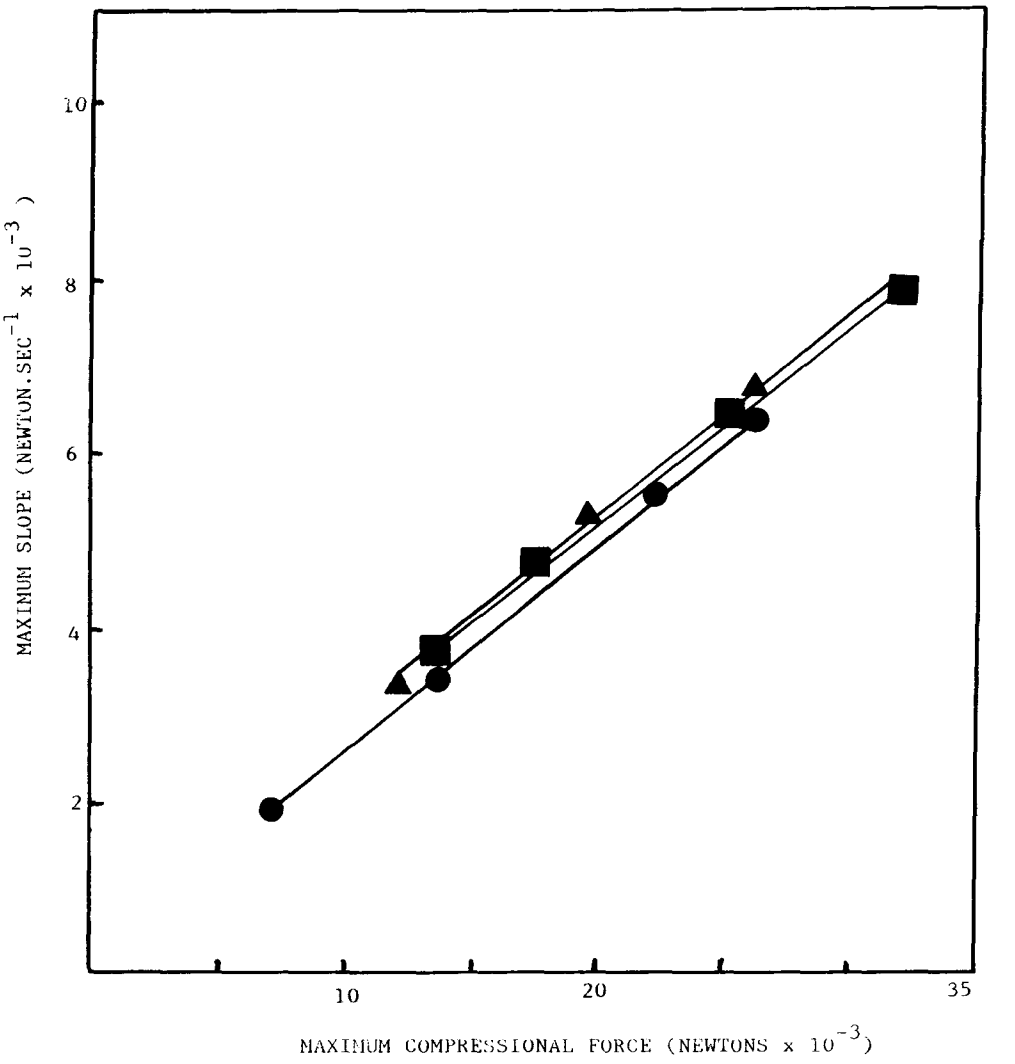

FIGURE 2

Maximum slope as a function of compressional force

Key: ● C & H Product A ▲ C & H Product B ■ C & H Product C

EXPERIMENTAL

Preparation of Tablets

The following formulae were compressed on an instrumented Stokes F-1 tablet press: placebo, pediatric aspirin, ascorbic acid, multivitamin, and antacid.

The tablet press was instrumented with piezo-electric transducers and interfaced with a PDP-11[1] computer and in some cases an Apple E-II[2] computer. The soft-ware used

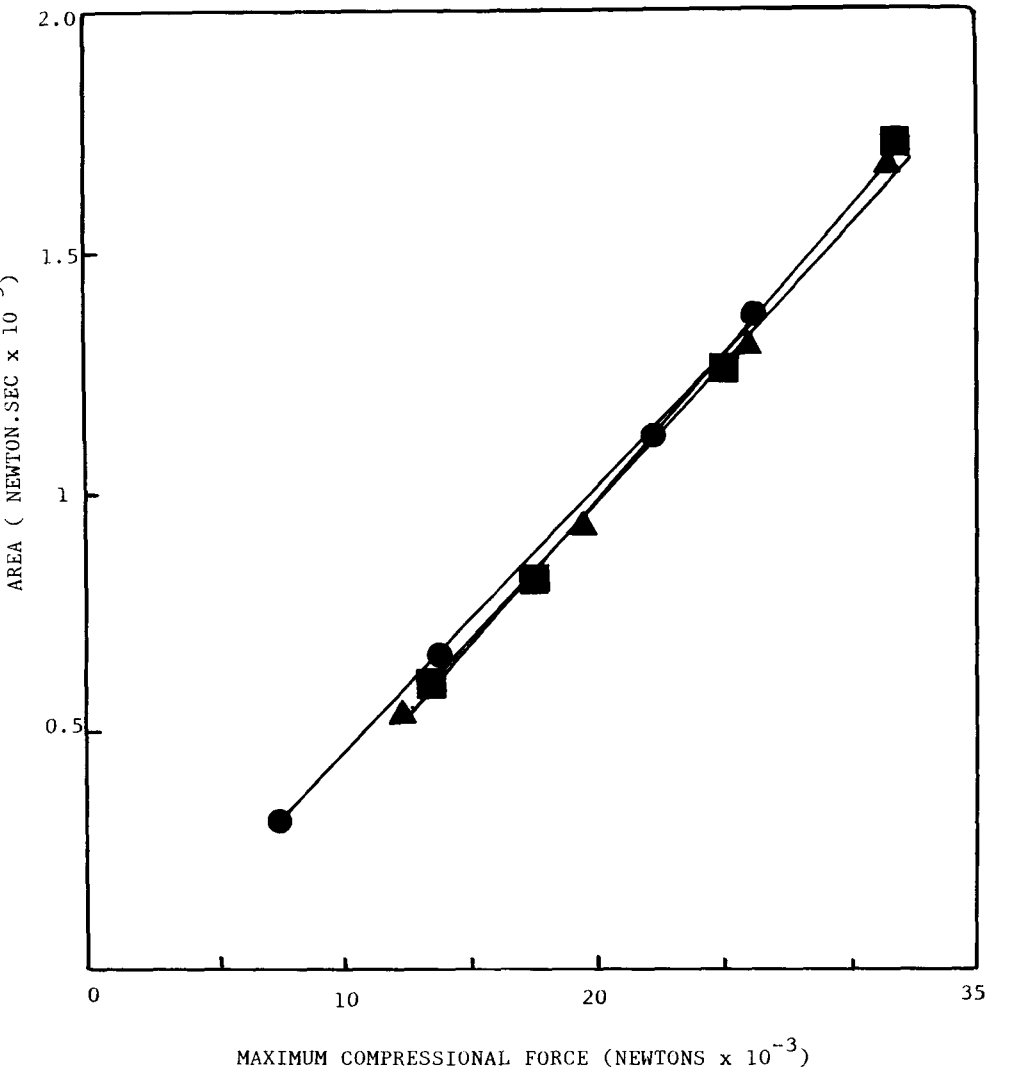

FIGURE 3

Area as a function of maximum compressional force

Key: ● C & H Product A ▲ C & H Product B ■ C & H Product C

with the computer enabled rapid collection of data corncerning a large number of tablets. The computer faclilitated the generation of several compression parameters. A transducer located in the upper punch holder, measured applied force as a function of time . Transmitted and ejection forces were measured by a transducer located in the lower punch holder. In order to generate force/time curves for applied and transmitted forces, the computer received signals at a rate of five hundred data points per second.

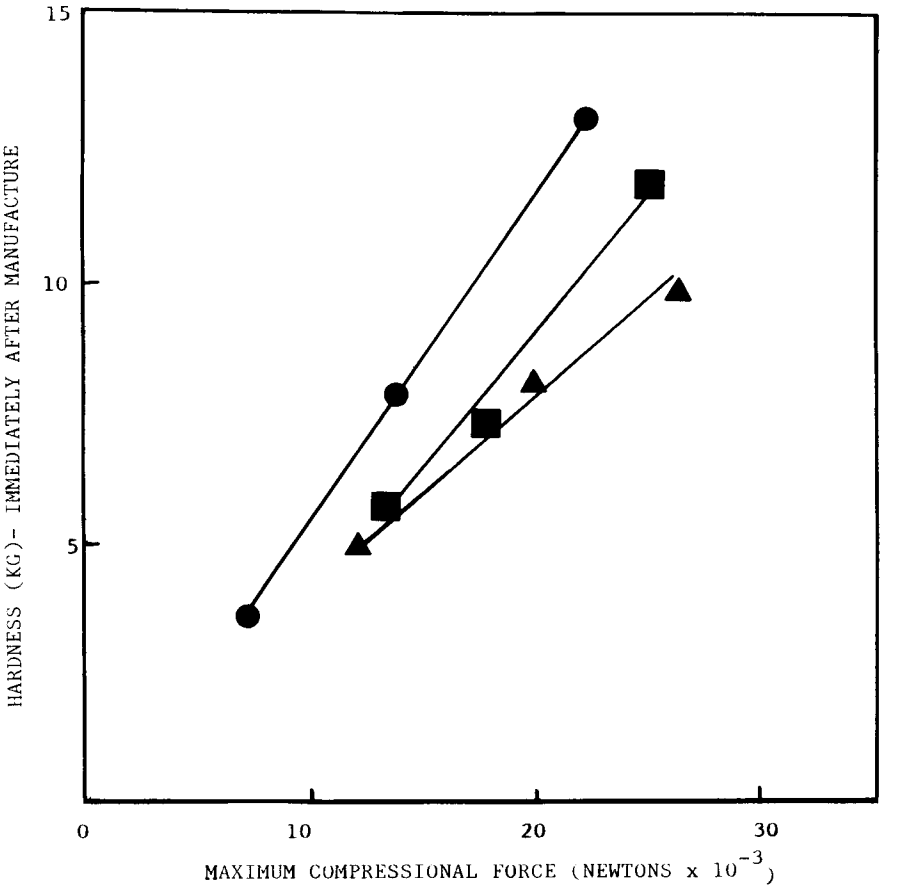

FIGURE 4

Tablet hardness as a function of compressional force.

(tested immediately after compression)

Key: ● C & H Product A ▲ C & H Product B ■ C & H Product C

The following parameters were genenareted for applied and transmitted force curves: peak width,center,maximum slope on the ascending curve, inflection point ordinate,and area as reported by Chilamkurti and co-workers(6). The tablets were compressed at four compression force levels.

Evaluation of Tablets

The tablets manufactured were evaluated for the following fundamental properties: weight uniformity,thickness, diameter, hardness, disintegration, friability, and in some cases , dissolution as reported earlier (1).

TABLE II

EFFECT OF COMPRESSION FORCE ON TABLET HARDNESS - ASCORBIC ACID FORMULATION.

MATRIX	INTERCEPT,N x 10^3	SLOPE ($Kg.N^{-1}$)	R^2(n)
C & H AI*	-1.1162	0.5760	0.99(4)
C & H AII	-2.8424	0.6684	0.99(4)
C & H B	-1.7957	0.5160	0.98(3)
C & H BROWN	-2.6600	0.4886	0.96(4)
NUTAB	-2.2549	0.3520	0.99(3)
DIPAC	-2.2579	0.3708	0.99(3)

*C & H Products AI and AII differed only in particle size distribution.

TABLE III

EFFECT OF COMPRESSION ON TABLET HARDNESS - MULTIVITAMIN FORMULATION

MATRIX	INTERCEPT,N x 10^3	SLOPE($Kg.N^{-1}$)	R^2(n)
C & H AI	0.5051	1.0150	0.98(4)
C & H AII	2.2998	0.7195	0.97(4)
C & H B	1.6543	0.5967	0.99(4)
C & H BROWN	-0.1218	0.6894	0.98(4)
NUTAB	-1.2282	0.6361	0.98(4)
DIPAC	0.1218	0.4431	0.98(3)

Acid neutralizing efficiency of the antacid tablets was evaluated by a method similar to that of the FDA (3). Two tablets , equivalent to an average dose of aluminum hydroxide antacid were placed in a beaker containing 70ml of 0.1N Hcl. The probes of a pH meter[3], standardized at pH 4.0 were then lowered into the 0.1N Hcl. The elecronic output of the pH meter was fed into a chart recorder[4] to provide a complete tracing of the acid neutralizing profile . The antacid tablets were analyzed for both acid neutralizing efficiency (rate), time to reach maximum pH, and acid neutralizing capacity, maximum pH value attained. These parameters were determined for both fresh and aged tablets.

TABLE IV

DISSOLUTION PARAMETERS* - ASPIRIN FORMULATION

MATRIX	COMPRESSION FORCE($Nx10^{-3}$)	R^2	INTERCEPT	SLOPE(-ve)
C & H AI	4.0	0.9667	61.14	1.07
	8.0	0.9779	99.68	1.06
	15.4	0.9871	97.59	0.86
	17.4	0.9888	101.38	0.80
C & H AII	3.0	0.9356	73.72	1.17
	7.9	0.9963	101.66	1.02
	10.1	0.9786	97.83	0.71
	16.4	0.9956	102.68	0.66
C & H B	3.9	0.9816	90.78	1.39
	9.0	0.9920	107.88	1.02
	10.3	0.9908	107.71	0.73
	18.4	0.9555	106.16	0.68
NUTAB	5.6	0.9368	81.98	1.36
	7.3	0.9930	109.76	1.15
	16.3	0.9916	109.78	0.98
	21.3	0.9889	109.50	0.76
DIPAC	4.7	0.9292	75.56	1.28
	9.0	0.9941	105.16	1.08
	17.1	0.9905	106.79	0.73
	19.8	0.9924	105.56	0.58

* Dissolution as percent remaining to be released at sixty minutes.

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MATRIX	INTERCEPT,N x 10^3	SLOPE($Kg.N^{-1}$)	R^2(n)
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RESULTS AND DISCUSSION

Table I and Figures 1 and 2 show the compression curve parameters obtained during the compression of placebo tablets. The maximum slope ,inflection point ordinate, and area under the curve were found to vary linearly with maximum compression force. Area to height (A:H) which has been shown to be related to related to the inherent compressibility of a system (2), appeared to increse in the order : Porduct A, Product B, and Product C. The greater the A:H value,the less the inherent compressibility. Thus, the three C & H matrices showed significant difference in compressibility , with Product A being the most compressible.This difference was parraled by the differences noted in the ralative laboring of the tablet press during the compression of the formulations. No significant difference was observed among the S_{max}:H values. This is was expected as these matrices are essentially similar chemically,and as was also reported by Chilamkurti et al. Inflection point ordinate , slope(maximum), varied linearly with compression force, although no significant difference was observed among the three C & H matrices.

Figures 3 and 4 show the effect of compression force on the hardness of tablets made from lubricated matrices (C & H A,B and C). The hardness values reflected in Figure 3 were obtained immediately after compression, while those shown in Figure 4 were obtained forty five days after manufacture. There appears to be an aging process in which a reduction in tablet hardness occurs.

Table II shows the effect of compression force on tablet hardness for ascorbic acid formulation. It is clearly discernable from the slope values, that the C & H Products A and B were the most compressible among the five matrices evaluated.

Table III illustrates the effect of compression force on the tablet hardness for the multivitamin formulation. Again, the C & H products appear to be more compressible than the other products investigated.

The effect of compression force on the dissolution of the aspirin tablets is shown in Table IV. Full dissolution profiles for the various tablets were determined, and hte data are presented as percent remaining to be released at sixty minutes. As would be expected, the rate of dissolution, the slope values, decreased with increases in the compression force. This is perhaps due to decrease in the porosity of the tablets and/or an increase in inter-particle interactions. In situations where the compression force was very high, the powder mix actually melted and resulted in a clear glass-like material.

Table V shows maximum pH recordings of acid neutralizing profiles obtained during the determination of the effect of aging on acid neutralizing effeciency of an aluminum hydroxide antacid formulation. The data suggest that an aging process does occur in this formulation, and process is most likely to occur in contant high temperature and humidity.

FOOTNOTES

1. Model IIE, Apple Computer Company, Cuperton,California.

2. Model PDP-11, Digital Computer Company,Marlboro,Massachusetts.

3. Markison pH Meter, Markison, Del Mar, California.

4. Linear Instruments Company, Dedham, Massachusetts.

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4. Brown et al, Pharmaceutical Technology,Feb. 1983.

5. Smyth et al, J. Pharm. Sci.,65,1045(1976).

6. Chilamkurti et al.,Drug Devel. and Ind. Pharm.,8,63(1982).