DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 14(4), 499-521 (1988)

SOME PHYSICAL PROPERTIES OF DIRECTLY COMPRESSED THIAMINE HYDROCHLORIDE TABLETS

O.K. Udeala and S.A.S. Aly
Department of Pharmaceutical Technology
and Industrial Pharmacy
University of Nigeria, Nsukka
Nigeria.

ABSTRACT

The effect of single direct compression vehicles or their binary blends on some physical properties of thiamine hydrochloride tablets was investigated. The pure drug has very poor flow and compression characteristics. It needed not less than 79% w/w of a direct compression vehicle to yield a flowable compressible mix. Tablets of high physical standards were produced with single vehicles such as Avicel PH 101, Celutab and Anhydrous lactose, USP respectively. On the contrary, neither STAR-x nor 'Emcompress could be used to produce thiamine hydrochloride tablets with good physical characteristics. The tabletting property of each of the unsatisfactory vehicle was improved by blending with a vehicle that has good tabletting property. An exponential relationship between hardness and friability of the compressed tablets was derived. There was no direct relationship between the hardness and disintegration of the tablets.

INTRODUCTION

The advantages of direct compression as a simple and advanced tabletting technique have been widely reviewed (1, 2). One of the many attributes of the direct compression method is the elimination of some physicochemical interactions which might occur during the wet granulation process (3, 4). There is increased product stability since the direct compression method involves only blending and compression. When a cohesive, active drug constitutes a large proportion of the tablet formula, the direct compression vehicle facilitates production by promoting flow. Henderson and Brune (5) stated that no single material has all the attributes of an ideal direct compression excipient. Nevertheless, some of these excipients serve more than one function in a tablet formula. Kwan and Milosovich (6) evaluated amylose as a direct compression vehicle and found that it could function as a filler, lubricant and disintegrant. Vehicles which do not show versatility in physical properties are improved upon through blending with other vehicles that possess the desired property. Microfine cellulose (7) Avicel (8), amylose V (7) anhydrous lactose dicalcium phosphate dihydrate, directly compressible starch (8) and spray dried lactose have been evaluated for tabletting either as single or binary blends. In their study of physical and chemical stability of thiamine hydrochloride tablets prepared with Emcompress, Shah and Arambulo (9) found that the tablets were soft and friable.

The present investigation was designed to evaluate the physical properties of thiamine hydrochloride tablets

prepared with either single or binary blends of some direct compression vehicles.

EXPERIMENTAL

Materials: Thiamine hydrochloride[1] represented the active constituent. The direct compression vehicles included Avicel PH 101[2], Anhydrous lactose, USP[3], Celutab[4], STAR-x 1500[5] and Emcompress[4]. Magnesium stearate and stearic acid[6], were used as lubricants.

Methods: The physical standards such as mean particle size, bulk density, packaging fraction and angle of repose were evaluated according to well known techniques. The mix for compression was formulated to contain 1 part of thiamine hydrochloride, 4-10 parts of a given single vehicle or binary blend of direct compression vehicles and 0.5% w/w of either magnesium stearate or stearic acid as lubricant. An F_3 single punch tabletting machine was used for compressing tablets of 250 mg average weight and 9.75 + 0.01 mm diameter using previously reported method (8). Altogether 300 tablets per batch were produced with each mix. The hardness of the tablets was measured with Erweka hardness tester[II] while the disintegration test apparatus[I]. The friability of the tablets was determined with a Roche friabilator[II] while the tablet thickness was determined using Baty dial micrometer[III].

RESULTS AND DISCUSSION

The physical characteristics of the pure drug and the vehicles are presented in Table I. Thiamine hydrochloride powder has a high angle of repose and would be expected to have poor flow characteristics.

TABLE 1 Some Physical Characteristics of Powdered Thiamine Hydrochloride and Direct Compression Excipients

Material	Particle Size Range "U"	True Density g/cc	Bulk Density g/cc	Packing Fraction	Angle of Repose
Thiamine HCl[a]	180.48	1.546	0.67	0.4366	64.00
Avicel[b]	82.99	1.502	0.355	0.236	40.00
Anhydrous[b] Lactose USP	185.07	1.683	0.559	0.332	40.00
Celutab[b]	342.58	1.720	0.683	0.397	31.58
STAR-x[b]	113.21	1.544	0.668	0.4326	28.30
Encompress[b]	280.75	2.215	0.903	0.4076	35.36

a. Mean of 5 Determinations

b. Data obtained on the physical properties of the vehicles are from ref. 8.

Ideally, the properties of tablets compressed with either single or binary blends of vehicles should be compared with control tablets produced with 100% of the lubricated pure drug substance. However, such control tablets could not be produced using either the tabletting machine or a hydraulic press. This was due to the very poor compression characteristics of thiamine hydrochloride. A reasonable approach was to use those tablets produced with the least possible concentration

of single or binary blend of vehicles as control tablets. The hardness-friability ratio (HFR) of the tablets was determined. Since Avicel, Celutab and Anhydrous Lactose, USP respectively yielded high HFR, these vehicles were each blended with other vehicles that possess poor HFR (10).

Uniformity of tablets:

The weight uniformity of the compressed tablets was evaluated according to the specifications of B.P. 1980. The uniformity of thickness which is an additional control for ensuring reproducibility in tablet dimensions (11) was determined. Both the single vehicles and the binary blend of vehicles produced uniform tablets as can be observed in Tables 2a & b. Although Lerk et al (12) described Avicel as a vehicle which has just adequate flow properties, the result shows that its mixture with thiamine hydrochloride has good flow properties which improves with increase in Avicel concentration. The effect of Avicel on flow is attributable to the glidant property of this type of cellulose (13). Thiamine hydrochloride tablets could not be compressed with STAR-x 1500 alone. This confirms the findings of Bolhuis and Lerk (14) who stated that this vehicle has poor tabletting properties. Tablets of good quality were however obtained by blending STAR-x 1500 and Avicel PH 101 in a 1:1 ratio. Non uniform tablet batches were produced with 1:3 blend of anhydrous lactose and STAR-x 1500. A blend of Avicel in 1:1 or 1:3 ratio with all other vehicles produced good tablets.

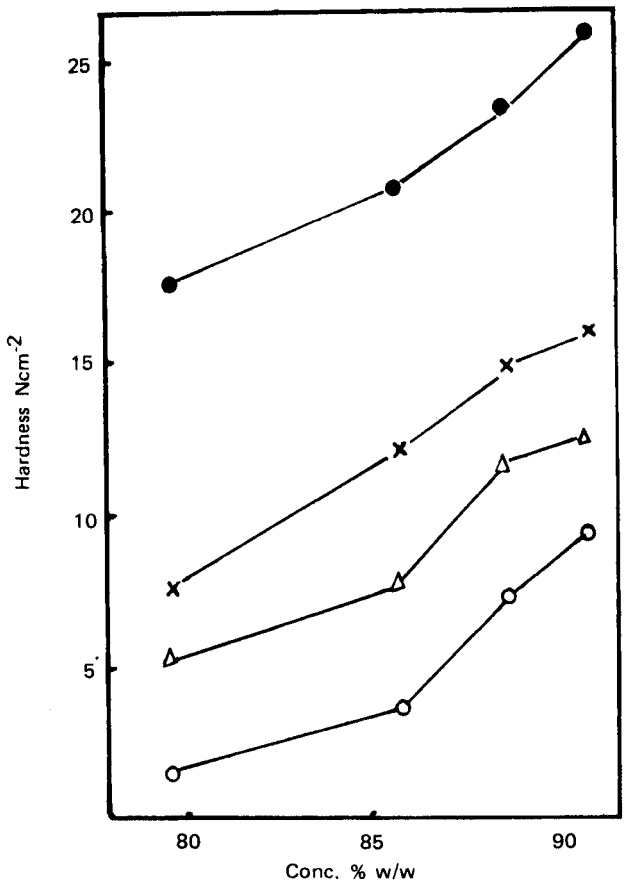

Fig 1. Effect of varying concentrations of single vehicles on the hardness of directly compressed thiamine hydrochloride tablets

Key: ● Avicel, × Encompress, Δ Celutab and ○ Anhydrous lactose.

Hardness and porosity:

The effect of varying concentrations of single or binary blends of vehicles on hardness is shown in Figs. 1 and 2. The hardness of the tablets was seen to be mainly dependent on the concentration and type of the single or binary blend of vehicle. Tablets prepared

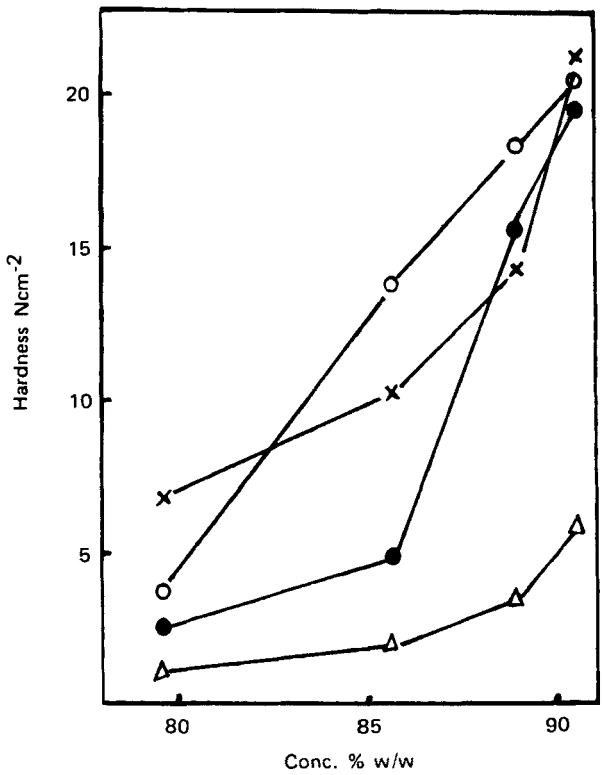

Fig 2. Effect of varying concentrations of 1:1 binary blend of Avicel and named vehicles on the hardness of thiamine hydrochloride tablets

Key: x Emcompress, O Anhydrous lactose

● Celutab and Δ Star-x

with Avicel alone yielded the highest hardness profile. A similar result was obtained by Richman et al (15) who investigated glyceryl trinitrate tablets prepared with Avicel. The high hardness profile of these tablets was attributed to the match-stick like bundles of microcrystalline cellulose which easily bond upon slight compression. The numerous hydrogen bonds on the molecule also contribute to bonding and hence to the

over all hardness of the tablets. The tablets which contained Anhydrous lactose as vehicle also showed good hardness profile. This confirms the findings of Batuyious (16) and Mendell (1) respectively. Good hard tablets were produced with Celutab as vehicle. Tablets produced with this vehicle are known to harden further with time (8) Fig. 2 shows that tablets produced with binary blends of vehicles possessed better hardness profile than tablets produced with all the single vehicles except Avicel. At 90% w/w concentration of vehicle the 1:1 blend of Avicel with Celutab, Anhydrous lactose, Emcompress respectively yielded tablets that were very close to each other in hardness. The tablets containing a blend of Avicel and STAR-x as vehicle possessed a lower hardness. This, however would be considered an improvement since thiamine hydrochloride tablets could not be compressed with STAR-x alone.

The porosity, ϵ of a tablet composed of more than two components is given by (17)

$$\epsilon = 1 - P_B \sum \frac{x_i}{P_i} \qquad \text{Eq. 1}$$

where P_B is the bulk density of the tablet calculated from its weight and dimensions, x_i is weight fraction of 1^{th} material and P_i is its true density. The porosity of the tablets formulated with the different single and binary blends of vehicles was calculated on the basis of Equation 1. The values obtained were presented in Table 2. A plot of the hardness of the tablets, H vs the calculated porosity on a semi-log scale is shown in Fig. 3. A good linear relationship exists between porosity and tablet hardness and thus

conforms to the empirical formula of Duckworth for hardness (18):

$$H = H_o \exp (- k\epsilon). \qquad \text{Eq. 2}$$

where H_o is the absolute hardness of a tablet at porosity zero and k is a constant. The porosity, in Eq. 2 may be replaced by the term representing this parameter in Eq. 1 above. Thus Eq. 2 assumes the form

$$\text{Log } H = \log H_o - K/2.303\left(1 - P_B \sum \frac{xi}{P_i} \right) \qquad \text{Eq. 3}$$

The bulk density P_B of the tablet is derived from the tablet weight and volume. If a tablet is compressed with a single vehicle, A, the equation becomes

$$\text{Log } H = \log H_o - K/2.303 \left(1 - \frac{wt}{Vo} \times \frac{100\%}{P} \right) \qquad \text{Eq. 4}$$

where P is the true density of the vehicle A and thus wt/P represents V_A, the true volume of the vehicle; V_o is the bulk volume of the tablet and 100% represents unity. The equation then assumes the form

$$\log H = \log H_o - K/2.303 \left(1 - \frac{V_A}{V_o} \right) \qquad \text{Eq. 5}$$

The hardness or crushing strength of a tablet depends on the solid content rather than the void fraction or porosity. If the porosity fraction is removed from the tablet which constitutes one whole, what is left is the fraction contributing to the tablet hardness. If this is effected in Eq. 5 above, the following expression results;

$$\log H = \log H_o - K/2.303\ 1 - \left(1 - \frac{V_A}{V_o} \right) \qquad \text{Eq. 6}$$

TABLE 2a Some Physical Characteristics of Thiamine Hydrochloride Tablets Directly Compressed with Varying Concentrations of Single Vehicles*

Vehicle Name	Conc. % w/w	Weight (g) Mean	Weight (g) C.V.%	Thickness (mm) Mean	Thickness (mm) C.V.%	HFR	Porosity %	Disinteg. Time (min) Mean	Disinteg. Time (min) C.V.%
Avicel	79.60	0.2432	4.90	3.08	1.21	5.64	26.80	8.10	17.16
	85.29	0.2440	4.20	3.06	1.00	13.38	25.20	4.70	36.70
	88.46	0.2460	2.60	2.94	1.00	22.42	21.50	1.90	40.55
	90.46	0.2550	1.60	2.96	0.71	44.85	19.06	1.20	48.84
Anhydrous Lactose USP	79.60	0.2360	6.10	2.67	3.85	0.1899	25.84	2.5	8.5
	85.29	0.245	5.30	2.78	2.39	1.490	24.86	2.56	22.6
	88.46	0.249	5.10	2.72	1.85	6.90	22.90	8.40	9.8
	90.46	0.256	3.20	2.72	1.33	16.08	20.90	10.20	2.90
Celutab	79.60	0.239	4.70	2.80	1.81	4.495	28.90	2.60	1.8
	85.29	0.244	3.90	2.79	1.30	11.660	27.16	3.10	13.7
	88.46	0.245	3.80	2.73	1.50	17.720	25.92	4.30	4.70
	90.46	0.249	2.30	2.77	1.31	30.94	25.29	5.50	11.10
Emcompress	79.60	0.247	4.6	2.35	2.10	4.170	25.04	14.0	10.30
	85.29	0.245	7.0	2.07	2.40	5.644	23.70	15.70	1.80
	88.46	0.246	4.2	2.17	10.80	9.522	20.96	16.40	9.50
	90.46	0.248	3.5	2.00	2.40	12.340	17.98	45.30	9.50

* Formulations prepared with STA-Rx could not be compressed.

TABLE 2b Some Physical Characteristics of Thiamine Hydrochloride Tablets Directly Compressed with Varying Concentrations of (1:1) Binary Blended Vehicles

Vehicle Name	Vehicle Conc. % w/w	Weight (g) Mean	Weight (g) C.V.%	Thickness (mm) Mean	Thickness (mm) C.V.%	HFR	Porosity %	Disinteg. Time (min.) Mean	Disinteg. Time (min.) C.V.%
Avicel/ STAR-x	79.60	0.225	3.6	3.14	7.20	0.178	35.24	0.898	3.68
	85.29	0.246	5.70	3.04	7.30	0.78	27.06	0.997	6.79
	88.46	0.247	6.70	3.10	4.3	1.33	26.60	0.952	11.33
	90.46	0.248	4.20	3.12	3.00	17.13	26.62	1.20	12.78
Avicel/ STAR-x	79.60	0.238	7.9	2.55	1.20	6.50	24.98	1.78	27.75
	85.29	0.234	5.0	2.48	1.80	9.50	24.36	1.95	26.50
	88.46	0.239	4.40	2.56	2.50	37.6	23.30	3.06	13.56
	90.46	0.258	4.10	2.60	1.50	100.65	20.60	6.388	6.98
Anhy- drous Lactose/ STAR-x	79.60	0.2192	6.496	2.86	1.53	0.52	32.42	1.48	11.75
	85.29	0.2381	5.115	2.93	3.35	1.04	28.60	2.48	6.71
	88.46	0.2466	4.97	2.98	2.215	1.4	27.30	3.05	8.88
	90.46	0.2513	3.98	3.11	3.41	4.20	23.110	5.11	2.33
Celutab/ STAR-x	79.60	0.2381	5.151	2.241	2.31	0.35	24.85	1.00	31.5
	85.29	0.243	0.869	2.41	3.11	1.13	13.30	1.236	2.25
	88.46	0.2413	6.30	2.41	1.50	1.74	11.96	1.76	10.64
	90.46	0.2581	5.78	2.511	3.78	5.50	10.60	2.8	4.55

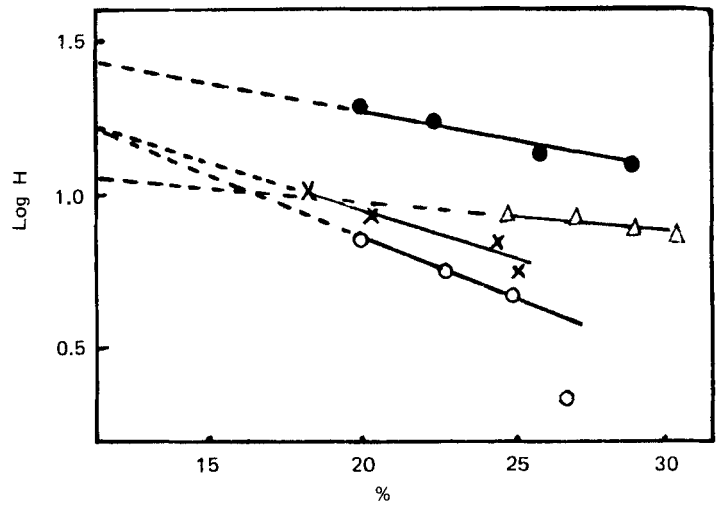

Fig 3. Arithmetic-log relationship between the porosity and hardness of thiamine hydrochloride tablets directly compressed with varying concentrations of different single vehicles

Key: ● Avicel, × Encompress, Δ Celutab and ○ Anhydrous lactose

which then reduce to

$$\log H = \log H_o - K/2.303 \left(\frac{V_A}{V_o} \right) \qquad \text{Eq. 7}$$

Since the vehicle, A was compressed under fixed compression force, the change in volume is a factor of change in the weight of the contributing vehicle and therefore

$$\log H = \log H_o - K/2.303 \frac{W_A}{W} \qquad \text{Eq. 8}$$

$$\text{or} \quad \log H = \log H_o - K/2.303 \frac{1}{C} \qquad \text{Eq. 9}$$

where C is weight fraction of the vehicle used for

compressing the tablets to a hardness of H and H_o is the absolute hardness of the tablet compressed from the vehicle alone at the compression force used. A plot of log H vs the reciprocal of the per cent vehicle concentration in a tablet formula is presented in Fig. 4. The values of H_o and K for tablets compressed with single direct compression vehicles are presented in Table 3. The data obtained by Sakr et al (19) for directly compressed with Eq. 9. The indication is that Eq. 9 is applicable. Statistical analysis of the hardness and concentration data shows that K is equal to the packing fraction $1/P_f$ of the vehicle.

Friability of tablets:

A graph of friability vs concentration of single direct compression vehicles is shown in Fig. 5. All the tablets prepared with each of the vehicles except anhydrous lactose possessed acceptable friability of 4% when a minimum concentration of 80% w/w of the vehicle was present in the tablet formula. At an optimum concentration of 90% w/w of each vehicle, the friability of the tablets was reduced to 1% or less. Fig. 6 shows that a 1:1 blend of Avicel with any other vehicle improved the friability of the tablets. At 80% w/w concentration of the binary blends the friability of the tablets were no higher than 3%. However, tablets containing STAR-x in the blend were still very friable. This however is considered an improvement since no tablets could be produced with STAR-x alone. The 1:1 blends did not produce friable tablets when 90% w/w concentration of vehicle was used

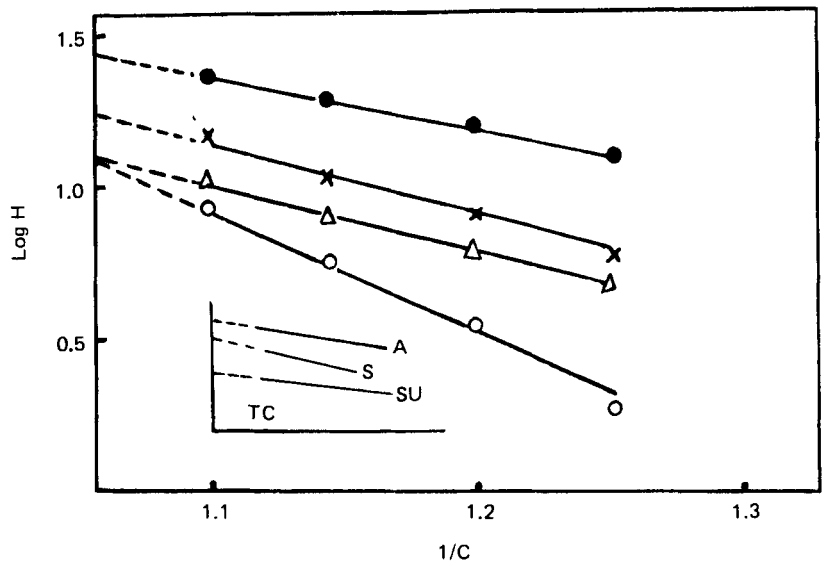

Fig 4. Log H as a function of 1/C (reciprocal % conc.) as given in Eq. 9.
Key: ● Avicel, x Emcompress, Δ Celutab and o Anhydrous lactose
TC for tetracycline hydrochloride tablets compressed directly from a, Avicel, S, Star-x and Su, Sugartab. Data obtained from ref. 19.

TABLE 3: Calculated Values of H_o and K for Different Thiamine Hydrochloride Tablets Formulated with 90.46% w/w Single Vehicles

Vehicle	H^o Ncm^{-2}	K
Avicel	25.18	3.455
Anhydrous Lactose USP	19.05	3.41
Celutab	14.79	2.34
STAR-x	-	-
Emcompress	19.95	2.21

TABLE 4: Experimental Values of F_w (%) and K_f for Thiamine Hydrochloride Tablets Formulated with 90.46% w/w Single Vehicles.

Vehicle	F_w	K_f
Avicel	10.0	0.4
AH.L	100.0	0.565
Celutab	6.76	0.40
STAR-x	-	-
Emcompress	5.012	0.24

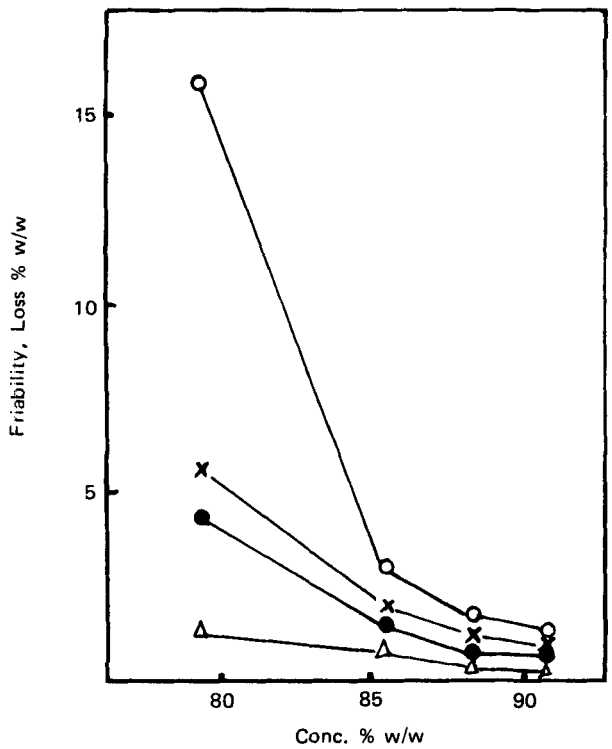

Fig 5. Effect of varying concentrations of single vehicles on the friability (loss % w/w) of directly compressed thiamine hydrochloride tablets

Key: See Fig 1.

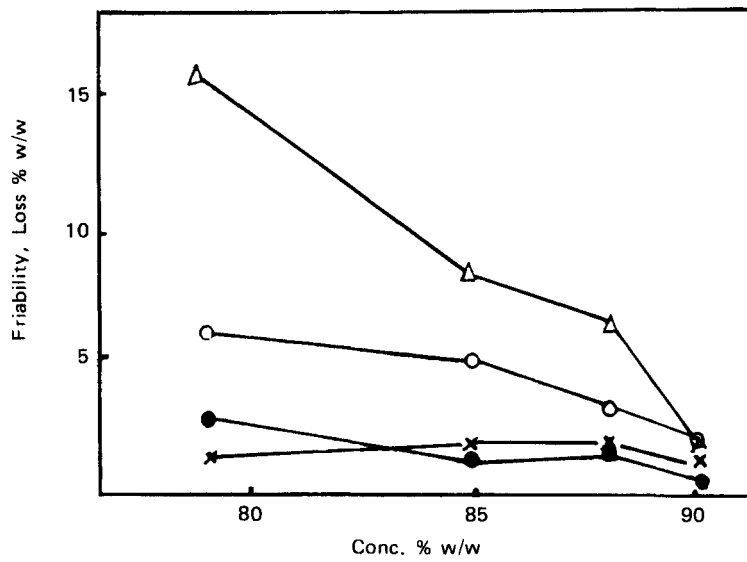

Fig 6. Effect of varying concentrations of 1:1 binary blends of Avicel and named vehicles on the friability (loss % w/w) of directly compressed thiamine hydrochloride tablets

Key: See Fig 2.

for compressing the tablets. Indeed the highest friability obtained with tablets produced with Avicel/anhydrous lactose blend was 1.5%. At this level of vehicle concentration, the hardness characteristics of tablets prepared with the 1:1 blend may be arranged as Avicel/Celutab>Avicel/Emcompress>Avicel/anhydrous > lactose Avicel/STAR-x. The nature of the friability vs vehicle concentration curves suggests that a direct relationship exists between log friability and concentration of the vehicles. This relationship can be expressed as

$$\log F = \log F_W - K_f C \qquad \text{Eq. 10}$$

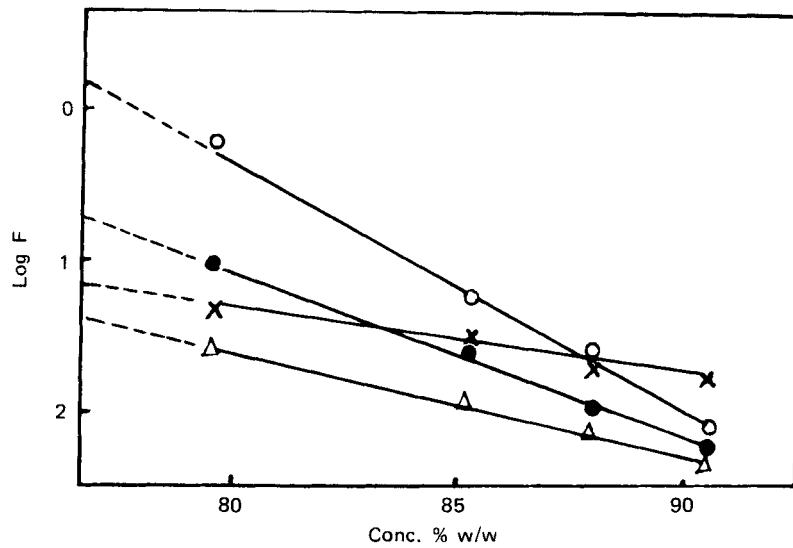

Fig 7. Log friability (loss % w/w) as a function of the concentration C % of contributing vehicle according to Eq. 10 for thiamine hydrochloride tablets directly compressed with varying concentrations of different vehicles

Key: See Fig. 1

where F and F_W are friabilities of tablets containing any experimental concentration, C and a limiting concentration W respectively of a given vehicle, K_f is a constant. F_W may vary as the concentration of vehicle between zero and the minimum required to obtain a compress. A plot of log F vs C is presented in Fig. 7. The intercept with the ordinate yields F_W. At a vehicle concentration of 66% w/w, the values of F_W and K_f respectively are presented in Table 5. In practice, tablets could not be compressed with 66% w/w and lower concentration of the direct compression vehicles. The friability at this concentration can therefore be assumed to be equal to the value at zero

TABLE 5: Experimental and Calculated Values of H_o and K^* for Thiamine Hydrochloride Tablets Formulated with 90.46% w/w Single Vehicles

Vehicle	H^o Ncm^{-2}	Calculated K^{-a}	Experimental K^{*b}	Correl. coeff (r)
Avicel	25.061	0.096	0.12	0.88
Anhydrous Lactose USP	10.965	0.25	0.32	0.92
Celutab	14.125	0.0992	0.115	0.94
STAR-x	-	-	-	-
Emcompress	17.789	0.992	0.12	0.897

a $K^* = K \times K_f$, which have been calculated from equations 9 & 10. See the text

b K^* Is the slope of the lines shown in Fig. 8

concentration of vehicle. Equations 9 and 10 have a common factor which is the concentration of the vehicle. Therefore both hardness and friability can occur in a single expression such as

$$\log H = \log H_o - K^*/\log F_w/F \qquad \text{Eq. 11}$$

A plot log H vs $1/\log F_w/F$ is presented in Fig. 8. The experimental, calculated values for K^* and their correlation coefficients are presented in Table 5. Except for anhydrous lactose, the values obtained for H_o are close to the values obtained earlier on

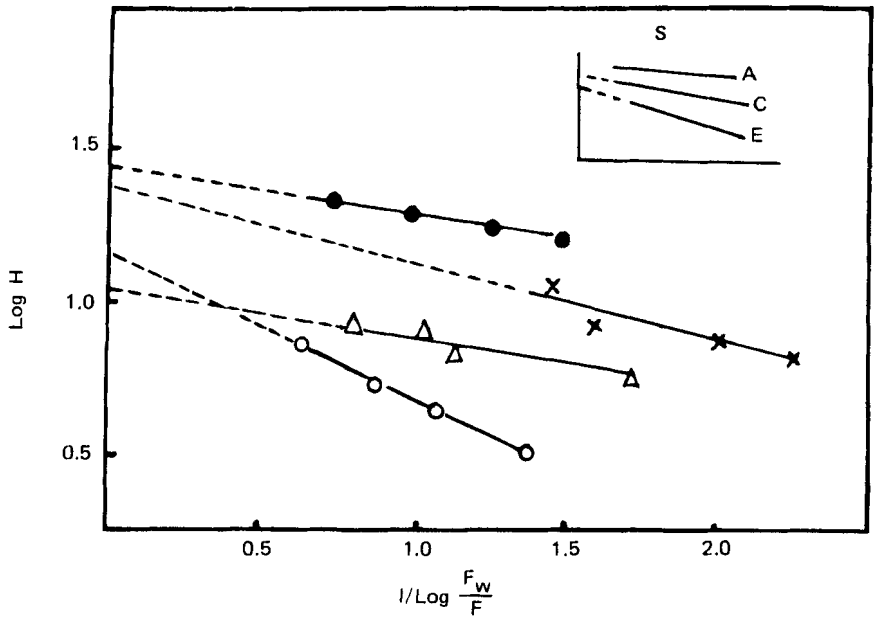

Fig 8. Log hardness (H) as a function of reciprocal log friability index of thiamine hydrochloride tablets directly compressed with varying concentrations of different vehicles. S for salicylamide data obtained from ref. 19: a,Avicel; a, Celutab and e, Emcompress.

Key: See Fig 1

(Table 3). The data obtained by Sakr et al (19) were treated with Eq. 11 and the result confirmed the validity of this expression.

Disintegration:

The disintegration time for the various tablets were presented in Tables 2a & b. All single vehicles except Emcompress yielded tablets that conformed to the B.P. disintegration test. An increase in vehicle concentration in the case of Avicel enhanced disintegration. When Emcompress is present in concen-

tration higher than 85% w/w, the tablets obtained failed the disintegration test. On the basis of effect on disintegration, the single vehicles may be arranged as

Avicel/Celutab> Anhy. lactose/Emcompress

At a concentration of 85% w/w, a 1:1 blend of Avicel with either anhydrous lactose or Celutab produced tablets with good disintegration time. Above this concentration the tablets failed the disintegration time. Above this concentration the tablets failed the disintegration test. On the contrary, a blend of Avicel with either STAR-x or Emcompress produced satisfactory tablets at all concentrations. The good disintegrating property of STAR-x is well known and it is not surprising that a blend of this vehicle and Avicel yielded tablets with the best disintegrating property. The contribution of Avicel in tablets containing Emcompress greatly improved their disintegration. This was probably due to the fact that fibrous Avicel which takes in liquid by a wicking action separated the more compact structure of Emcompress. On the basis of effect on disintegration the blends can be arranged in the following order:

Avicel/STAR-x < Avicel/Emcompress < Avicel/Celutab Avicel/Anhydrous lactose.

CONCLUSION

Thiamine hydrochloride powder was found to possess bad flow properties such that no less than 79% w/w of direct compression vehicle was needed to impart good flow properties. Single vehicles such as

Avicel PH 101, Celutab and anhydrous cellulose, USP were found suitable for compressing the drug into tablets. A blend of either of the vehicles in a 1:1 ratio with Avicel produced good tablets. On the other hand a blend of Avicel with either anhydrous lactose (1:3) or STAR-x (1:3) proved the best vehicle for this drug. In all cases, a good linear relationship between hardness and friability was established.

ACKNOWLEDGEMENTS

We are indebted to E. Mendell Co., Inc. U.S.A. and FMC, Corporation, U.S.A., for their free gifts of Emdex Emcompress and Avicel respectively.

FOOTNOTES

1. Roche Nig. (Ltd.) Lagos, Nigeria
2. FMC Corporation, Avicel Dept. Pennsylvania USA
3. Shiffield Union, N.L., 07083 USA.
4. E, Mendell Co. Inc., USA.
5. Slaley Mfg. Co. III. USA.
6. E. Merk N.J. USA.

I. Manesty Machine Ltd., Liverpool, U.K.

II. Erweka - Apparatabeau, Model HTB. 28 W. Germany

III. Model 120 - 1206, Baty Co. Ltd., Sussex, U.K.

REFERENCES

1. Mendell E., J. Manuf. Chem. & Aerosol News 43 43 (1972).

2. Kan, K.A. and Rhodes, C.T., Canad. J. Pharm. Sci, 8, (1973)

3. Warren, J.W. and Price, J.C., J. Pharm. Sci., 66, 1406 (1977).

4. Ibid, 66, 1409 (1977).

5. Henderson, N.J. and Bruno, A.J., J. Pharm. Sci, 59 1336 (1970).

6. Kwan, K.C. and Milosovich G., Ibid 55, 340 (1966)

7. Lerk C.F. and G.K. Bolhuis Pharm. Weekblad, 108, 469 (1973).

8. Aly, S.A.S. and Abu-Taleb, A.E., Drug Devel. & Ind. Pharm. in Press.

9. Shah, D.H. and Arambulo, A.S., This Journal, 1, 495 (1974 - 1975).

10. Broadbent, J.E., Mitchell, A.C. and O'Reilly, W.J., Aust. J. Pharm. Sci., 47, 592 (1966).

11. Sakr, A.M., A.H. Kassem, A.A. Aziz, A.H. Shalaby, Canad. J. Pharm.

12. Lerk, C.F. Bolhuis, G.K. and DE Boer, A.H., Pharm. Weekblad, 109, 945 (1974).

13. Fox, C.D., M.D. Richman, G.E. Riev and R.F., Shangraw, Drug Cosmetic Ind., 92, 258 (1963).

14. Bolhuis, G.K. and Lerk, C.F., Pharm. Weekbland 108, 46 (1973).

15. Richman, M.D., Fox, C.D., and Shangraw, R.F., J.Pharm. Sci., 54, 447, (1965).

16. Batuyias, M.A., ibid, 55, 727 (1966)

17. Mastuda, Y., Minamida, Y., and S.I. Hyashi, ibid, 65, 1155 (1976).

18. Duckworth, W., J. Am. Ceram. SOC., 36, 68 (1953).

19. Sakr, A.M. Kassem, A.A., Abu-Taleb A.E., Khidr, S.H. and Saleh, S.E., Egypt. J. Pharm. Sci., 17, 335 (1976).