DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 16(7), 1203-1216 (1990)

THE TABLETTING PROPERTIES OF DIKA FAT LUBRICANT

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ABSTRACT

The lubricant property of dika fat, a solid vegetable oil extracted from the kernels of Irvingia gabonensis var gabonensis and var excelsia was investigated. An instrumented tablet machine (ITM) was used to evaluate the effect of dika fat on the unit ejection force (EJF/A) of a model direct compression formulation. Dika fat, at equivalent concentration levels, performed better than magnesium stearate, stearic acid and a hydrogenated vegetable oil STEROTEX, in reducing EJF/A of tablets compressed from the model direct compression formulation. Dika fat imparted no adverse effect on the hardness, disintegration and dissolution of directly compressed hydrochlorothiazide tablets prepared in this study.

INTRODUCTION

A tablet dosage form contains in addition to the active drug other substances known as excipients which include fillers, disintegrants, binders and lubricants. Each of these confers on the material to be compressed some desirable characteristics.

Lubricants have been classified, based on their function as true lubricants, glidants and anti-adherents (1).

While some workers (2) have classified lubricants on the basis of their chemical structures other investigators have provided some other forms of classification (3-9).

The pharmaceutical literature is replete with lubrication studies and tests for lubricity using instrumented tablet machines. Several of the parameters used as indices for evaluating lubricants are investigated on instrumented eccentric and rotary presses (10-11).

Dika fat derived from Irvingia gabonensis var gabonensis and var excelsia is a solid vegetable oil. The technological step of hydrogenation is not necessary in its preparation since it is solid at room temperature.

In a previous study, dika fat was evaluated as a tablet lubricant in tablets made from basic lactose granulation (18). The purpose of the work reported here is the use of an instrumented tablet machine in evaluation of the effect of dika fat on the unit ejection force, EJF/A of a model direct compression formulation. Also, the effect of dika fat on the hardness, disintegration and dissolution of tablets compressed from some direct compression tablet formulations is reported.

EXPERIMENTAL

Materials.

Dika fat was obtained from Irvingia gabonensis by soxhlet extraction as previously described (18). The fat was further purified, bleached and deodorized by standard techniques (19).

The following substances were used as received from their manufacturers: hydrochlorothiazide (Industria Chimica, Italy), magnesium stearate (Amend Drug and Chem. Co., USA), maize starch, (A.E. Staley Co., USA), stearic acid (Baker Co., USA), STEROTEX (Capitol City Products, USA), unmilled dicalcium phosphate dihydrate, DITAB (Stauffer, USA) and hydrous lactose NF, FAST FLO LACTOSE (Foremost, USA).

Methods

Preparation of Dika Fat for Lubrication

Dika fat was mixed with dry ice and then milled in a Molineaux grinder (Type 530, Molineaux, France). The milled dika fat was

vacuum dried for 24 h and suitably stored in a dessicator containing calcium chloride granules as dessicant.

Composition of Tablet Formulations

Model direct compression formulation

DITAB	1 part
FAST FLO LACTOSE	1 part
Lubricant	2 and 4% w/w

Hydrochlorothiazide tablets

Hydrochlorothiazide	25 mg
DITAB	1 part
FAST FLO LACTOSE	1 part
Maize starch	7% w/w
Lubricant	1-4% w/w

Blending and Lubrication of Powder Mixtures

In all the formulations drugs and excipients except the lubricants were preblended for 5 min in a twin shell blender (model LB-3794, Patterson Kelly Co., PA, USA). Calculated quantities of required lubricants which had been bolted through a 250 micron aperture sieve were then added. Blending was then continued for 10 and 30 min respectively for the model direct compression formulation and the hydrochlorothiazide tablet formulations.

Compression of Tablets

A Stokes model RB-2 rotary tablet press (Stokes Engineering Philadelphia, PA, USA) which was instrumented as described previously (20) was used in this study. Metal foil resistance 'self temperature compensating strain gages" were used for the measurement of forces. The eyebolt of the tablet press was instrumented to measure compression forces in the manner of Wray et al (21). Tablet ejection forces were monitored by instrumenting a modified ejection cam according to Vincent et al (22). To eliminate bias due to differences in tablet thickness, recorded ejection forces were converted to unit ejection force by the relationship

$$\text{Unit ejection force, EJF/A} = \frac{\text{Ejection force, EJF}}{\pi . d . t .}$$

where d = diameter of the tablets and

t = thickness of the tablets.

Values of unit ejection force are reported in kg/cm^2. Tablets were compressed only on a single station of the tablet press to avoid possible tooling errors. The press speed during compression was fixed at 24 r.p.m. Tablet thickness and diameter were measured with a micrometer callipers (Tubular Micrometer Co., St. James, Minnesota) immediately after tabletting. The temperature and relative humidity in the tabletting room were maintained at 25 ± 2°C and 50 ± 10% respectively. The target ablet weight was 400 mg for the model direct compression and hydrochlorothiazide tablets.

Evaluation of Tablet Hardness

The hardness of ten tablets at each compression force was determined on a Pharma Test Hardness Tester (model HT-300, Key International Inc., NY) 24 h after the tablets had been made.

Disintegration Time Studies

Disintegration time of tablets was determined by the USP method using the Van der Kamp Disintegration Apparatus (model VK-5, Techne, Cambridge Ltd., England). The apparatus has the facility for testing six tablets simultaneously. The disintegration medium was 0.1 N HCl. Six tablets were tested at the same time and the average of the longest disintegration time within each group of six tablets was recorded. Disintegration time tests were performed for hydrochlorothiazide tablets only.

Dissolution Studies

The dissolution rate of tablets was monitored using an automated Van der Kamp-600 six spindle dissolution tester (model VK 600, Van Kel Industries, NJ, USA). The dissolution medium was 1000 ml of 0.1 N HCl maintained at 37°C. The revolution of the stirrer carried by the spindle was maintained at 50 r.p.m.

The dissolution medium was circulated through a UV spectrophotometer (model 25, Beckman Instruments, USA) by means of a Manostat Cassette pump (Manostat, NY, USA). Samples of the dissolution medium were analysed for hydrochlorothiazide at absorbance of 272 nm. Six dissolution studies were performed on tablets for each batch of tablets and the average percent drug dissolved plotted against time to generate a dissolution curve.

RESULTS AND DISCUSSION

Ejection force

The model direct compression formulation containing FAST FLO LACTOSE and DITAB was chosen for ejection force measurements because of the relatively high ejection forces required by the compacts. Therefore, the effectiveness of a lubricant can easily be monitored. A compression force range of 300 - 1800 kg was used so as to provide data over a wide range of tabletting conditions. A limitation was also imposed by the ITM which allows a maximum ejection force of 40 kg. The properties of the materials being investigated also influenced choice of range of compression force.

Hydrogenated vegetable oils when used as lubricants in tabletting often consist of 1-5% w/w of the final blend. Lubricant concentrations of 2 and 4% w/w were therefore used in the tabletting of mixtures containing DITAB and FAST FLO LACTOSE. Since lubricants are used at low concentrations in tabletting, their uniform distribution throughout the powder mix must be ensured. In this investigation, blending times were fixed at 10 and 30 min respectively. It was intended that a 10 min blending time would ensure proper mixing while 30 min would give indications of possible effects of prolonged blending.

The effect of dika fat on the ejection force of tablets compressed from the model formulation is shown in Fig 1. Fig 1 shows that ejection force increases with increase in compression force. These results are to be expected since both increase in lubricant concentration and prolonged blending should ensure a more efficient coating of particles being mixed thus ensuring decrease in ejection force. Knoechel et al (23) have stated that the relationship between compression force and ejection force is predictable and is independent of the material being compressed. The effect of 2 and 4% dika fat concentration on ejection force are significantly different from each other. Lower ejection force values were obtained at 4% dika fat concentration. Blending time similarly affected the ejection force of tablets containing dika fat. At all lubricant concentrations, tablets compressed

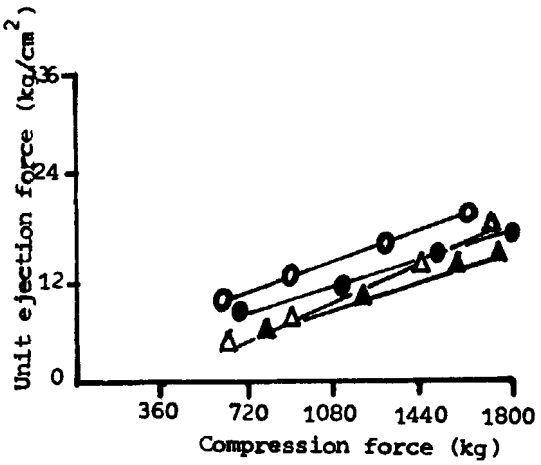

FIGURE 1

Effect of varying concentration and blending time of dika fat on the ejection force of tablets compressed from the model formulation.

O , 2% dika fat concentration and 10 min blending time
● , 2% dika fat concentration and 30 min blending time
Δ , 4% dika fat concentration and 10 min blending time
▲ , 4% dika fat concentration and 30 min blending time.

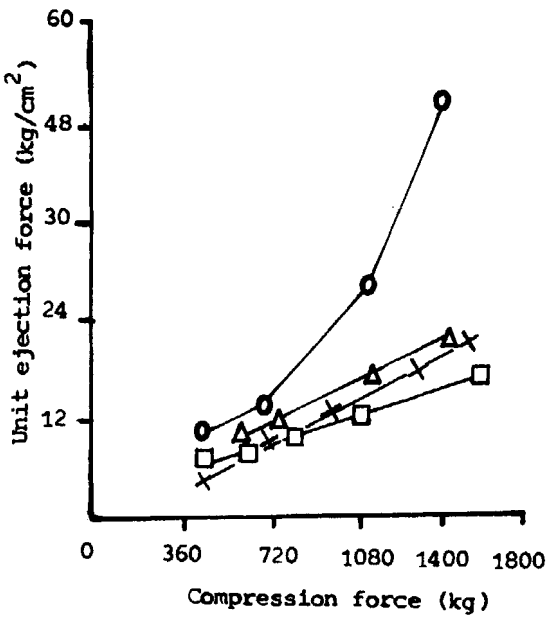

FIGURE 2

Effect of 2% w/w concentration of O, stearic acid; Δ, STEROTEX; X, magnesium stearate and □, dika fat at 30 min blending time of lubricant on the unit ejection force of tablets compressed from the model formulation.

from mixtures blended for 30 min yielded lower ejection force values than tablets compressed from mixtures blended for only 10 min.

The ejection force profiles of tablets compressed from the model formulation containing 2% of named lubricants and blended for 30 min are shwwn in Fig 2. Comparatively, dika fat performed better than stearic acid, STEROTEX and magnesium stearate with which it has been compared. A probable explanation for this result may be the relatively lower melting point of dika fat when compared with other lubricants. Bowden and Tabor (24) reported that the frictional contacts that occur during tabletting generate heat. The heat, these authors asserted, is capable of melting lubricants. The lower ejection force associated with tablets containing dika fat may therefore be due to enhanced boundary lubrication because of the ability of the fat to melt at the temperature of the tabletting process.

Hardness

The use of hardness in tablet formulation development includes determination of the basic properties of pure materials, quality control specification for in-process validation and the study of the effect of formulation and manufacturing variables on tablet strength. The formulation and manufacturing variables include the effects of granule size, moisture and lubricants. The effect of dika fat on the hardness of tablets compressed from the model formulation was determined at each compression force level. Fig 3 indicates that as compression force is increased tablet hardness is increased. It is well known that the hardness of tablets depends on the type, amount and length of blending of the lubricant. At 10 min blending time increase in the concentration of dika fat from 2 to 4% resulted in a decrease in tablet hardness. This decrease was more pronounced at higher compression forces. At 30 min blending time a similar effect of dika fat concentration was observed. The hardness of the tablets compressed from mixtures blended for 30 min were generally lower than those from mixtures blended for only 10 min. It is obvious that both the concentration and blending time of dika fat affect the hardness of tablets compressed from the model formulation. Lubricants, in order to function as such coat powder particles.

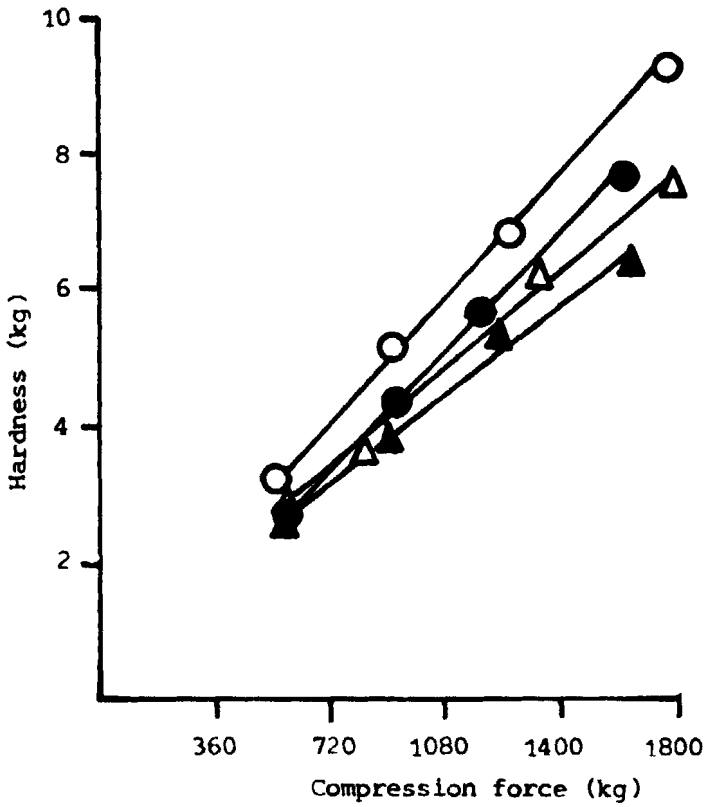

FIGURE 3

Effect of dika fat on the hardness of tablets compressed from the model formulation.
○, 2% dika fat concentration and 10 min blending time
●, 2% dika fat concentration and 30 min blending time
△, 4% dika fat concentration and 10 min blending time
▲, 4% dika fat concentration and 30 min blending time.

Shangraw et al (25) have stated that the smaller mean particle size of direct compression blends when compared with granulations, necessitate the use of higher concentration of lubricants to achieve fluidity. Because there are many more surfaces available to be covered with lubricants in direct compression, the softening effect upon compression is magnified. Increasing the concentration of dika fat obviously conformed with this expectation. Also increasing blending time lowered tablet hardness as expected.

Disintegration

Although used in small amounts in a formulation (0.5 to 5% w/w), lubricants can significantly affect the important tablet properties of disintegration and dissolution rate. It is important therefore, to evaluate the extent to which any substance proposed as a tablet lubricant may affect these tablet properties.

The disintegration time of the hydrochlorothiazide tablets prepared in this study is presented in Table 1. All the tablets passed the BP disintegration time test of 15 min for plain uncoated tablets. Increasing both the concentration and blending time of the lubricants did not have a significant effect on the disintegration time of the hydrochlorothiazide tablets. The concentrations of the lubricants investigated are within the range normally recommended for lubricants of the hydrogenated vegetable oil or fatty acid origin. Even at a concentration level as high as 4% and 30 min blending time dika fat did not prolong the disintegration time of hydrochlorothiazide tablets. Rather, relatively low disintegration times were obtained.

Dissolution

It is now routine to use dissolution tests in formulation work on solid dosage forms. It is used to compare the effect of additives such as lubricants on the bioavailability of tabletted dosage forms. The effect of dika fat on the dissolution behaviour of several formulations were evaluated.

The dissolution profile of hydrochlorothiazide tablets containing 1 to 4% dika fat are shown in Fig 4 a and b. Fig 4 a shows the profile of tablets compressed from powder mixes blended for 10 min while Fig 4 b shows those blended for 30 min. These figures show that increasing the concentration of dika fat affects the dissolution profile of the hydrochlorothiazide tablets. There is a discernible decrease in dissolution rate with increase in the concentration of dika fat. The effect of dika fat lubricant concentration on the dissolution of hydrochlorothiazide tablets is more marked and distinct in Fig 4 b which contains the dissolution profile of tablets compressed from powder mixtures blended for 30 min. The

TABLE 1

Effect of Varying Concentration of Lubricants and Blending Time on the Disintegration Time of Hydrochlorothiazide Tablets

Lubricant Conc. (%w/w)	Blending time (min)	Disintegration time (min) of Hydrochlorothiazide tablets containing			
		Magnesium stearate	STEROTEX	Dika fat	Stearic acid
1.0	10	2.61(1.63)	0.49(0.30)	0.44(0.13)	0.51(0.09)
	30	5.35(1.61)	1.51(0.83)	0.46(0.10)	0.66(0.14)
2.0	10	5.61(1.89)	0.70(0.34)	0.85(0.26)	0.69(0.29)
	30	7.17(2.03)	0.47(0.60)	0.48(0.29)	0.83(0.48)
3.0	10	-	1.55(0.99)	0.54(0.15)	1.06(0.40)
	30	-	1.38(0.72)	0.37(0.08)	1.17(0.29)
4.0	10	-	3.08(1.07)	0.39(0.07)	1.55(0.34)
	30	-	2.48(1.49)	1.27(0.60)	1.53(0.38)

• Values in brackets are the standard deviation

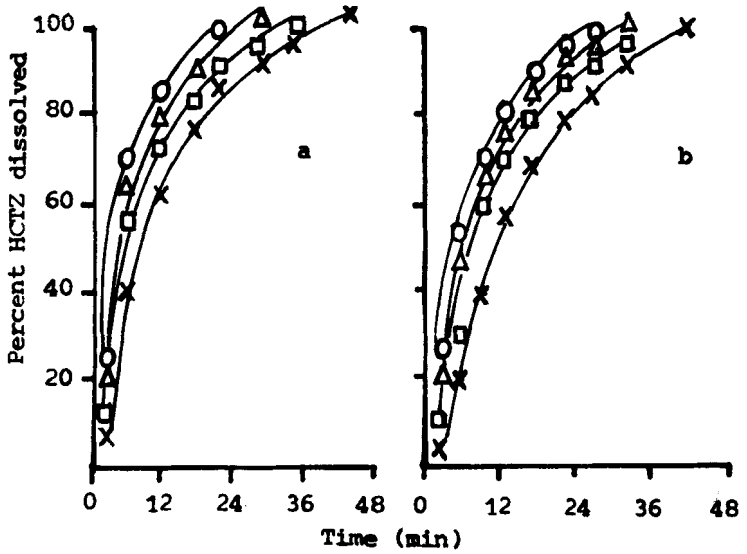

FIGURE 4

Dissolution profile of batches a and b hydrochlorothiazide (HCTZ) tablets compressed from powder mix blended for 10 and 30 min respectively to yield tablets containing O , 1%; Δ , 2%; □ , 3% and X, 4% w/w dika fat.

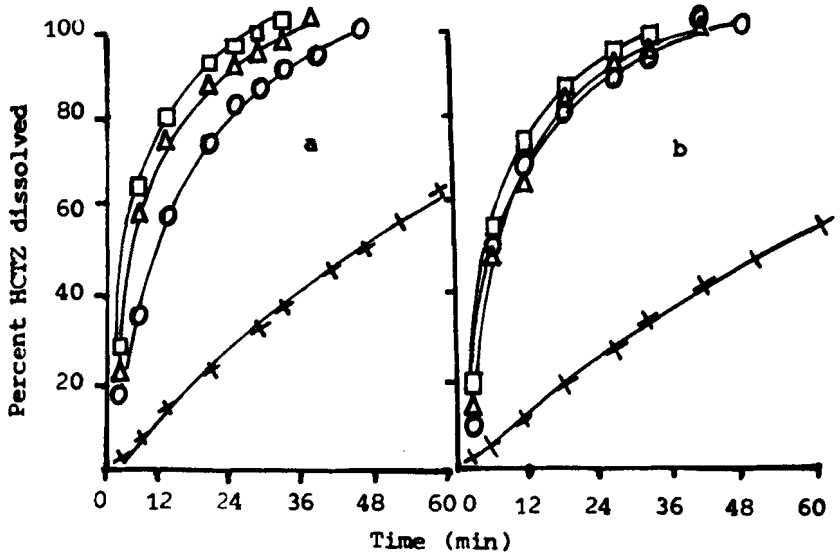

FIGURE 5

Dissolution profile of batches a and b hydrochlorothiazide (HCTZ) tablets compressed from powder mix blended for 10 and 30 min respectively to yield tablets containing 2% □, dika fat; Δ, STEROTEX; O, stearic acid and X, magnesium stearate.

observed effect is probably due to more distribution of the lubricant at a longer blending time. The observed effect of dika fat on dissolution is typical of hydrophobic lubricants which retard the dissolution of drugs from compressed tablets. The magnitude of this retardation is dependent on the type, concentration of lubricants and blending time of the powder mix.

The dissolution profile of hydrochlorothiazide tablets containing 2% of named lubricants are shown in Fig 5 a and b. Fig 5 a which shows the profile for tablets compressed from powder mixtures blended for 10 min indicates that tablets containing dika fat and STEROTEX recorded 100% hydrochlorothiazide release within 30 min of the dissolution test. On the other hand, tablets containing stearic acid attained 100% drug release at 40 min. Tablets lubricated with magnesium stearate released only 70% of the labelled hydrochlorothiazide content after 60 min of the dissolution test. A similar pattern of release previously described for hydrochlorothiazide tablets is repeated in Fig 5 b which shows the dissolution profile of tablets compressed from mixtures blended for 30 min. In both Figs 4 and 5, dika fat lubricant clearly performs better than all the other lubricants with which it has been compared.

CONCLUSION

Data from this investigation indicate that dika fat has potential as a tablet lubricant. On the basis of ejection force, tablets containing dika fat showed the least increase in ejection force as compression force was increased in the model direct compression formulation. Dika fat performed better than magnesium stearate, STEROTEX and stearic acid which were used as basis for comparison in the model formulation.

At concentration levels up to 4%, dika fat had no deleterious effect on the hardness of tablets compressed from the model formulation. Also, prolonging the blending time did not have any untoward effect on the hardness of tablets compressed from the model formulation.

Results obtained with the hydrochlorothiazide formulations should give an insight into the optimum use levels in dosage form

development work with dika fat. It was established that up to 4% dika fat can be used in the hydrochlorothiazide formulation. It was also established that variation in blending time from 10 to 30 min did not remarkably influence both properties of disintegration and dissolution of the hydrochlorothiazide tablets.

It is reasonable therefore to classify dika fat into the group of hydrophobic lubricants such as stearic acid and the hydrogenated vegetable oils which can be used at concentration levels up to 5% without significant adverse effect on the tablet properties of disintegration and dissolution.

The lack of a hydrogenation step in the processing of dika fat makes it an inexpensive substitute or supplement in tabletting technology. Thus, dika fat should find industrial application as a tablet lubricant.

ACKNOWLEDGEMENTS

One of us J. O. Onyechi would like to thank Professor Ralph Shangraw and Dr. Larry Ausburger of the Department of Pharmaceutics, University of Maryland at Baltimore for permission and assistance in the use of the instrumented tablet machine of the Department.

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