Auxilliary Dry Binding Properties of Some Hydrogenated Vegetable Oils in Direct Compression Tabletting

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Abstract

The ability of some hydrogenated vegetable oils to act as dry binder in direct compression tablet formulations was investigated using an instrumented rotary tablet press. The effect of these widely used tablet lubricants was compared to Avicel® PH 102, a standard, dry binding excipient in direct compression tablet formulations. The effects of the hydrogenated vegetable oils on the hardness, friability, disintegration time and dissolution of tablets made from the direct compression tablet formulations were evaluated. Dika fat, Lubritab®, Sterotex®, Stearolac-S® and stearic acid improved the hardness and friability profiles of a model direct compression tablet formulation as well as ascorbic acid and aspirin-acetaminophen tablet formulations. Prolonged mixing had no deleterious effect on the properties of the hydrochlorothiazide, ascorbic acid and aspirin-paracetamol tablets prepared. The hydrogenated vegetable oils appear to be a good alternative to Avicel® PH 102 as dry binder in the formulations evaluated.

Keywords: Hydrogenated vegetable oils, Auxiliary dry binding, Hardness, Friability, Disintegration time, Dissolution, Direct compression tablet formulations

Introduction

In pharmaceutical tabletting technology, hydrogenated vegetable oils are used as lubricants, and are made from fully hydrogenated refined vegetable oils that are sprayed onto dry, fine powder (Edward Mendell Co. Inc., USA, 1982). They are specifically created for application in the production of pharmaceutical tablets. Generally, they are used as lubricants in the range of 1 – 5% w/w (Shangraw, 1985) and as auxiliary dry binder when tablets and capsules tend to cap and laminate (Edward Mendell Co. Inc., USA, 1982). Used as dry binder, addition of up to 5 - 10% w/w can eliminate these problems and aid in producing satisfactory tablets. They are most effective when added in the dry state in the last blending operation before compression and mixed for 10 – 15 minutes (Edward Mendell Co. Inc., USA, 1982). When using hydrogenated vegetable oils as auxiliary binders, it is important that their effect on the tablet properties of hardness, friability, disintegration and dissolution be ascertained.

The objective of the present investigation was to evaluate the potential application of some hydrogenated vegetable oils as auxilliary dry binders in direct compression tabletting. The effects of the fats (Dika fat, Lubritab®, Sterotex®, Stearolac-S® and stearic acid) on the hardness, friability, disintegration time and dissolution rate of tablets made from three direct compression tablet formulations were compared to those of tablets containing Avicel® PH 102, a widely used auxilliary dry binder.

Materials and Methods

Dika fat was obtained from Irvingia gabonensis by soxhlet extraction as previously described (Onyechi, 1987). The fat was further purified, bleached and deodorized by standard techniques (Onyechi, 1987).

Lubritab® (Edward Mendell Co. Inc., USA), Sterotex® (Capitol City Products, USA), Stearolac-S® (Paniplus Coy., USA) and stearic acid (Baker Co., USA) were used as received from the manufacturers. The other excipients used were unmilled dicalcium phosphate, Ditab ® (Stauffer Chemical Coy., USA), hydrous lactose, Fast Flo ®Lactose (Foremost Foods, USA), compressible sugar, Dipac ® (Amstar, USA), Sta-Rx®1500 (A.E. Staley Co., USA), colloidal fumed silicon dioxide, Cab-O-Sil® (Carbot Corp., USA) and magnesium stearate (Amend Drug and Chem. Co., USA).

The drugs aspirin granules (Monsanto Chemical Co., USA), ascorbic acid (Roche, US), paracetamol granules (Mallinckrodt,

USA), hydrochlorothiazide (Industria Chimica, Italy) were used as received from their manufacturers.

Blending and lubrication of powder mixtures: In all the formulations (Table 1), drugs and excipients with no dry binders added were preblended for 5 min in a twin shell blender (Model LB-3794, Patterson Kelly Co., PA, USA). Calculated quantities of the dry binders were then added after being passed through a 250 µm aperture sieve. Blending was then continued for 5, 10 and 30 min respectively for the model direct compression formulation. The aspirin-acetaminophen, ascorbic acid and hydrochlorothiazide tablet formulations were blended for a further 10 and 30 min respectively.

Table 1: Composition of tablet formulations

Content	Quantity
Model direct compression formulation	
Unmilled dicalcium phosphate (Ditab®)	1 part
Hydrous lactose (Fast Flo ®Lactose)	1 part
Hydrogenated vegetable oils	1-5, 10% w/w
Hydrochlorothiazide tablets	
Unmilled dicalcium phosphate (Ditab®)	1 part
Hydrous lactose (Fast Flo ®Lactose)	1 part
Hydrochlorothiazide	25 mg
Sta-Rx®1500	7% w/w
Hydrogenated vegetable oils	1-5, 10% w/w
Ascorbic acid tablets	
Ascorbic acid	210 mg
Compressible sugar (Dipac ®)	40 mg
Colloidal fumed silicon dioxide (Cab-O-Sil®)	0.5% w/w
Hydrogenated vegetable oils	5, 10 % w/w
Aspirin-Paracetamol tablets	
Aspirin granules	345 g
Paracetamol granules	290 g
Hydrogenated vegetable oils	5, 10 %w/w

Dika fat at a range of 1 - 5 and 10% w/w concentration levels were used in all the formulations. Tablet properties evaluated were hardness, friability, disintegration time and dissolution rate. Other dry binders used as basis for comparison were Avicel® PH 102 and the hydrogenated vegetable oils Sterotex® , Lubritab®, Stearolac-S® and stearic acid

Instrumentation of rotary tablet press: A Stokes model RB-2 rotary tablet press (Stokes Engineering Philadelphia, PA, USA) which was instrumented as described previously (Salpekar and Augsburger, 1974) was used in this study. Metal foil resistance 'self temperature compensating strain gauges' 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* (1966).

Measurement of compression forces: The eyebolt of the Stokes RB-2 machine was instrumented to measure compression forces. The instrumentation technique has been described previously (Salpekar and Augsburger, 1974, 1974).

Compression of tablets: Tablets were compressed on a Stokes model RB-2 rotary tablet press (Stokes Engineering) which can simultaneously monitor compression and ejection forces. Only a single station of the tablet press was used to avoid possible tooling errors. The press speed during compression was fixed at 24 rpm. Tablet thickness and diameter were measured with a micrometer calipers (Tubular Micrometer Co., St. James, Minnesota) immediately after tabletting. The temperature and relative humidity in the tabletting room were maintained at 25 ± 2 ^{0}C and 50 ± 10% RH respectively. The tablet press was adjusted to give tablets of 400 mg weight for the model direct compression and hydrochlorothiazide tablet formulations. The weights were 300 mg for ascorbic acid tablets and 630 mg for aspirin-paracetamol tablets

A compression force range of 300-1800 kg was used for compressing mixtures containing Ditab ® and Fast Flo ®Lactose. The range of force for mixtures containing ascorbic acid was 200 -1000 kg. The range of compression forces were chosen to provide data over a wide range of tabletting conditions. A limitation was also imposed by the instrumented tablet press which allows a maximum ejection force of 40 kg. The properties of the materials being investigated also influenced choice of range of compression forces. The poorly compressible ascorbic acid was compressed at a lower range of compression force. On the other hand the mixture of Ditab® and Fast Flo ®Lactose was compressed at the higher range of compression force.

Evaluation of tablet hardness: Ten tablets were used to determine hardness at each compression force on a Pharma Test Hardness Tester (Model HT-300, Key International Inc., NY) 24 h after the tablets had been made. The HT-300 model incorporates an automated push button

activated printer which supplies a reading for every tablet tested as the high, low and average force values.

Evaluation of friability: The friability loss of 20 tablets from each batch at each compression force was determined on a Van der Kamp 'Roche type' friabilator (Model No. 10809, Van-Kel Industries, Inc., NJ, USA). Per cent friability was calculated from the relationship:

Friability % = $W_I - W_F / W_I \times 100$,

where W_I = the initial weight of 20 dedusted tablets and W_F = the weight of the tablets after revolution of the friabilator drum.

Evaluation of disintegration time of tablets: Disintegration time of tablets was determined by the USP method using the Van der Kamp Disintegration Apparatus (Model VK-5, Techne, Cambridge Limited, England). A 0.I N HCl was the disintegration medium. The Van der Kamp apparatus has the facility for testing six tablets simultaneously. Two runs in which six tablets were tested at the same time were made. The average of the longest disintegration time within each group of six tablets was recorded. Disintegration time tests were performed for ascorbic acid, aspirin-paracetamol and hydrochlorothiazide tablets only.

Dissolution studies on tablets: The dissolution rates of tablets were 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.I N HCl maintained at 37 ^{0}C. The stirring rates of the spindles of the dissolution apparatus was maintained at 50 r.p.m.

Analysis for the drug content of the dissolution medium was performed with a UV spectrophotometer (Model 25, Beckman Instruments, USA.). Samples were circulated to the spectrophotometer via a Manostat Cassette pump (Manostat, NY). The absorbance of ascorbic acid, hydrochlorothiazide, aspirin and paracetamol were measured at 245, 272, 229 and 249 nm respectively. Dissolution studies were performed on six tablets for each batch of tablets. The dissolution data were plotted as percent drug dissolved against time and each datum point represents the average of the six.

Statistical analyses of data: All statistical analyses (linear regression, ANOVA, stepwise regression) were performed with the aid of "canned" software programs written for a desktop calculator/computer.

Results and Discussion

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 variable include the effects of granule size, moisture and lubricants. The effects of the hydrogenated vegetable oils on the hardness of tablets compressed from a model direct compression tablet formulation containing equal parts of Ditab ® and Fast Flo® Lactose are shown in Fig. 1. Tablet hardness was determined at each compression force level. Fig. 1 illustrates that at the 4% w/w concentration level, as compression force increased tablet hardness also increased. Similar results were obtained by other workers. Lerk *et al* (1974) reported increase in the crushing strength of tablets with increase in applied force. The system investigated by these workers contained direct compression dicalcium phosphate and microcrystalline cellulose. Goh and co-workers (2008) also showed that increasing compression force resulted in corresponding increase in the hardness of tablets prepared from salt, starch and fat mixtures.

In Fig. 2, the effect of Lubritab® concentration and mixing time on the hardness of tablets made from the model formulation is shown. It can be seen that prolonged mixing of Lubritab® for 30 min did not influence the hardness of the tablets adversely. This is typical of results obtained for the hydrogenated vegetable oils used in this study. It is well known that the hardness of tablets depends on the type, amount and length of blending of the lubricant. Fig. 3 showed the effect of the hydrogenated vegetable oils on the hardness of ascorbic acid tablets at 4 %w/w level of concentration. The hardness increased as compression force increased. However, the dika fat and stearic acid containing ascorbic acid tablets exhibited higher hardness values compared to those containing Sterotex® and Lubritab®. There was no deleterious effect on the hardness of the ascorbic acid tablets.

Fig. 4 showed the effect of Lubritab® concentration and blending time on the hardness of ascorbic acid tablet formulation.

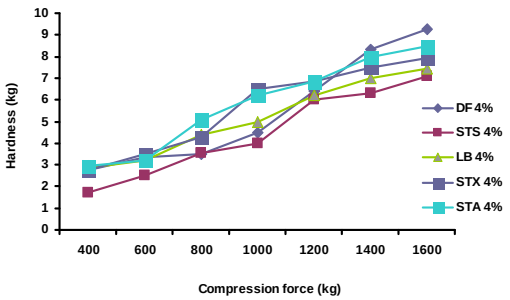

Fig. 1: Typical effect of hydrogenated vegetable oils on the hardness of tablets from a model direct compression tablet formulation

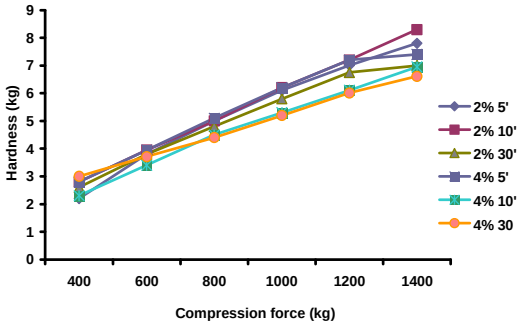

Fig. 2: Effect of Lubritab concentration and mixing time on the hardness of tablets from the model direct compression tablet formulalion

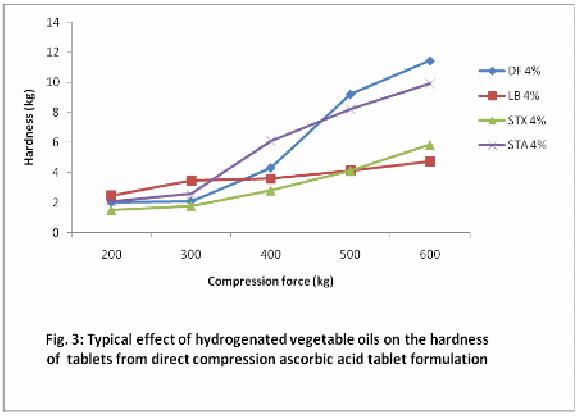

Fig. 3: Typical effect of hydrogenated vegetable oils on the hardness of tablets from direct compression ascorbic acid tablet formulation

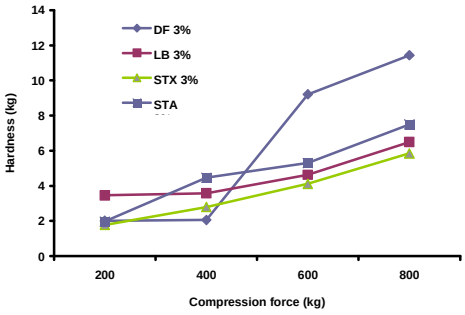

Fig. 4: Typical effect of hydrogenated vegetable oils on the hardness of a direct compression ascorbic acid tablet formulation

Figure 4 illustrates that prolonged mixing did not affect the hardness of the ascorbic acid tablets at all concentrations and blending times investigated.

The typical effect of the hydrogenated vegetable oils on the hardness of tablets compressed from direct compression aspirin-acetaminophen formulation is shown in Fig 5. It can be seen that increasing the concentration of dika fat from 5 to 10 %w/w resulted in a marginal decrease in tablet hardness. This decrease was more pronounced at higher compression forces. The effect of increasing Lubritab® concentration from 5 to 10% w/w, on the hardness of tablets compressed from the aspirin-paracetamol formulation was opposite to that obtained for dika fat. The hardness of tablets containing 10 %w/w Lubritab® was higher than that of those containing 5 %w/w (Fig. 5). Dika fat in this regard acted like a typical lubricant by decreasing tablet hardness at higher concentration while Lubritab® on the other hard exhibited auxiliary dry binding characteristic (Edward Mendell Co. Inc., USA, 1982). Tablets containing 10 %w/w Avicel® PH 102 and PEG 6000 exhibited higher hardness values compared to tablets containing equivalent concentrations of dika fat or Lubritab® indicating potential dry binding capability.

The effect of named excipients on the friability of the aspirin-paracetamol tablets was evaluated and is shown in Fig. 6. Fig. 6 showed that friability decreased as compression force of the tablets increased. Lubritab® containing tablets exhibited friability profiles better than those of tablets containing Avicel® PH 102 or PEG 6000.

Fig. 7 showed the effect of Sterotex® concentration and mixing time on the friability of tablets compressed from the model formulation. Fig. 7 showed that at all compression force levels, increasing compression force caused a corresponding decrease in the friability of the tablets. The friability tended to a constant regime. Fig 7 also indicates that prolonged blending of the formulations did not adversely affect the friability of the tablets containing Sterotex®.

Fig. 8 showed the effect of concentration and blending time of the hydrogenated vegetable oils on the disintegration time of hydrochlorothiazide tablets. Comparatively, the order of decreasing disintegration time was Avicel® PH 102 < dika fat < PEG 6000 < Lubritab®. However, the tablets all met the BP requirement for standard tablets, all the tablets disintegrating within 15 minutes of the test.

Fig 9 showed the effects of the hydrogenated vegetable oils on paracetamol dissolution from the aspirin-paracetamol tablet formulation.

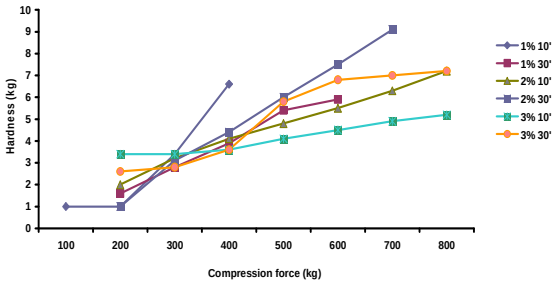

Fig. 5: Effect of Lubritab concentration and mixing time on thehardness of ascorbic acid tablets

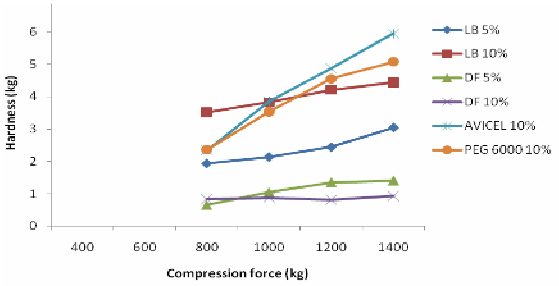

Fig 6: Typical effect of named excipients on the hardness of tablets compressed from a direct compression acetaminophen tablet formulation

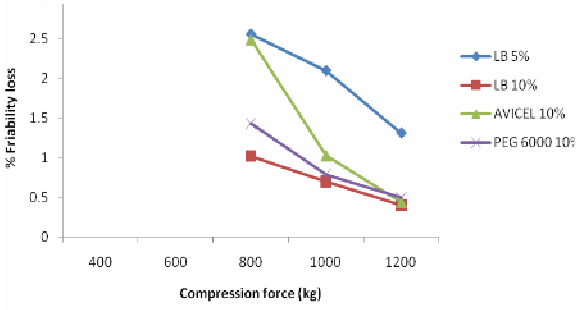

Fig. 7: Typical effect of excipients on the friability of tablets from direct compression aspirin-acetaminophen tablet formulation

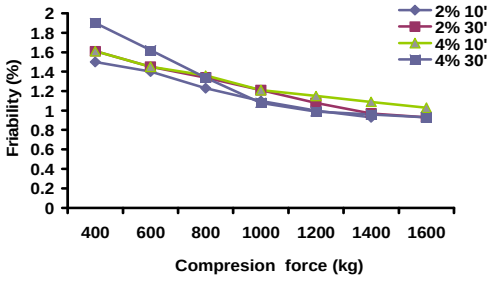

Fig 8: Effect of STX concentration and mixing time on the friability of tablets compressed from the model direct compression formulation

There was no significant difference in the dissolution from tablets containing 5 and 10 %w/w dika fat. Dissolution from tablets containing 10 %w/w PEG 6000 was similar to that from tablets containing 10 %w/w Lubritab®. Dissolution was more from tablets containing 5 %w/w Lubritab® compared to those containing 10% w/w of the hydrogenated vegetable oil. The $T_{50\%}$ and $T_{90\%}$ for aspirin dissolution from the aspirin-paracetamol tablets are shown in Table 2. The $T_{50\%}$ and $T_{90\%}$ for paracetamol dissolution from the aspirin-paracetamol dissolution is shown in Table 3. The release of either aspirin or paracetamol from the aspirin-paracetamool tablets met BP (2003) requirements. Neither the concentration of the hydrogenated vegetable oils nor the prolongation of blending time caused delay in the release of the actives from the formulations.

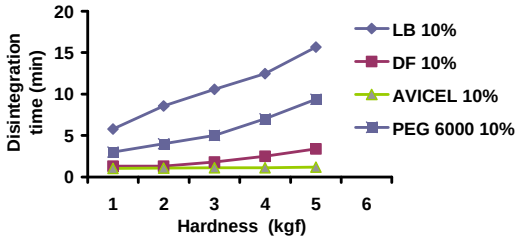

Fig 9: Typical effect of excipients on the disintegration time of tablets compressed from a direct compression hydrochlorothiazide tablet formulation

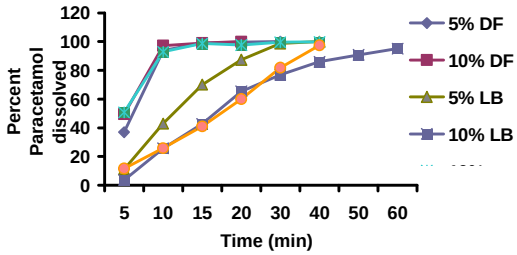

Fig. 10: Typical effect of excipients on paracetamol dissolution from aspirin-paracetamol tablets

Table 2: The $T_{50\%}$ and $T_{90\%}$ for aspirin dissolution from aspirin-paracetamol tablets containing 4% named excipients and compressed to 6.0 ± 1 kg hardness

Named excipient	$T_{50\%}$ (min)	$T_{90\%}$ (min)
Dika Fat	6.00	13.50
Stearolac-S®	5.00	11.50
Sterotex®	7.00	14.00
Lubritab®	8.50	24.00
Stearic acid	13.00	39.00

Table 3: The $T_{50\%}$ and $T_{90\%}$ for paracetamol dissolution from aspirin-paracetamol tablets containing 4% named excipients and compressed to 6.0 ± 1 kg hardness

Named excipient	$T_{50\%}$ (min)	$T_{90\%}$ (min)
Dika Fat	6.50	17.50
Stearolac-S®	8.00	19.50
Sterotex®	9.50	22.50
Lubritab®	11.50	27.50
Stearic acid	12.00	28.00

Conclusions: The effects of dika fat, Lubritab®, Sterotex®, Stearolac-S® and stearic acid on the tablet properties of direct

compression tablet formulations have been determined. Overall, these hydrogenated vegetable oils, at 5 - 10 %w/w concentration levels, produced desirable hardness and friability profiles in the direct compression tablet formulations evaluated. All the fats produced formulations that passed the USP 23 requirements of 60% hydrochlorothiazide dissolution within 60 minutes Lubritab® was found to be a good auxilliary dry binder for aspirin-paracetamol tablets. The hydrogenated vegetable oils appear to be a good alternative to Avicel® PH 102 as auxiliary dry binder in the direct compression tablet formulations evaluated.

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