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USE OF HYDROGENATED VEGETABLE OIL AS A TABLET LUBRICANT

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A tablet machine instrumented using piezo-electric load cells was used to study the influence of hydrogenated vegetable oil (H.V.O.) on tablet ejection forces, in comparison with magnesium stearate. Whilst it was found that magnesium stearate was a more efficient tablet lubricant than H.V.O. alone, when mixed with some anti-adherent excipients, H.V.O. was found to produce comparably low ejection forces.

The strength and toughness of tablets containing H.V.O. were markedly higher than those containing magnesium stearate.

Unlike magnesium stearate-containing tablets, those made using H.V.O. maintained virtually constant strength and toughness even following prolonged mixing.

Dry powder mixes containing H.V.O. were found to be more resistant to segregation following vibration under conditions encountered during tablet production, than similar mixes containing magnesium stearate.

INTRODUCTION

Successful tablet production depends on the ability to eject completed tablets without disrupting or damaging them and without causing excessive wear of punches or dies. Many tablet formulations produce significant die wall friction which prevents tablet production without addition of a lubricant or lubricants.

As a class of excipients, tablet lubricants act by reducing inter-surface friction, so that lubrication is achieved by reduction of friction between die walls and powder particles. However, the ability of lubricants to efficiently reduce friction also means that they may be effective as anti-adherents, in reducing die wall sticking and punch face picking and as glidants where reduction of inter particle friction can improve powder flow properties.

Of the tablet lubricants currently in use it appears that magnesium stearate is frequently the lubricant of choice for a given formulation. The reason for this is probably due to the highly efficient performance of magnesium stearate purely as a lubricant.

The lubricant action of magnesium stearate appears to be due to the formation of a thin molecular film around the surface of powder particles or granules which has the ability to be sheared easily [1] However, the very presence of this hydrophobic film of magnesium stearate may be responsible for many of the adverse effects it is found to have on both powder and tablet properties, including loss of homogeneity and loss of mechanical strength [2,3,4].

For these reasons, alternative materials have been proposed which would enable tablet lubrication to be achieved without detriment to other formulation factors.

In the present study, hydrogenated vegetable oil (H.V.O.) has been investigated alone and in combination with other excipients, in comparison with magnesium stearate-containing formulations. The properties studied include the influence of hydrogenated vegetable oil on lubricity; tablet strength and toughness; compressibility following mixing; homeogeneity and physical stability of powder mixes.

MATERIALS AND METHODS

(i) Lubricity

Prior to tableting, powders were mixed for 30 min in a cube blender fitted with intensifier bars (Type AR400, Erweka GmbH, Frankfurt, FRG) rotated at approximately 40 rev min^{-1} and containing 500 g of powder. The principle excipient with which all lubricant and anti-adherent powders were mixed was Emcompress, a direct compression form of dibasic calcium phosphate dihydrate (Edward Mendell Co Inc, New York, USA and Redhill, UK). The lubricants used were hydrogenated vegetable oil, H.V.O. (LUBRITAB, Edward Mendell Co Inc) and magnesium stearate (GPR grade, batch 937972OD, BDH Chemicals Ltd, Poole, UK). Some other materials were used as anti-adherents in combination with H.V.O. : Purified Talc B.P. (Evans Medical ltd., Speke, UK); a sucrose ester (TAL 160T, Contract Chemicals, Warrington, UK); magnesium lauryl sulphate (Albright & Wilson, Whitehaven, UK).

10 mm flat-faced tablets weighing 400 mg were compressed on a reciprocating tableting machine (type F3, Manesty Machines Ltd, Liverpool, UK) instrumented using load cells (type 9021 and 9031,

Kistler Instruments, Switzerland). The output signal from each load cell was amplified and fed to a microcomputer (model B, BBC, Acorn Ltd, Cambridge, UK) via a fast analogue - digital converter. At each compression event, upper and lower punch forces were monitored as was ejection force.

(ii) **Tablet strength**

Following compression the mechanical strength of each 400 mg tablet was determined using a tensile testing apparatus (type T22K, JJ Instruments, Southampton, UK) fitted with a 500 N load cell and a linear variable displacement transducer (type AG2.5, Sangamo Schlumberger, Bognor Regis, UK). The amplified signals from both load cell and LVDT were passed via a fast a-d converter to a microcomputer which calculated tablet tensile strength and normalized work of failure. Tensile strength, σ, was calculated using the relation in equation 1:

$$\sigma = \frac{2F}{Dt}\pi \qquad (1)$$

where F is diametral peak force at failure, D is tablet diameter and t is tablet thickness. Normalized work of failure, e, was calculated using equation (2):

$$e = \frac{\left[\int_{F_o}^{Fmax} F.dx\right]}{A} \qquad (2)$$

where x is cross-head displacement and A is cross-sectional area of failure.

The influence of powder mixing time on the strength and toughness of compressed tablets was also studied. Lubricant powders were mixed with microcrystalline cellulose powder (EMCOCEL, Edward Mendell and Co Inc, Carmel, New York) for different lengths of time using a cube blender (Erweka, GmbH, Ludwigshafen, FRG).

(iii) **Powder mixing and segregation**

In all cases, an initial geometric mixing stage was carried out to disperse the cohesive lubricant particles throughout the other component powders and this was followed by mixing for approximately 30 min in a cube blender (Erweka GmbH). After this time samples each weighing 400 mg were removed at random from the blended powder. The samples were analyzed for ascorbic acid content (Batch 3050039, Roche Ltd, Welwyn Garden City, UK) using UV absorption spectrophotometry at λ_{max} = 264 nm. When an acceptable level of drug homogeneity had been achieved, the powder mix was subjected to vibration in a model system previously described elsewhere [5]. Each powder system was vibrated for 15 min at a frequency of 50 Hz and an acceleration of 3g (29.43 ms^{-2}). Following vibration, a further 10 samples each weighing 400 mg were removed at different levels in the powder bed for analysis. The homogeneity of a given powder system during mixing or vibration was characterized using measurements of coefficients of variation (CV) calculated according to equation 3:

$$CV = \frac{\sigma_{n-1}}{\bar{x}} \times 100\% \qquad (3)$$

where σ_{n-1} is the standard deviation of spot samples and $\bar{x}$ is the mean drug content of spot samples.

In some cases colloidal silica (Aerosil, Degussa, FRG) was added to the other component powders during mixing.

RESULTS AND DISCUSSION

(i) Lubricity

Tablets compressed using Emcompress mixed with 0.5% HVO showed a tendency for sticking to occur, and there was also some evidence of sticking at 2% although this was absent at 5% concentration. At a level of 5% HVO acted as a satisfactory lubricant although the magnitude of ejection forces were consistently slightly higher than the corresponding compression force/ejection force profile for magnesium stearate (fig 1).

In view of the slight tendency for HVO to cause sticking, the influence of some potential anti-adherents was investigated. A mixture of 2% talc with H.V.O. produced variable upper punch forces and there was evidence of picking, especially on the lower punch. Increasing the concentration of talc to 5% reduced the picking effect and at 7.5% talc it was virtually absent. Mixing talc with HVO had little effect on the ejection force profiles (fig.2) and it appears that H.V.O. was acting as the principle lubricant whereas talc was effective as an anti-adherent at higher concentrations. Use of maize starch in place of talc, at a concentration of 5% also acted as an efficient anti-adherent, again with no significant influence on ejection force (fig.2).

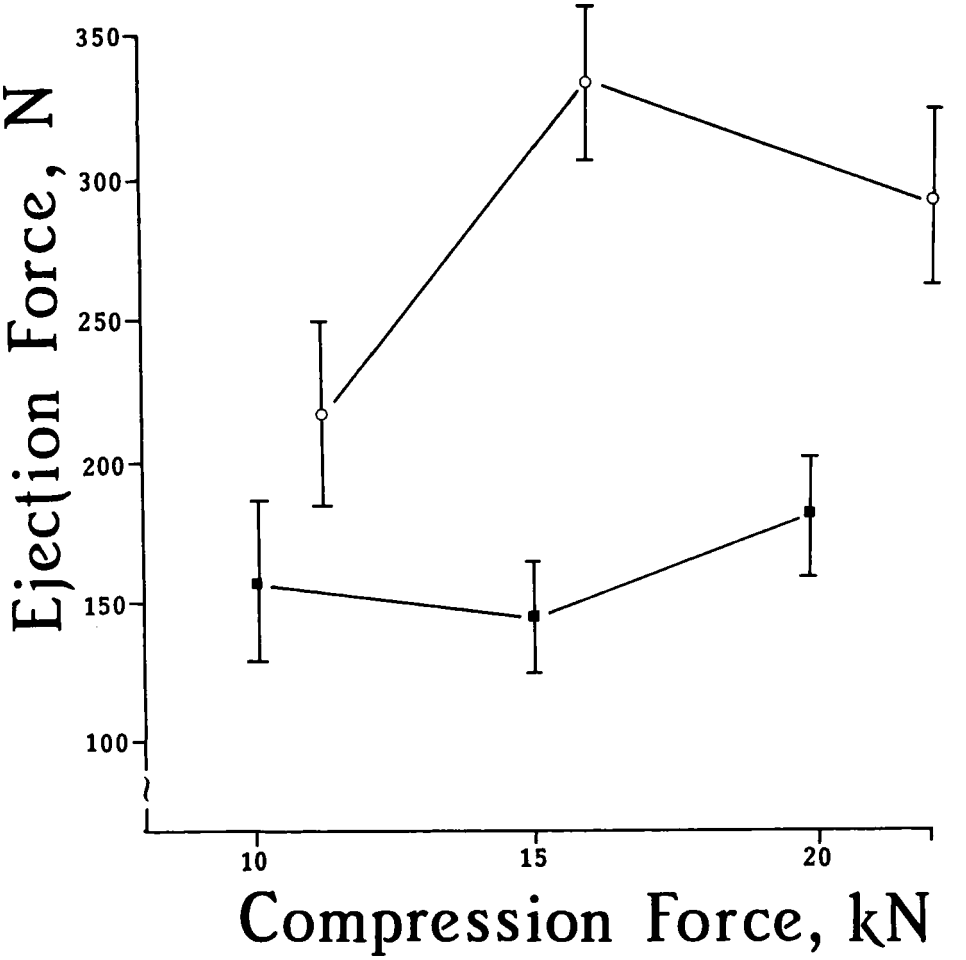

FIGURE 1
Relationship between tablet ejection forces and compression forces for mixtures of dicalcium phosphate (Emcompress) with 5% HVO (Lubritab) O , and 0.5% magnesium stearate ■ .

Use of meagnesium lauryl sulphate at a concentration of 2% in combination with HVO produced an improved lubrication effect, such that ejection forces fell to levels comparable with or below those for magnesium stearate (fig.3). The combination of HVO and magnesium lauryl sulphate also improved the anti-adherent qualities of the system.

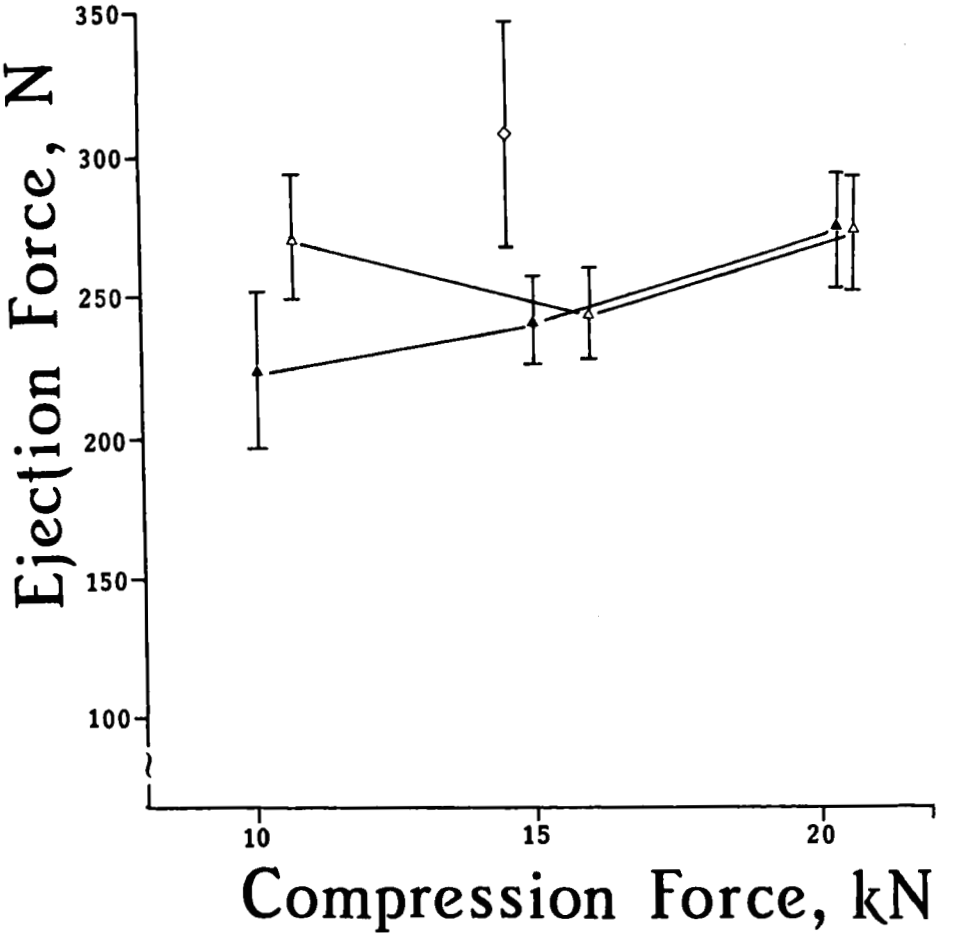

FIGURE 2
Relationship between tablet ejection forces and compression forces for mixtures of dicalcium phosphate (Emcompress) with : 5% HVO + 5% talc △ ; 5% HVO and 7.5% talc ▲ ; 5% HVO and 5% maize starch ◇

Use of sucrose ester 160T also improved the lubricant qualities over use of HVO alone (fig. 4), although in this case there was no reduction in tablet picking or sticking.

(ii) **Tablet Toughness**

The tensile strength and normalized work of failure profiles for tablets compressed from Emcompress with HVO were found to be

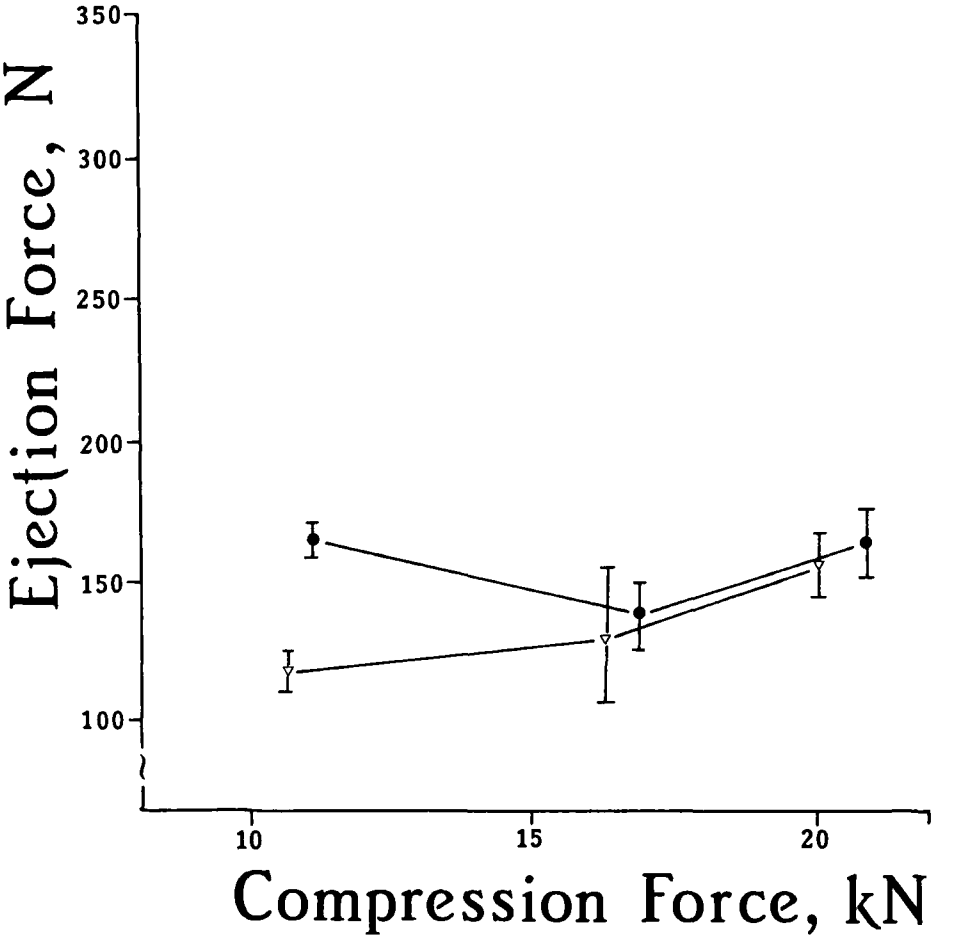

FIGURE 3
Relationship between tablet ejection forces and compression forces for mixtures of dicalcium phosphate (Emcompress) with : 5% HVO + 2% magnesium lauryl sulphate ● ; 5% HVO and 5% magnesium lauryl sulphate ▽

significantly higher than in cases where magnesium stearate was used as the lubricant (fig.5).

At some compression forces the tensile strength of tablets containing HVO were found to be twice that for magnesium stearate - containing tablets, and the normalized works of failure for HVO

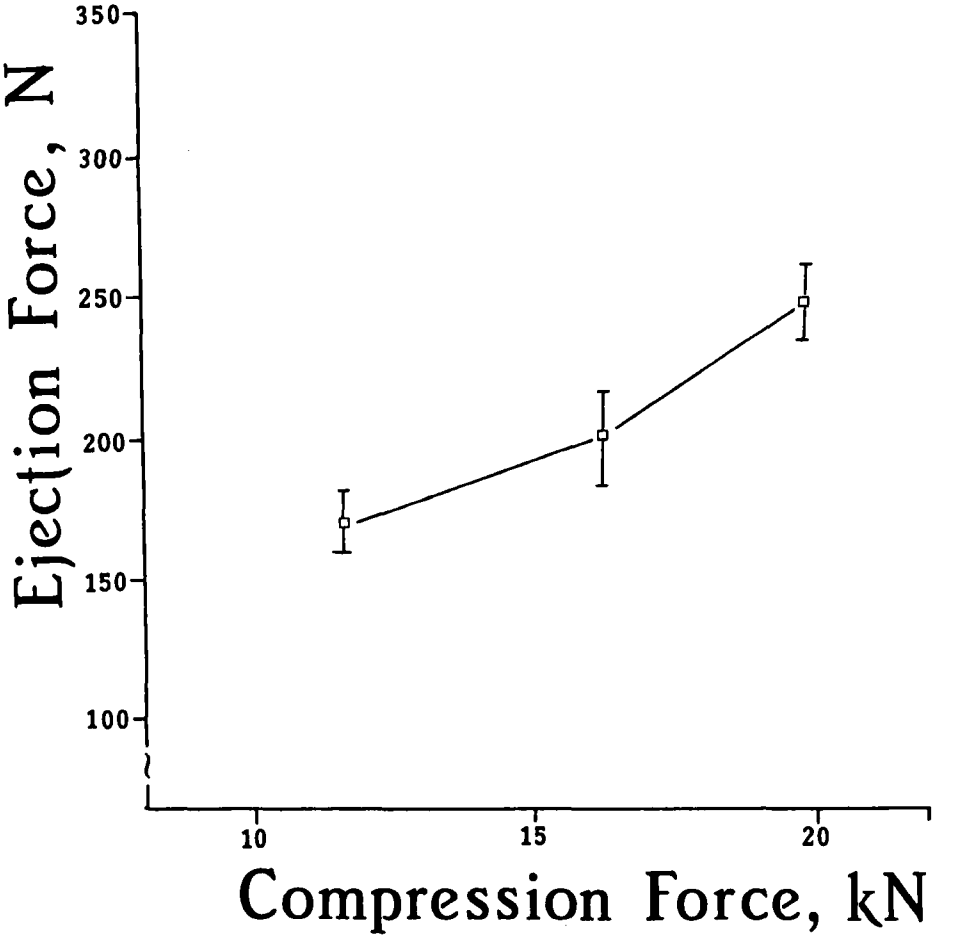

FIGURE 4
Relationship between tablet ejection forces and compression forces for mixtures of dicalcium phosphate with : 5% HVO and 2% sucrose ester.

tablets were three times the magnitude of magnesium stearate tablets. In the case of complex lubricant/anti-adherent systems, use of 5% talc in combination with HVO further improved the work of failure of tablets, although $7\frac{1}{2}$% talc had a deleterious effect on compression strengths and toughnesses (fig 6).

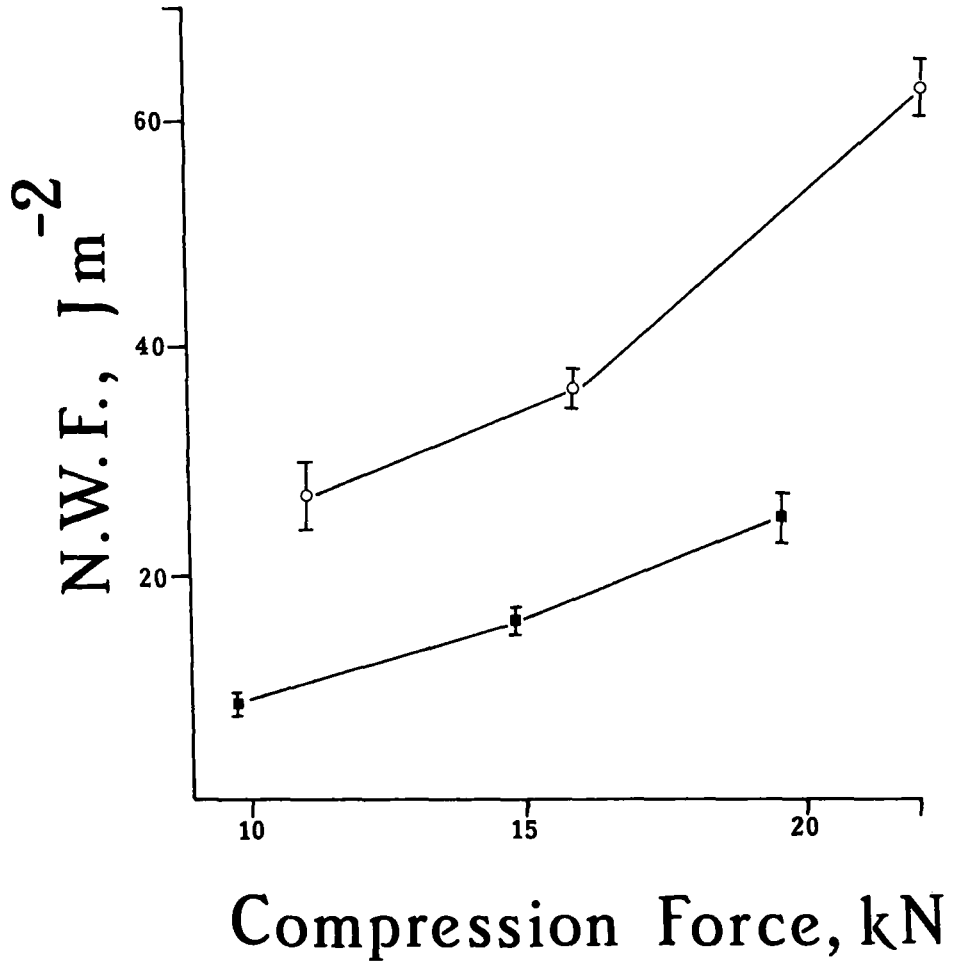

FIGURE 5
Relationship between normalized work of failure (NWF) values and compression forces for dicalcium phosphate tablets lubricated with : 0.5% magnesium stearate ■ ; 5% HVO (Lubritab) ○ .

Use of sucrose ester 160T had virtually no influence on the strength or toughness in comparison with use of lubritab alone, whereas use of magnesium lauryl sulphate at a concentration of 5% further increased the strength and toughness of tablets (fig.7).

It was also found that mixing time influenced the strength and toughness of tablets containing microcrystalline cellulose and

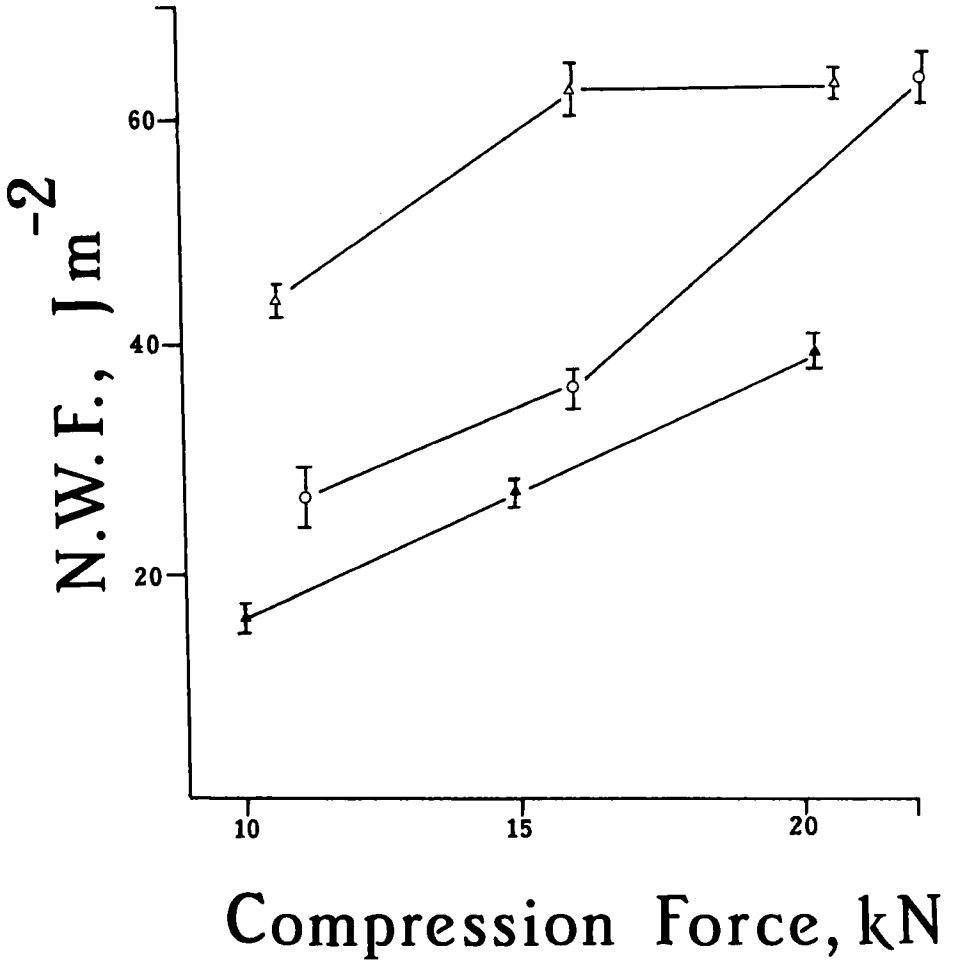

FIGURE 6
Relationship between normalizrd work of failure (NWF) values and compression forces for dicalcium phosphate tablets lubricated with : 5% HVO and 5% talc △ ; 5% HVO and 7.5% talc ▲ .

magnesium stearate far more than those containing HVO (fig.8). Indeed, accepting that the presence of HVO, like all efficient lubricants, reduced the strength of tablets, there was very little subsequent change in strength, even after prolonged mixing. In contrast, fig.7 shows that tablets containing magnesium stearate continued to lose compressibility as mixing continued.

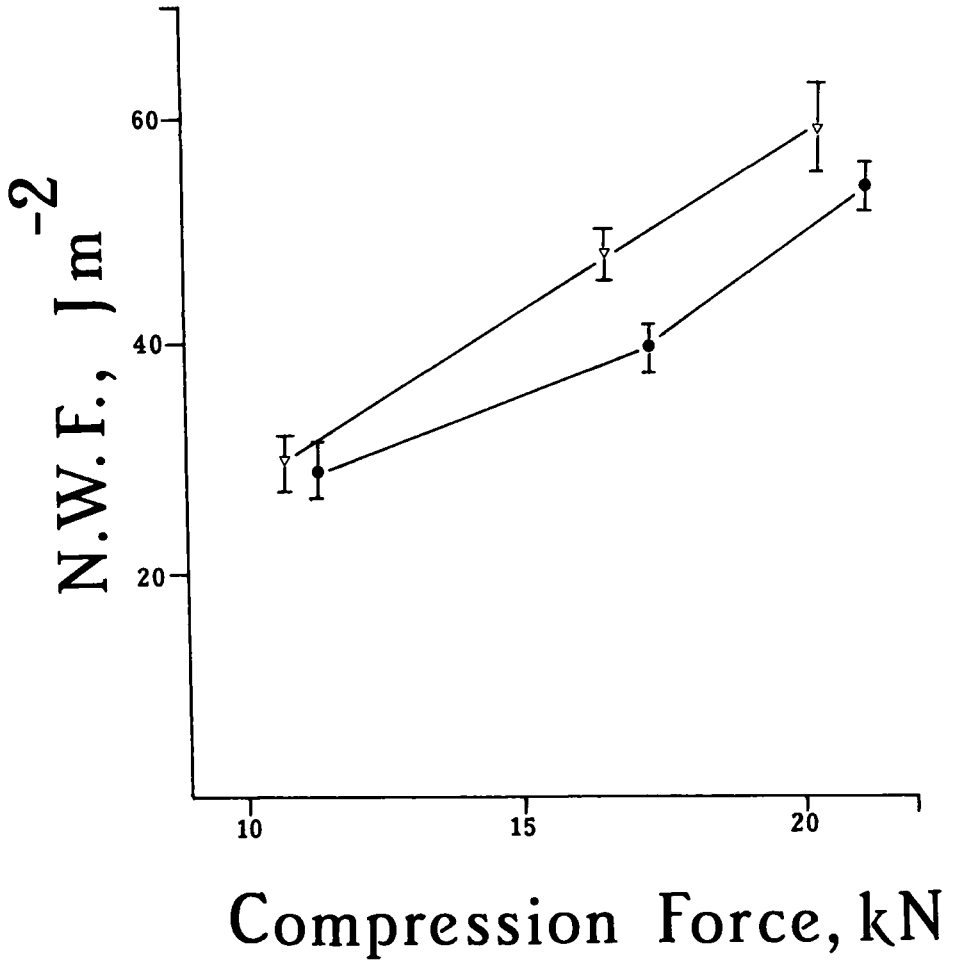

FIGURE 7
Relationship between normalized work of failure (NWF) values and compression forces for dicalcium phosphate tablets lubricated with : 5% HVO and 2% magnesium lauryl sulphate ● ; 5% HVO and 5% magnesium lauryl sulphate ▽ .

Interestingly, the ejection forces for magnesium stearate were also found to decrease with mixing time (fig.9) and this together with loss of compressibility appears to support this view of other workers concerning formation of a continuous hydrophobic film during mixing [1,2,3].

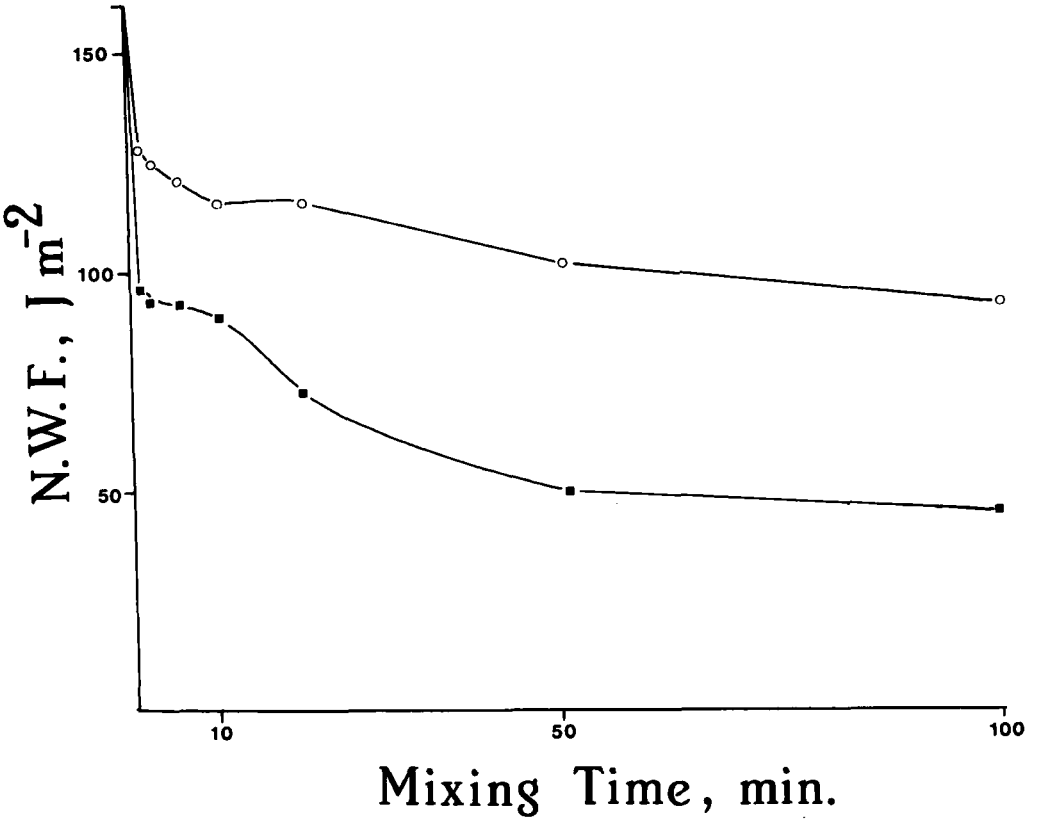

FIGURE 8
Relationship between tablet toughness (NWF) and mixing time for tablets compressed using microcrystalline cellulose (Emcocel) with 0.5% magnesium stearate ■ ; 2% HVO (Lubritab) ○ .

(iii) **Powder Mixing and Segregation**

A binary powder mix containing Emcompress and 1% w/w ascorbic acid was found to have a homogeneity characterized by a coefficient of variation of 6.92% following 30 mins mixing. Following vibration for 15 mins at 50Hz and 29.42 ms^{-2} the coefficient of variation (CV) of spot samples rose to 16.43% indicating that some segregation had occurred (fig 10). The influence of addition of a ternary lubricant

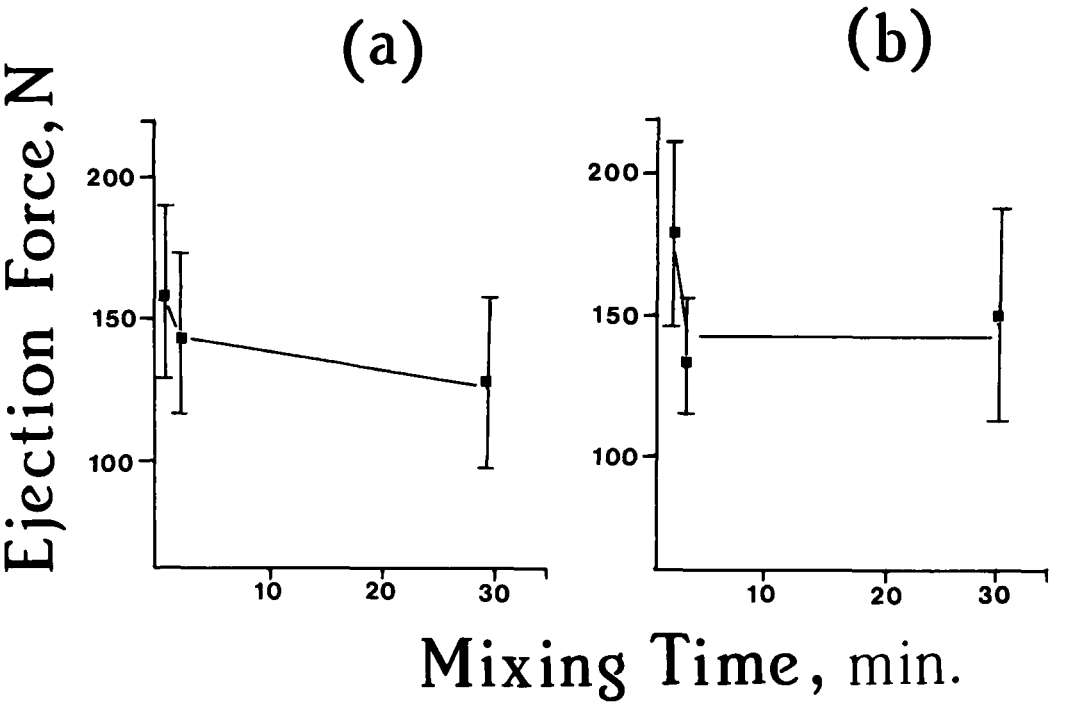

FIGURE 9
Relationship between tablet ejection forces and mixing times for tablets compressed at (a) 15 kN and (b) 20 kN.

component on homogeneity was similar. When $\frac{1}{2}$% $^{w}/_{w}$ magnesium stearate or 2% $^{w}/_{w}$ HVO was added to the binary mix the homogeneity of both ternary mixes was found to be better than the vibrated binary mix, although slightly worse than the binary powders following 30 mins mixing (fig 10). However, on vibration, the 2 ternary mixes exhibited very different behaviour. Whereas the ternary mix containing $\frac{1}{2}$% magnesium stearate showed marked drug segregation, the homogeneity of the mix containing 2% HVO remained virtually unchanged (fig 10).

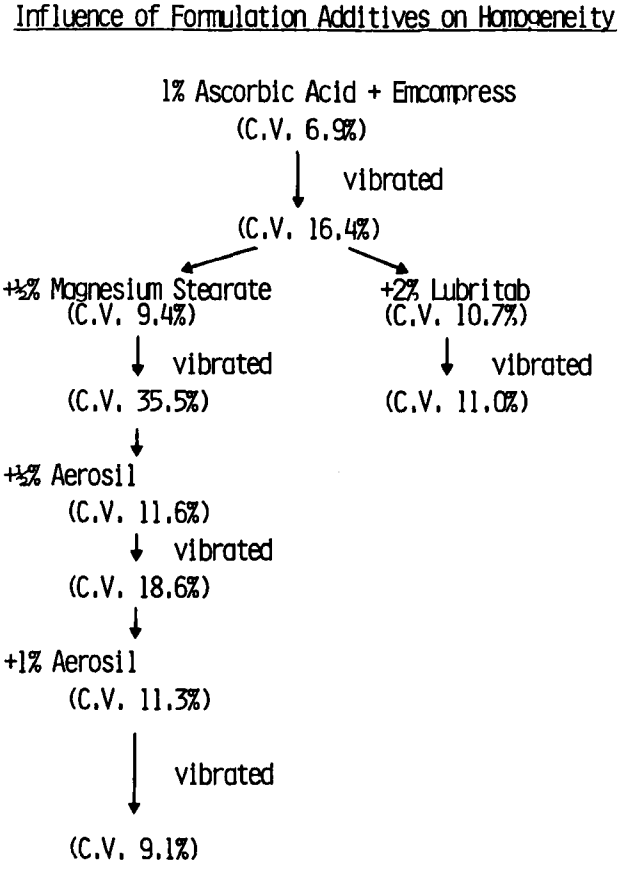

FIGURE 10
Schematic chart showing the influence of formulation additives on the homogeneity of various powder systems after blending and vibration.

It was considered that the adverse influence of magnesium stearate on drug homogeneity was probably due to formation of a continuous hydrophobic film around particles and ordered units causing weakening of drug-excipient particle bonds and leading to displacement of fine drug particles which were then free to segregate through the powder bed. Work carried out elsewhere [4] showed that finely divided colloidal silica could be used to

preferentially attract magnesium stearate particles so that the magnesium stearate was itself coated with silicon dioxide which did not interfere with other mix components. For this reason the ternary mix containing magnesium stearate was mixed with $\frac{1}{2}$% colloidal silica. Although a reduction of aggregation was achieved (fig 10), the quaternary mix lost homogeneity when vibrated (fig 10). Vibration conditions were important since they represented frequency and acceleration levels commonly encountered during tablet production [5]. A further 1% colloidal silica was added to the previous quaternary mix and this was found to reduce segregation both before and after vibration to levels produced using HVO alone (fig 10). Addition of similar quantities of silicon dioxide to HVO ternary mixes was found to have little influence on homogeneity. This was probably because HVO did not produce the same 'stripping' of drug particles from ordered units that magnesium stearate was found to cause in the present study and which was first reported by Lai and Hersey [6].

CONCLUSIONS

1. The lubricity of hydrogenated vegetable oil is lower than that of magnesium stearate in the same formulation.

2. In combination with some anti-adherent powders, hydrogenated vegetable oil can be used to produce tablets with comparable ejection forces to those produced using magnesium stearate.

3. Normalized work of failure values for tablets compressed using

hydrogenated vegetable oil were at least twice as high as those for tablets containing magnesium stearate compressed at comparable forces

4. Mixing time was found to have virtually no effect on the compression properties of tablets containing hydrogenated vegetable oil, whereas the strength and toughness of tablets containing magnesium stearate were found to be adversely affected by increased mixing times.

5. Powder mixes containing hydrogenated vegetable oil were found to undergo less segregation following vibration than those containing magnesium stearate.

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