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Preliminary evaluation of dika fat, a new tablet lubricant

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Dika fat, a solid vegetable oil extracted from the kernels of *Irvingia gabonensis* var excelsia has been evaluated as a lubricant* on the basis of its effect on the flow rate of granules, disintegration time and dissolution rate of tablets. The fat shows a maximal effect on flow at a concentration of 2·5% w/w. It produces better disintegration and dissolution profiles than magnesium stearate at all concentrations tested. The indication is that there is less degradation of aspirin in tablets containing this oil than there is in tablets containing magnesium stearate. The use of Dika fat (m.p. 39–40 °C) eliminates the hydrogenation step often necessary for vegetable oils.

Dika fat is a solid vegetable oil extracted from the kernels of *Irvingia gabonensis* var excelsia. The fat is generally used for food (Platt 1975) and is therefore easily available. We have examined its use as a tablet lubricant and compared it with magnesium stearate. Considering that it needs no hydrogenation before use, Dika fat's potential in tableting may exceed that of any hydrogenated vegetable oil.

MATERIALS AND METHODS

Materials

Dika fat was obtained by soxhlet extraction of decorticized and pulverized *I. gabonensis* kernels using n-Hexane (Merck). The solvent was removed by evaporation under vacuum. Lactose, maize starch, magnesium stearate, acacia, aspirin powder, microcrystalline cellulose were all purchased from Merck.

Granulation

The basic lactose granulation contained in each tablet, 425 mg lactose, 50 mg maize starch, 0·5% w/w to 3% w/w magnesium stearate or Dika fat. The powder mix in 250 g batches was wet granulated in an Erweka oscillating granulator, carrying a 1·7 mm screen, dried at 60 °C for 1 h and re-screened through a 1·00 mm screen. The aspirin mix contained 600 mg aspirin per 700 mg tablet. Microcrystalline cellulose was used as the filler and the concentration of lubricant in each tablet was varied as in the basic lactose granulation. The lubricants were passed through a 0·250 mm sieve before incorporation into the powder mix or granules.

* The term lubricant used in the text includes glidant.
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Flow rate measurement

An Erweka granule flow tester, Type G.D.T., was used for measuring the flow rate of granules containing varying amount of a given lubricant. The apparatus is fitted with an impulse counter that records the flow time of 100 g of granules with 10^{-1} s precision.

Compression of tablets

Tablets were compressed in an Erweka tablet machine Type EKD 9228 fitted with ½ inch flat-faced punches. The basic lactose granules were compressed into tablets of 500 mg weight while the aspirin mix was compressed into tablets of 700 mg weight. The hardness of all tablets was fixed at 6 kg Monsanto units.

Disintegration time measurement

The average disintegration time of five tablets was measured using an Erweka disintegration apparatus, Type T4, 32440. The disintegration time for each batch of tablets was determined five times in distilled water maintained at a temperature of 37 ± 0·5 °C.

Dissolution rate study

The rotating basket technique was employed. A basket constructed with No. 90 mesh sieve, 45 mm in height and 25 mm in diameter, was used for the investigation. The cover, firmly attached to the basket by thumb screws, had soldered onto it a shaft connected to a stirrer motor (Gallenkamp). Revolution was maintained at 100 rev min^{-1}. The dissolution medium was 900 ml distilled water maintained at an acid pH of 3 and a temperature of 37 ± 0·5 °C in a thermostatic bath. The basket was centrally placed in the dissolution medium so that its lowest part was 30 mm from the bottom of a one litre capacity bottle which constituted the dissolution

chamber. The screw cap cover of the chamber carried ports for a thermometer, the stirrer shaft and for sampling.

Analysis for dissolved aspirin

At pre-determined time intervals, 2 ml samples were withdrawn from the dissolution medium and replaced with an equivalent amount of acidified distilled water. Analysis of dissolved aspirin was carried out according to methods set out by Gibaldi & Weintraub (1970). Optical densities were read at 302 nm on a Pye Unicam Spectrophotometer, SP-8000. For each batch of tablets, the entire dissolution profile was determined twice.

RESULTS

The flow rate data are presented as graphs of flow rate in g s^{-1} as a function of per cent w/w lubricant content (Fig. 1). This shows that at 1·5% w/w, magnesium stearate has its optimum effect on flow after which the flow rate declines sharply. Dika fat

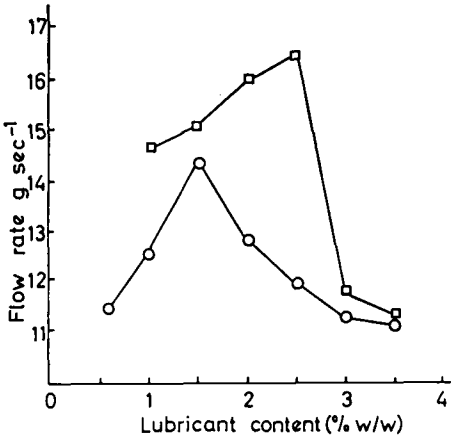

FIG. 1. Flow rate of basic lactose granules lubricated with ○ magnesium stearate □ Dika fat.

shows a similar effect but at a higher concentration, 2·5% w/w. This effect is in agreement with Jones & Pilpel (1966) who stated that for every real powder system, there should be an optimum combination of glidant size and concentration which leads to a maximum in the flow rate.

The British Pharmacopoeia, 1973, specifies a disintegration time of 15 min for uncoated tablets. At a concentration of 1·5% w/w tablets containing magnesium stearate lubricant showed a disintegration time of 14·8 min (Table 1) and thus satisfy the pharmacopoeial requirement. It is at this concentration that magnesium stearate has its maximal effect on flow rate. The same Table shows that tablets containing 1·5% w/w Dika fat have disintegration time of 7·3 min. Even at 2·5% concentration, where this fat has its highest effect on flow rate the disintegration time, 11·6 min is still within the pharmacopoeial requirement. This is not the case with magnesium stearate which fails at this concentration with disintegration time of 21·2 min.

The disintegration time of aspirin tablets was monitored and this did not exceed 7 min at all concentrations of lubricant. The use of microcrystalline cellulose as a filler is therefore justified, since it helped to produce rapid disintegration of these tablets.

Table 1. Mean disintegration time for tablets containing varying concentrations of lubricants.

Concn. of lubricant % w/w	Mean disintegration time (min) Magnesium stearate	Dika fat
0·5	9·1	3·9
1·0	12·2	5·2
1·5	14·8	7·3
2·0	17·5	9·3
2·5	21·3	11·6
3·0	24·7	14·7

Two representative dissolution rate profiles for tablets containing 1·0 and 1·5% w/w lubricants respectively were considered. The per cent concentration of dissolved aspirin was calculated and in Figs 2A, B and C are shown graphs of per cent aspirin dissolved as a function of time. The nature of the curves except in Fig. 2B for magnesium stearate, is similar to that expected of tableted drugs (Khan 1975). For lubricant concentrations of 0·5 and 1·0% respectively, tablets containing Dika fat have the same dissolution profile as tablets containing no lubricant. Deviation only becomes apparent at a concentration of 1·5% (Fig. 2B). With magnesium stearate, deviation is apparent at all concentrations and a discernible lag in dissolution develops at a concentration of 1·5%. This is reminiscent of the pattern seen in encapsulated drugs (Khan 1975). At all concentrations of lubricant tested, the curves are generally steeper for those tablets containing Dika fat, thus indicating a higher rate of drug release. These tablets attained 100% dissolution faster than tablets containing magnesium stearate. Fig. 2C shows that aspirin tablets containing Dika fat are stable after a relatively short storage time of 14 days at 30 °C. The dissolution curves obtained for these tablets after 24 h and 14 days respectively are super-

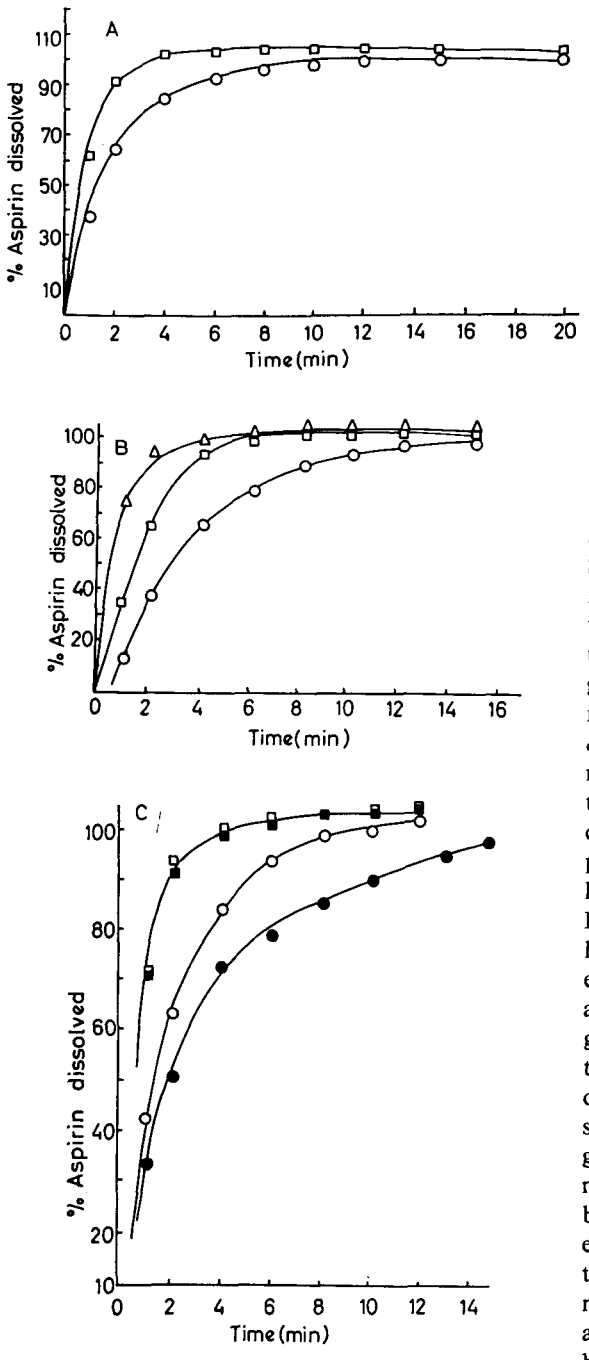

FIG. 2A. Dissolution profile of aspirin tablets containing ○ 1·0% magnesium stearate □ 1·0% Dika fat.
B. Dissolution profile of aspirin tablets containing ○ 1·5% magnesium stearate □ 1·5% Dika fat △ 0·0% lubricant.
C. Dissolution profile of aspirin tablets after storage at 30 °C ●, magnesium stearate (14 days), ○ magnesium stearate (24 h), ■ Dika fat (14 days), □ Dika fat 24 h).

imposable on one another. This is not the case with tablets containing magnesium stearate; the curve obtained after 14 days deviates significantly from that obtained after 24 h.

DISCUSSION

Jones & Pilpel (1966) have recognized the difference in the mode of action of a chemically different powder added to improve flowability and a fine fraction added to a coarse granulation of the same material for the same purpose. The first category of glidant is thought to separate individual powder particles thereby reducing van der Waal's type cohesive forces which act between them. The second type is thought to improve flow by adhering to the surfaces of the coarser granules. This coating smooths out surface irregularities and thus reduces inter-particular resistance to flow. This mode of action agrees with findings by Augsburger & Shangraw (1966), who attributed tablet weight increases to the coating of filler particles with glidant, thereby allowing them to flow more readily and uniformly into the dies. As the concentration of fine glidant material is increased, a point is reached when its particles begin to interact with each other (Jones & Pilpel 1966). It is possible to explain the action of magnesium stearate in terms of coating or adherence to granules. It is known that this lubricant prolongs disintegration of tablets because of its water-proofing property whereas its soluble analogue, magnesium lauryl sulphate does not (Caldwell & Westlake 1972). Dika fat is not expected to be soluble like magnesium lauryl sulphate, but on the basis of its favourable effect on disintegration, it certainly allows the permeation of water into the tablet matrix. If coating of granules is assumed to be the mode of action of the two lubricants, on the basis of their respective effect on disintegration, it may be argued that magnesium stearate forms a more efficient coat around the granule than Dika fat. Since Dika fat improves flow more than magnesium stearate, it would not do this by forming a poor coat around the granules. However, an efficient coat and a favourable disintegration time would not agree with the obvious hydrophobic nature of Dika fat. It is, therefore, reasonable to assume that Dika fat acts as a better glidant/lubricant by a mechanism different from coating or adherence. Its action may be explained in terms of reduction of surface van der Waal's type cohesive forces on particles. With the two lubricants, critical concentrations were attained at 1·5% w/w for magnesium stearate and 2·5% for Dika fat. At these concentration, the flow rate of each batch of granules (Fig. 1)

decreased sharply. It may be assumed that the particles of these lubricants begin to interact with each other and thus hinder flow.

The Dissolution Efficiency (D.E.) of a tabletted drug has been mathematically represented by Khan (1975) as

$$\text{Dissolution Efficiency} = \frac{\text{y.dt}}{\text{y.100t}} \times 100\%$$

D.E. can be calculated from experimental data in terms of the proportion of the area of curve at time t relative to the area of the curve for 100% dissolution (see Khan 1975). Khan has pointed out that when a relation is to be established between dissolution and another variable, in this instance, lubricant concentration, it is more realistic to use D.E. which takes into account the dissolution profile as a whole as opposed to either t50 or t90 values which are single points on a plot. It is further suggested that in calculating D.E. the time interval chosen should be such that the range of values of the dissolved drug obtained during that interval be greater than 90% of the total drug contained in the tablet. An 8 min time interval satisfies this requirement for the tablets being investigated. Table 2 shows the D.E. calculated

Table 2. Mean dissolution efficiency for tablets containing varying concentration of lubricant at 8 min interval.

Concn. of lubricant % w/w	Mean dissolution efficiency Magnesium stearate	Dika fat
0·0	91·9	91·9
0·5	76·9	91·3
1·0	77·5	90·0
1·5	58·9	82·3

for the various tablets. Tablets formulated with Dika fat lubricant show better D.E. than tablets formulated with magnesium stearate. Since Dika fat is insoluble in water, this result lends support to the supposition that its mode of action is not dependent on the coating of granules. A change of lubricant concentration from 1·0 to 1·5% lowers D.E. for magnesium stearate to 58·9% while D.E. for Dika fat is reduced to 82·3%. It is at this concentration that the effect of Dika fat lubricant becomes noticeable. Since a D.E. of 82·3% is still reasonable, 1·5% may be the optimum concentration of Dika fat that may be used as lubricant. In Table 3 where the t50 and t90 values are shown, the same type of effect by each lubricant is manifest. For both 50% and 90% dissolution a longer time (t) is invariably required for tablets containing magnesium stearate.

Table 3. Mean time for dissolution of 50 and 90% aspirin contained in tablets lubricated with magnesium stearate and Dika fat respectively.

Concn. of lubricant % w/w	Mean t50 (s) Mg stear.	Mean t50 (s) Dika fat	Mean t90 (s) Mg stear.	Mean t90 (s) Dika fat
0·0	36	36	84	84
0·5	75	48	297	108
1·0	75	48	295·8	108
1·5	163·8	84	475·8	176

The result of the storage test is not surprising. Magnesium stearate and other alkali stearates are known to increase the degradation of aspirin both in tablets and suspension (Kornblum & Zoglio 1967; Maulding et al 1969). The former graded the relative acceptability of tablet lubricants in combination with aspirin as follows: hydrogenated vegetable oil, stearic acid, talc and aluminium stearate. The stearates in this grading are the least acceptable. Dika fat would obviously fall into the same rank as hydrogenated vegetable oil. The use of Dika fat in place of hydrogenated vegetable oil will no doubt prove more convenient and economical since no hydrogenation step is needed for its production. The fatty acid content of Dika fat is well known (Litchfield 1971), it is edible and therefore has some potential for use as a tablet lubricant.

Acknowledgements

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