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THE EFFECT OF LUBRICANTS ON THE PROPERTIES OF CHLOROQUINE PHOSPHATE TABLETS

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ABSTRACT

The properties of tablets prepared from different size fractions of chloroquine phosphate granules using different lubricants were evaluated. Lubricants used were magnesium stearate, stearic acid and talc, tablet properties studied include weight variation, crushing strength, friability and disintegration time.

The effects obtained were largely dependent on the type and concentration of lubricant. Generally, as granule size increased, tablets were found to show increased weight variation, decreased hardness and increased friability. With tablets containing talc as lubricant,

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disintegration time was shown to decrease with increase in granule size.

There appears to be an optimum lubricant concentration for the compression of different granule size fractions.

INTRODUCTION

In addition to other variables that affect tablet properties, the constituents of a formulation may have profound effects on both the physical properties of the tablets and the biological availability of the active component. Of particular importance is the lubricant which in many cases has to be present to make compression on a tablet machine possible.

Munzel and Kagi (1) have investigated the distribution of lubricant in a granulation and its role in reducing friction.

From the work of Bowden and Tabor (2) it has been indicated that the strongest bonds are formed between clean surfaces. Thus, the presence of lubricant can reduce the hardness of the tablets, produced by weakening the bonds between particles (3).

Magnesium stearate is a popular die wall lubricant in the tabletting process because of its low shear strength (4). The disadvantages of adding hydrophobic lubricants such as magnesium stearate to tablets have

been considered by Ganderton (5). Increasing the lubricant concentration was shown to reduce the rate of aqueous penetration and tablets containing lubricant showed greater variation than unlubricated tablets due to uneven distribution of hydrophobic material.

Lubrication is therefore a surface phenomenon and for a given lubricant, the extent of lubrication may depend on how much of the lubricant particles are adsorbed on the tablet material. It is the purpose of this work to find out the effect that lubricants and granule size can have on the tabletting properties of chloroquine phosphate granules.

MATERIALS AND METHODS

Materials

Chloroquine phosphate (ICI), Magnesium stearate, stearic acid and talc (BDH) were all used as fine powders. Polyvinyl pyrrolidone (Courtin and Warner) dissolved in water to form 5% w/v solution was used as granulating agent.

Methods

Preparation of Granules:

The granulations were prepared by the massing and screening process. 1kg batches of chloroquine phosphate powder was dry mixed in a blade mixer (Erweka Apparatebau)

for 4 minutes. The total required weight of the granulating solution was then added in two aliquots while massing was carried out for 5 minutes. The wet mass was forced through a No. 10 mesh screen aperture on a Reciprocating granulator (Jackson and Crockatt). The wet granules were dried in a fluid bed dryer (Glatt) at an inlet air temperature of 45 - 48°C for 20 minutes. The dry granules were rescreened through a No. 10 mesh screen.

The granules obtained from various batches were thoroughly mixed and fractionated into different sizes by placing 500g batches on a nest of sieves (Endecotts Test sieves), which was then tapped for 5 minutes on a mechanical sieve shaker (Pascall Engineering Company). The different fractions were then stored in tightly closed jars.

Compression and Analysis of Tablets

Different formulations were obtained by mixing granules of selected size range with the required concentration of the lubricants used. The granules were then compressed at a constant pressure and speed, on a single Punch tablet machine (Diaf, Denmark) fitted with a 10mm flat faced punch. Tablets were stored for an average period of 2 days before analysis.

The tablet properties measured include weight variation (20 tablets per batch), crushing strength (using a Pfizer hardness tester), Friability (using a Roche friabilator) and disintegration time (British Pharmacopoiea method using a Manesty disintegration Unit).

RESULTS AND DISCUSSION

Effect of Lubricant Type and Granule Size

Tablet properties are shown in Tables 1 - 3 and Figures 1 - 3, illustrating the effects of lubricants in relation to the initial granule size. Granule size was represented by the average of the sieve apertures used in the classification. As control, none of the size fractions of chloroquine phosphate granules could compress in the absence of a lubricant. Lubricants that were employed include magnesium stearate (0.5%) stearic acid (1.5%) and Talc (5%) and for each of these lubricants, weight variation was shown to increase as granule size increased from 375μm to 1200μm (Table 1), the differences between the 605 and 855μm being non significant (P=0.95). This observation is in agreement with the findings of previous workers (6, 7, 8), that weight variation in tablet batches could be affected by the granule size, since larger granules would exhibit more irregular

Table 1: Effect of Lubricant on weight variation of tablets prepared from different sized granules.

Lubricant		Coefficient of weight variation (%) Granule size (μm)			
Type	Concentration (%)	375	605	855	1200
Talc	5	0.72	1.30	1.20	2.60
Stearic acid	1.5	0.90	1.60	1.30	-
Magnesium stearate	0.5	0.51	0.78	1.70	2.20
"	0.7	0.89	0.99	0.81	2.00
"	0.9	1.33	1.15	0.53	0.91

Table 2. Effect of Lubricant on the Crushing Strength of tablets prepared from different sized granules.

Lubricant		Hardness (Kg) Granule size (μm)			
Type	Concentration (%)	375	605	855	1200
Talc	5	9.3	7.3	7.4	4.1
Stearic acid	1.5	9.6	7.5	8.6	-
Magnesium Stearate	0.5	10.0	7.5	8.5	2.6

packings that could result in non uniform die fills during compression.

Values obtained for the coefficient of weight variation (Table 1) of tablets also varied with the type of lubricant. Due to the nature of the lubricants, it was necessary to use different concentrations that would allow compression and ejection of the tablets. It was noted that the biggest granule batch (1200 μm) would not compress with stearic acid at a concentration of 1.5%.

The relationship between Crushing strength and granule size for each lubricant is shown in Table 2. Tablets produced from the 375 μm granule fraction showed the greatest resistance to crushing while those produced from the very big granules showed least resistance. The differences between the crushing strength of the 605 μm and 855 μm batches are however not significant (P=0.95). Tablet strength could therefore appear to decrease with an increase in granule size as previously observed by Kassem and others (7). A decrease in granule size could mean an increased area of contact and decrease in void space, leading to stronger bonding in the tablets. With the three lubricants used, the strength of the tablets did not appear to differ significantly within each size fraction.

In the work of Rubinstein and Blane (8), there was no obvious relationship between granule size and crushing strength of Bendrofluazide tablets, when tablets contained up to 1% of magnesium stearate as lubricant. Also shotton and Lewis (3) studied the effect of Base particle size on tablet crushing strength in the presence of 2% magnesium stearate as lubricant. Results obtained by the latter work indicated a large dependence on the nature of the base material.

Tablet friability, like hardness is also an indication of the compactness of the tablets, and was shown to increase with increase in granule size (Table 3). This result is a reflection of the hardness of the tablets which decreased as granule size increased (Table 2).

Table 3: Effect of Lubricant on the friability of tablets prepared from different sized granules.

Lubricant		Friability percent Granule size (μm)			
Type	Concentration (%)	375	605	855	1200
Talc	5	1.3	1.5	1.9	2.5
Stearic acid	1.5	1.4	1.7	2.1	-
Magnesium stearate	0.5	1.4	1.8	1.9	8.1

The effect of lubricant and granule size on disintegration time is shown in Fig. 1. With magnesium stearate, the highest disintegration times were observed for the 605 and 855 μm batches. The disintegration time for the 1200 μm batch was however much shorter.

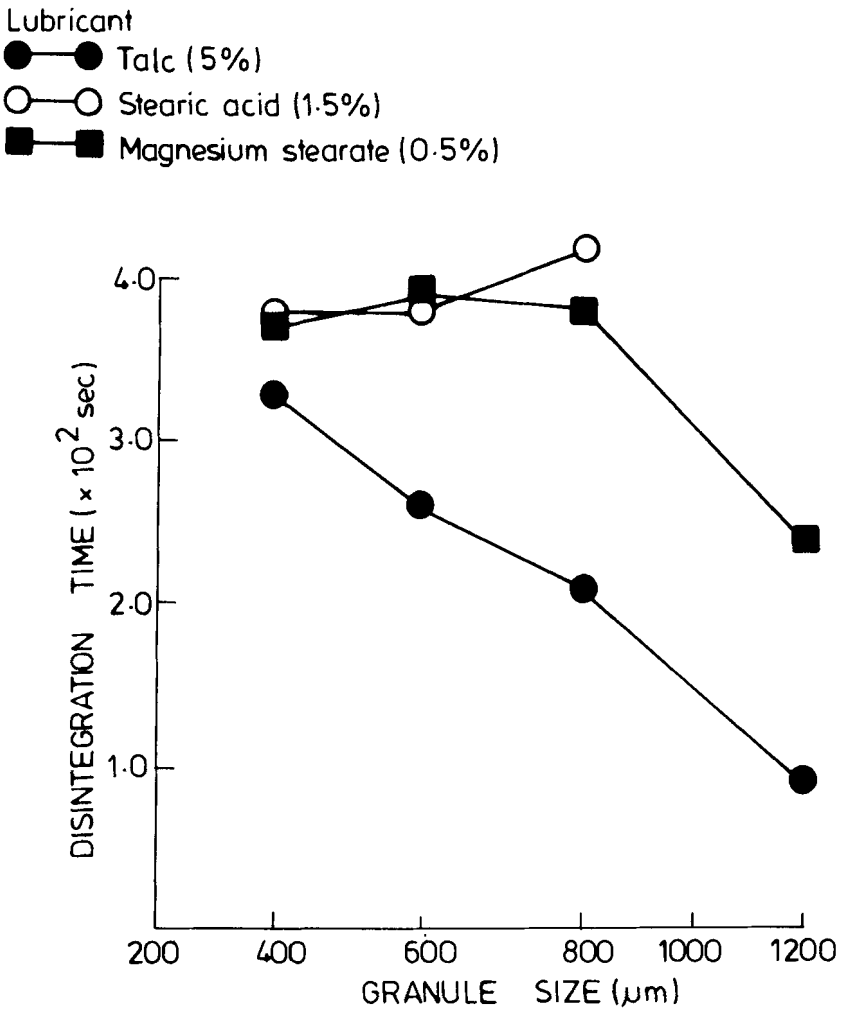

Fig. 1. The effect of lubricant type on disintegration time of tablets prepared from different sized granules

With talc, disintegration time decreased with increase in granule size, agreeing with an earlier work by Kassem and others (7). However, there appears to be no general trend in the effect of granule size on disintegration of tablets containing magnesium stearate and stearic acid. Other workers have observed that granule size does not directly influence tablet disintegration time (8,9). From their work, it seems that the compaction pressure would affect the disintegration time more, particularly when a disintegrant is present in the tablet. However, from Fig 1. there is sufficient variation in the results to show that granule size exerts an influence on disintegration time of tablets. Overall talc produced tablets with the shortest disintegration time in all the batches. Magnesium stearate and stearic acid had similar effects on the tablets. The higher disintegration times produced by these two lubricants could be due to the hydrophobicity of the substances, which can cause an increase in the angle of contact between the tablet and the disintegration medium (5, 10). The increased angle of contact can cause a reduction in the rate of penetration of tablets by the medium.

Effect of lubricant concentration and granule size

To show the effect of increasing lubricant concentration on tablet properties, different concentrations

of magnesium stearate was included into the granule formulation. From Table 1, it was shown that 0.5% of lubricant produced the lowest variation in weights of tablets obtained from the 375 μm granules. Increasing or decreasing the concentration of the lubricant in this particular granule batch resulted in an increase in weight variation. With the larger granules (605 μm - 1200 μm), tablets could not be compressed adequately with lubricant concentrations below 0.5%. From this observation, it could appear that lower concentrations of magnesium stearate was insufficient to lubricate the bigger granules to facilitate compression and ejection.

In addition, weight variation of tablets decreased as the lubricant concentration increased above 0.5% for bigger granules indicating an increase in the uniformity of die fill as the proportion of finer particles increased.

Generally, at all lubricant concentrations, the 375μm granules produced relatively stronger tablets than the 1200μm granule batch (Fig. 2). A similar observation has been explained earlier. Considering the smallest granule batch (375μm), tablet crushing strength decreased slightly, as lubricant concentration was increased. This is in agreement with the findings of

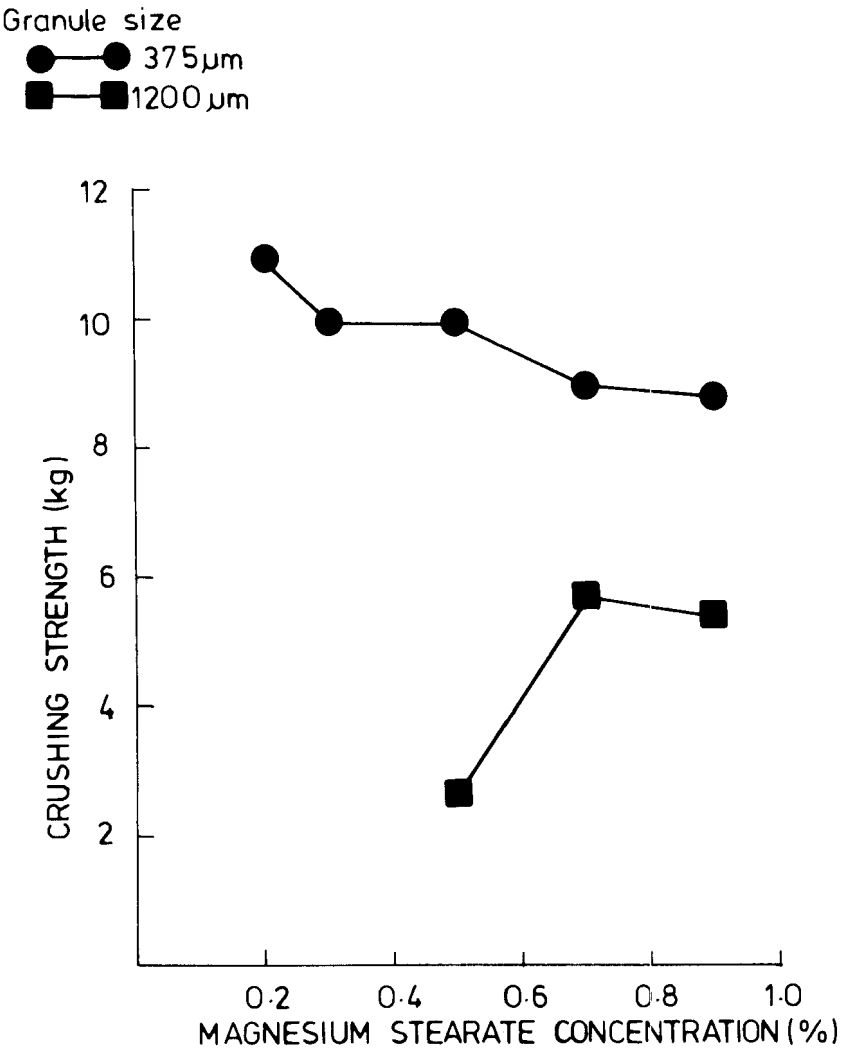

Fig. 2. The effect of magnesium sterate concentration on the crushing strength of tablets prepared from different sized granules

Strickland and others (10) as well as Shotton and Lewis (3). The results obtained by the latter also varied with the nature of the base material.

However, a different trend was observed with the bigger granules where the tablets initially increased in

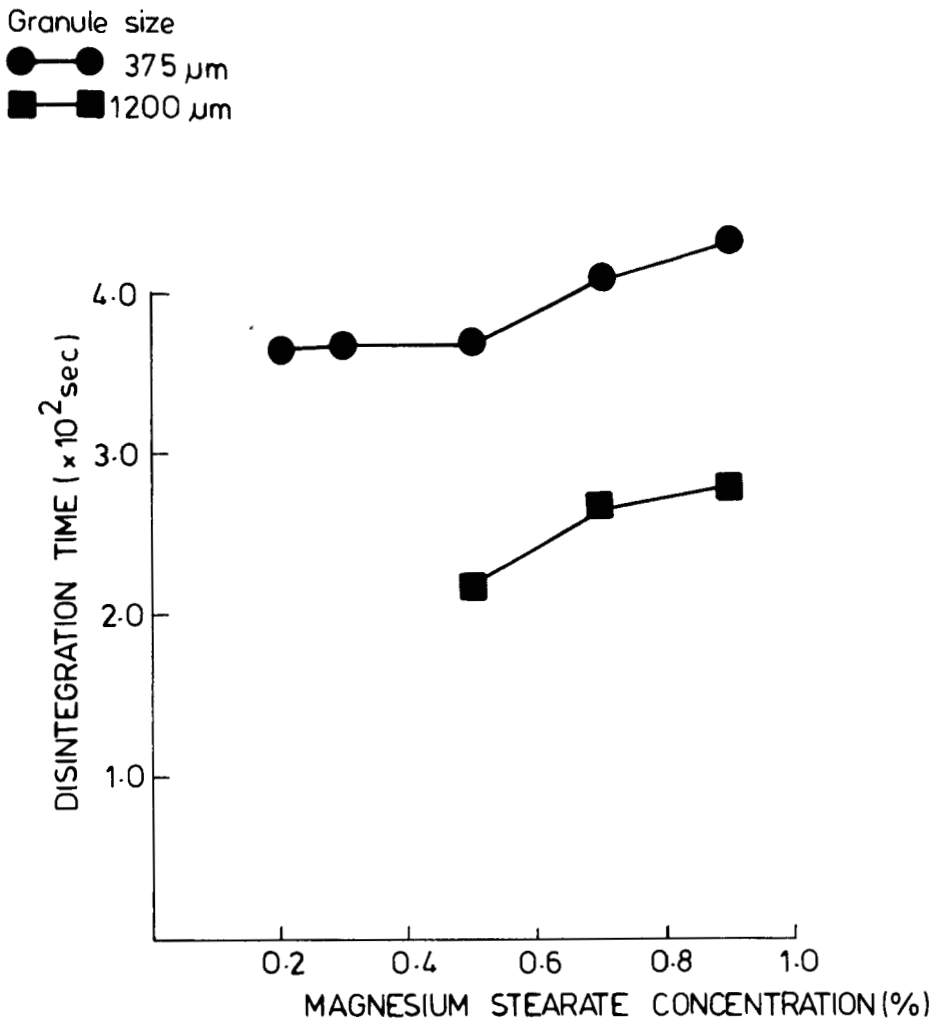

Fig. 3. The effect of magnesium sterate concentration on the disintegration time of tablets prepared from different sized granules

crushing strength and then decreased slightly as lubricant concentration increased.

Fig. 3 shows the disintegration time of tablets in relation to lubricant concentration and granule size. Tablets obtained from the big granules (1200μm) distinctly

differed from those prepared from small granules (375μm) regardless of concentration of magnesium stearate. The same observation was noted earlier when other lubricants were considered. In addition, there was an increase in disintegration time as lubricant concentration increased. This is not unexpected and may be a consequence of the hydrophobicity of magnesium stearate which becomes more pronounced, with increase in concentration.

SUMMARY AND CONCLUSION

Different sized fractions of Chloroquine phosphate granules were compressed at same compaction pressure and properties of the tablets have been investigated in relation to the type and concentration of lubricants as well as the size of granules used for the compression.

Weight variation was shown to increase while tablet crushing strength decreased with increasing granule size, the magnitude of effect depending on both the type and concentration of lubricant. Two observations were made on disintegration time. While with talc, disintegration time decreased with increase in granule size, no general trend was observed in the disintegration time of tablets containing magnesium stearate and stearic acid. Disintegration of tablets is however dependent on other factors that affect the rate of penetration of the tablets by the liquid.

In general, the effects produced by lubricants on the properties studied, are dependent on the size of the granules from which the tablets were made. This could be due to the variation in the surface area of the granules as granule diameter and geometry are changed. For instance, considering a single spherical granule of diameter D being broken into n smaller but similar granules of diameter d, the surface area of the granule would have increased by a factor of the cube root of n (i.e. $\sqrt[3]{n}$).

Therefore, by reducing granule size, the total exposed surface of the granules is increased. On application, a certain amount of lubricant can spread effectively to cover the smaller granules in monolayers, the same amount when applied to the bigger granules will coat the latter with multilayers of the lubricant, leaving a large proportion of the granules enclosed and unexposed to the lubricant during compression.

It then appears that there could be an optimum lubricant concentration for the compression of granules of different sizes. This may account for the inability of bigger granules to compress adequately without picking and sticking to punch faces at very low concentrations of the lubricant. However, when there were sufficient lubricant to facilitate compression and ejection of the

tablets, then, other factors such as fragmentation and elasticity of the granules can exert appreciable influence on the properties of the tablets.

In conclusion, the concentration of lubricant is shown to influence the compression characteristics of different granule size fractions. This could also account for the non-agreement between various reports as to the actual involvement of granule size on the determination of tablet properties. Many reports are usually based on different materials and methodology. For instance, the presence and concentration of the added lubricant may not be accounted for. Also, interactions between lubricants, diluents and disintegrants such as could affect tablet physical characteristics have been reported (11, 12). It would therefore be acknowledged that any effect on tablet property would depend to some extent on the nature of the base material as well as other components of the tablets.

REFERENCES

1. K. Munzel and W. Kagi, Pharm. Acta Helv., 29, 53 (1954).

2. F.P. Bowden and D. Tabor, The Friction and Lubrication of Solids, Clarendon Press, Oxford. (1954).

3. E. Shotton and C.J. Lewis, J. Pharm. Pharmac., 16, 111T (1964).

4. C.J. Lewis and E. Shotton
ibid., 17, 825 (1965).

5. D. Ganderton, ibid., 21, 9S (1969).

6. A.S. Arambulo, H.S. Fu and D.L. Deardoff,
J. Amer. Pharm. Ass. (Sci. Ed.) 42, 692 (1963).

7. A.A. Kassem, A.M. Sakr and M.S. Mesiha, Mfg.
Chem. 43, 24 (1972).

8. M.H. Rubinstein and M.C. Blane,
Pharm. Acta Helv., 52, 5 (1977).

9. A.M. Marks and J.J. Sciarra,
J. Pharm. Sci., 57, 497 (1968).

10. W.A. Strickland, E. Nelson, L.W. Busse, and T. Higuchi.,
J. Amer. Pharm. Ass. (Sci. Ed.) 45, 51 (1956).

11. E. Yumioka and M. Hrokazau, Yakazaigaku, 26, 201 (1966)

12. K.T. Jaiyeoba and W.O. Opakunle, Mfg. Chemists
49, (5), 60 (1978).