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# Disintegrants: effects of interacting variables on the tensile strengths and disintegration times of sulphaguanidine tablets

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## Summary

The effects of separately varying the packing fraction ($P$), the nature ($N$) and concentration ($C$) of disintegrants on both the tensile strength and disintegration times of sulphaguanidine tablets are in the orders, respectively, of $P > N > C$ and $N > P \gg C$. The combined effects of these variables on the tensile strength are found to be very close to zero and are in the order of $N\&C > P\&N > P\&C$ while those for the disintegration times are significantly removed from zero and the order is $P\&N \gg P\&C > N\&C$. Thus, the results indicate that the type and relative proportions of the disintegrants in the formulation have a more complex effect on the disintegration time of the tablets than on their tensile strengths. The ranking of the effects of the various disintegrants on disintegration times is potato starch > alginic acid ≫ methylcellulose.

Disintegrants are added to tablet formulations for the purpose of causing the compressed tablet to break apart when placed into an aqueous environment in order that the active ingredient is released. The type and proportions of the disintegrant present in a tablet formulation have been shown (Khan and Rhodes, 1973; Pilpel et al., 1978; Bolhuis et al., 1982) to influence the mechanical properties of the tablets and disintegration and dissolution characteristics. Processing variables such as the granulation technique, temperature and rate of compression and the compression pressure employed can also affect the properties of compressed tablets. Many workers have evaluated the separate (Khan and Rhodes, 1973; Pilpel et al., 1978; Bolhuis et al., 1982) and combined (Kurup and Pilpel, 1977; Adeyemi and Pilpel, 1983, 1984; Bangudu and Pilpel, 1985; Zubair et al., 1988) effects of formulation and processing variables with the objective of optimizing the production and therapeutic performance of various tablet formulations. In fact, it has recently been suggested (Bangudu and Pilpel, 1985) that this type of analysis will prove useful in the future development of commercial tablets. The purpose of the present study has therefore been to determine how the packing fraction and the type

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and amount of some disintegrants added to sulphaguanidine separately and in combination, affected the tensile strengths and disintegration times of the resulting tablets.

The materials were sulphaguanidine BPC, alginic acid BPC, methylcellulose M20 BPC, and gelatin BP all from Halewood Chemicals, Middlesex, U.K.; potato starch from BDH Chemical, Poole, U.K. and magnesium stearate from Hopkin and Williams, Essex, U.K. They were all used as supplied.

The sulphaguanidine formulation was made in batches of 40 g with the various disintegrants: potato starch, alginic acid and methylcellulose added in proportions of 5, 10 and 15% w/w which were dry-mixed for 5 min in a Kenwood planetary mixer. The mixtures were moistened with 38 ml of 2.5% w/v of freshly prepared gelatin solution and massing continued for 3 min. The wet masses were granulated manually through a 1.7 mm aperture sieve, the granules dried for 12 h at 60 °C and the dried granules resieved through a 1.4 mm aperture sieve.

1% w/w of finely sifted magnesium stearate was mixed with the sulphaguanidine granules in a ball mill for 5 min to act as lubricant. 600 mg of the final mix was then compressed manually into tablets at the rate of 0.22 $mm \cdot s^{-1}$ on a single punch (Kilian & Co. Koln-NIEHI Type S5) machine using a 12.7 mm diameter die, flat-faced punches and different compression pressures in order to achieve packing fractions of between 0.75 and 0.85. The tablets were stored for 24 h in screw-capped jars to allow for hardening and elastic recovery before measurements were carried out on them. Their dimensions and weights were then accurately measured and their packing fractions calculated (Kurup and Pilpel, 1977; Zubair et al., 1988).

The load required to break the tablets diametrically was determined using the Schleuniger Hardness Tester on 10 tablets from each batch and the results accepted only if the samples split clearly into two halves. Their tensile strengths were calculated using the same equation as in previous papers (Esezobo and Pilpel, 1976; Adeyemi and Pilpel, 1984; Zubair et al., 1988).

The disintegration times of the tablets were measured individually on 10 tablets from each batch in distilled water at $37 \pm 1$ °C using the BP 1973 method and a Manesty Disintegration Tester, and an average calculated.

The experiments were performed in a factorial design. Each of the 3 variables, packing fraction ($P$), nature of disintegrant ($N$) and concentration of disintegrant ($C$) was selected at a "low" level ($P = 0.75$ and $C = 5\%$ w/w), a "medium" level ($P = 0.80$ and $C = 10\%$ w/w), and a "high" level ($P = 0.85$ and $C = 15\%$ w/w) for comparing the 3 disintegrants. The method adopted for analysing

TABLE 1

*Values of tensile strength and disintegration times for the tablets at packing fractions of 0.75, 0.80 and 0.85*

| Disintegrant type ($N$) | Concentration of disintegrant ($C$) (% w/w) | Packing fraction (P) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 0.75 | 0.80 | 0.85 | 0.75 | 0.80 | 0.85 |
| | | Tensile strength (MN $m^{-2}$) | | | Disintegration time (min) | | |
| Potato starch | 5 | 0.31 | 0.62 | 1.26 | 7.50 | 8.00 | 13.50 |
| | 10 | 0.29 | 0.55 | 1.10 | 0.50 | 1.10 | 5.70 |
| | 15 | 0.27 | 0.48 | 0.87 | 0.25 | 0.30 | 0.50 |
| Alginic acid | 5 | 0.37 | 0.60 | 1.15 | 27.00 | 40.00 | 76.00 |
| | 10 | 0.30 | 0.56 | 0.83 | 3.00 | 6.00 | 18.50 |
| | 15 | 0.28 | 0.45 | 0.69 | 1.00 | 1.00 | 3.50 |
| Methylcellulose | 5 | 0.44 | 0.82 | 1.12 | > 180 | > 180 | > 180 |
| | 10 | 0.50 | 0.90 | 1.26 | 24.00 | 55.00 | 87.00 |
| | 15 | 0.65 | 1.12 | 1.58 | 8.00 | 13.00 | 29.00 |

TABLE 2

*Quantitative effects of packing fraction (P), nature of disintegrant (N) and concentration of disintegrant (C) on tensile strength and disintegration of the tablets*

(A) Employing potato starch and alginic acid

| Transitional level | Independent coefficient: Tensile strength ($MNm^{-2}$) Variables | | | Independent coefficient: Disintegration time (min) Variables | | |
|---|---|---|---|---|---|---|
| | *P* | *N* | *C* | *P* | *N* | *C* |
| Low-High | 0.70 | −0.07 | −0.23 | 14.56 | 20.06 | −29.06 |
| Low-Medium | 0.26 | 0.02 | −0.02 | 5.03 | 14.98 | −17.73 |
| Medium-High | 0.36 | −0.12 | −0.14 | 7.19 | 5.59 | −25.95 |
| | First-order interaction coefficient Interaction coefficient between | | | | | |
| | *P & N* | *P & C* | *N & C* | *P & N* | *P & C* | *N & C* |
| Low-High | −0.08 | −0.20 | −0.02 | 11.44 | −12.94 | −18.94 |
| Low-Medium | −0.03 | −0.04 | 0.03 | 4.48 | −2.73 | −10.78 |
| Medium-High | −0.11 | −0.05 | 0.01 | 2.31 | −3.11 | −3.51 |

(B) Employing potato starch and methylcellulose

| | Independent coefficient: Tensile strength ($MNm^{-2}$) Variables | | | Independent coefficient: Disintegration time (min) | | |
|---|---|---|---|---|---|---|
| | *P* | *N* | *C* | *P* | *N* | *C* |
| Low-High | 0.80 | 0.28 | 0.06 | * | * | * |
| Low-Medium | 0.32 | 0.21 | 0.02 | * | * | * |
| Medium-High | 0.44 | 0.47 | 0.06 | 13.44 | 44.34 | −26.24 |
| | First-order interaction coefficient Interaction coefficient between | | | | | |
| | *P & N* | *P & C* | *N & C* | *P & N* | *P & C* | *N & C* |
| Low-High | 0.02 | −0.02 | 0.28 | * | * | * |
| Low-Medium | 0.04 | −0.003 | 0.07 | * | * | * |
| Medium-High | −0.03 | −0.02 | 0.21 | 11.06 | −4.86 | −23.26 |

* These values could not be calculated as the disintegration times of tablets prepared with 5% w/w methylcellulose exceeded 180 min.

the independent and interacting coefficients is identical to that described in detail in Adeyemi and Pilpel (1983), Bangudu and Pilpel (1985) and Zubair et al. (1988).

As expected from previous studies (Adeyemi and Pilpel, 1984; Bangudu and Pilpel, 1985; Zubair et al., 1988), the results given in Table 1 show that increasing the packing fraction, $P$, increases both the tensile strength and disintegration times of the tablets.

The order of the relative effects of the independent variables at all levels on the tensile strengths is found to be $P > N > C$ (see Table 2). The packing fraction is a measure of the extent to which particles are brought together during consolidation to form bonds resulting in hard tablets. Furthermore, York and Pilpel (1973) showed that the tensile strength of materials increases exponentially with packing fraction. Therefore, a small increase in packing fraction would be expected to have a large effect on tensile strength and this may well account for the much larger effect on tensile strength observed by increasing $P$ than by changing $N$ or by increasing $C$ of the disintegrants in the formulation. The positive values of $P$ at all 3 levels (see Table 2) indicate that it is an important variable to consider in the tabletting of drugs. The relatively low negative values of $N$ and $C$ (Table 2) indicate respectively that the difference in the effects of starch and alginic acid on tensile strength is insignificant and that a change from starch to alginic acid or increase in their $C$ decreased the tensile strength of the tablets (see Fig. 1). This latter effect may be due to the softness and plasticity of these two materials and it may be presumed that their incorporation in the formulation before the wet granulation process weakened the interparticle bonds between the drug particles similar to the effects of lubricant on tablet strength (Holzer and Sjogren, 1981).

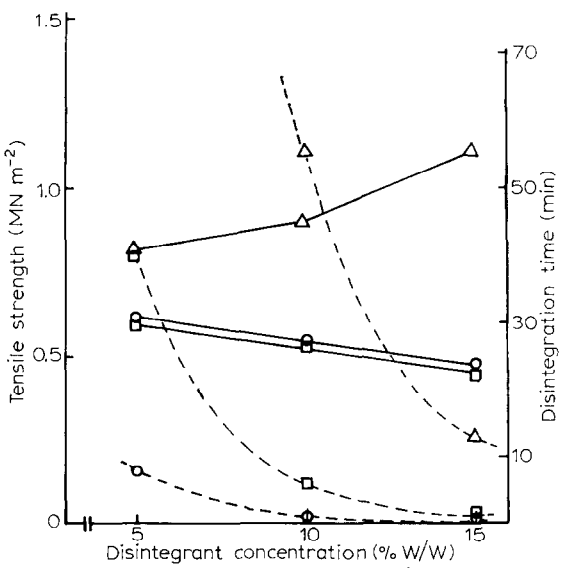


Fig. 1. Effects of the nature ($N$) and concentration ($C$) of the disintegrants on the tensile strength and disintegration time of the tablets at $P = 0.80$. ———, tensile strength; - - - - -, disintegration time; ○———○, potato starch; □———□, alginic acid; △———△, methylcellulose.

However, a change from the use of starch to methylcellulose or increasing its $C$ in the formulation resulted in an increase in tensile strength (see Table 1 and Fig. 1). This may be ascribed to the formation of strong bonds by some form of mechanical interlocking due to the fibrous nature and irregularly shaped particles of methylcellulose and possibly to its binding action (Shangraw et al., 1980).

The order of the relative effects of the independent variables at all levels on the disintegration times is found to be $N > P \gg C$ (see Table 2). This indicates that a change from starch to alginic acid or to methylcellulose increased the disintegration times of the tablets (see Table 1 and Fig. 1). It may well be that alginic acid and methylcellulose when moistened do not develop a swelling capacity or a bursting power similar to an equivalent weight of starch. This is because when these materials are wetted, they rapidly absorb water, swell to many times their original size and rupture the tablets' interparticle bonds (Khan and Rhodes, 1973; Bolhuis et al., 1982). The relatively large negative values of the independent coefficient obtained for $C$ (Table 2) indicates that increasing $C$ decreased markedly the disintegration times of the tablets. This is shown in Fig. 1 and it is consistent with the use of these materials as tablet excipients for improving the disintegration of tablets.

With methylcellulose, however, it appears that its effect on the disintegration times of the tablets depends considerably on the amount of the

material present in the formulation. From Table 1 and Fig. 1 it is seen that at the 5% level it prolonged the disintegration time, but at higher levels (10% and 15%) it decreased the disintegration time of the tablets. This may be ascribed to the different roles that methylcellulose can play in tablet formulations. This is because on coming into contact with water, the material first swells and then produces a gel. For this reason the material functions both as a binder and as a disintegrant or disintegrant activator depending on the amount employed (Huber et al., 1966; Shangraw et al., 1980; Itiola and Pilpel, 1986).

Table 2 also shows that the 3 variables $P$, $N$ and $C$ are interacting with each other at the 3 levels employed to alter the tensile strength and disintegration time of the tablets. For both the starch/alginic acid and starch/methylcellulose systems, the interacting effects on the tensile strengths are very close to zero indicating little interaction between the variables on this parameter. However, their effects on the disintegration times are significantly removed from zero indicating that all the variables influenced the disintegration times to a larger extent than the tensile strength. In addition, it is seen (Table 2) that the interaction between $P$ and $N$ increased the disintegration times while that between $N$ and $C$ as well as between $P$ and $C$ produced decreasing effects on the disintegration times for all the formulations indicating, once more, that the concentration of a disintegrant in a formulation has a profound effect on improving the disintegration times of tablets.

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