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The effect of some excipients on the physical properties of a paracetamol tablet formulation

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The effects of the addition of the excipients sorbitol, sodium lauryl sulphate and Aerosil on the physical properties of a paracetamol tablet formulation have been evaluated. Increase in the concentration of sorbitol and sodium lauryl sulphate caused a decrease in the hardness with a corresponding increase in the friability, disintegration and dissolution rates of the tablets.

The mode of incorporation of the excipient, Aerosil, greatly influenced the physical properties of the paracetamol tablets. When added internally, the tablets' strength decreased while the friability, disintegration and dissolution rates increased. However, when Aerosil was added externally, the strength of the tablets increased while their friability, disintegration and dissolution rates decreased.

Paracetamol is generally administered as tablets containing 500 mg of active drug formulated with the appropriate amounts of other excipients in order to confer desirable properties on the granules and on the final products. The excipients may be added as an inert diluent (bulking excipient), as a wetting agent to improve penetration of the internal pores or as a lubricant (glidant) to improve granule flow.

The addition of excipients in tablet formulations and the method of incorporating them have often been shown to influence such tablet properties as their mechanical strength, friability, disintegration and dissolution times (Chow 1958; Wurster & Seitz 1962; Levy & Gumtow 1963; Wurster & Taylor 1965; Walters 1968). Thus Chow (1958) and Walters (1968) have shown that increasing the sorbitol content of paracetamol tablets caused a corresponding increase in their disintegration and dissolution times and faster absorption rate of the drug; Wurster & Seitz (1962), Levy & Gumtow (1963) and Wurster & Taylor (1965) showed that increase in the concentration of sodium lauryl sulphate substantially increased the dissolution of the drugs benzoic acid and prednisolone from their tablets.

Some studies have shown Aerosil (colloidal silica) to behave as a disintegrant as well as a lubricant or glidant in tablet formulations. For example, Wai et al (1966), Lerk & Bolhius (1977) and Ragnarsson et al (1979) have shown that the presence of Aerosil in a tablet formulation reduces their disintegration and dissolution times while its lubricant property in powder mixtures has been reported by York (1975).

Reports on some commercial brands of paracetamol tablets in Nigeria have suggested that availability of the drug in this preparation is variable (Obiorah & Nasipuri 1976; Nasipuri et al 1982). In particular, Obiorah & Nasipuri (1976) showed that some commercial brands did not disintegrate even after 1 h.

The purpose of the present work has therefore been to see to what extent the properties of paracetamol tablets could be improved by the incorporation of excipients such as sorbitol, sodium lauryl sulphate and Aerosil, and in addition, to determine how the method of incorporation influences the behaviour of Aerosil in a tablet formulation.

Material and methods

The materials used were: paracetamol powder BP (Bayer W. Germany); maize starch and sodium lauryl sulphate (BDH Laboratories, UK); Aerosil (Merck, W. Germany), sorbitol 150 mesh (Laporte Industries Ltd.) and magnesium stearate (Evans Medical, UK). The paracetamol and the other materials were dried at 100 °C for 24 h and stored in screw cap jars.

Preparation of granules. The granulation was formulated to contain in each tablet, 500 mg paracetamol and 25 mg maize starch. The formulation was made in batches of 160 g and the different excipients, sorbitol (between 1 and 8% w/w), sodium lauryl sulphate (between 0·25 and 2% w/w) and aerosil to act as an internal disintegrant, (between 1 and 8% w/w) were added respectively.

The formulation and the various excipients were intimately mixed in a planetary mixer (Kenwood) and 105 g of freshly prepared 14% w/w maize starch mucilage added. The wet masses were granulated through a No. 8 mesh sieve, the granules dried for 12 h

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at 60 °C and screened through a No. 16 mesh sieve. The moisture content of the granules which ranged between 1·25 and 1·65% w/w was determined by heating to a constant weight.

Preparation of tablets. Magnesium stearate 1% w/w, was mixed with the formulated paracetamol granules in a ball mill for 5 min to act as lubricant. To a batch of the granules prepared without the inclusion of any of the excipients, dry Aerosil powder (1 to 8% w/w) was added and mixed in a ball mill for 5 min. The final mix was then compressed in a single punch machine (The Kilian and Co. GMBH, KOLN-NIEHI Type K5) fitted with 12·5 mm flat-faced punches at a constant dial machine compression reading of 6·5 units.

Hardness determination. The hardnesses of the tablets were determined using the Schleuniger Hardness Tester, (Esezobo & Ambujam 1982) and the mean of ten determinations calculated.

Friability determination. The friability of the tablets was measured as described by Esezobo & Ambujam (1982) but employing a Roche Friabilator.

Disintegration time measurement. Ten tablets from each batch were individually assessed using the BP disintegration test apparatus (Manesty Ltd) and a mean time calculated (Esezobo & Ambujam 1982).

Dissolution test. The dissolution rate of single tablets was measured in 0·1 M HCl at 37 °C ± 0·5 °C using the modified beaker method of Levy & Hayes (1960) as described by Esezobo & Pilpel (1976). Samples were periodically assayed spectrophotometrically at 243 nm for drug in solution. Three replicate determinations of each formulation were averaged.

Results and discussion

Table 1 summarizes the results of the effects of the excipients on the hardness, friability and disintegration times of paracetamol tablets. It is seen that an increase in the concentrations of sorbitol, sodium lauryl sulphate and Aerosol (added internally) all resulted in a slight decrease in hardness with a corresponding increase in the friability of the tablets. This result is in good agreement with those previous studies (Ragnarsson et al 1979; Holzer & Sjogren 1981). It may be assumed that the incorporation of these excipients before wet granulation weakened the interparticulate bonds between the drug particles similar to the effects of lubricants on tablet strength (Shotton & Ganderton 1961; Shotton & Lewis 1964).

In contrast, the addition of dry Aerosil powder to the granules before compression (i.e. added externally) resulted in the production of harder tablets with a corresponding decrease to their friability (See Table 1).

Table 1. Mean hardness, friability and disintegration time for paracetamol tablets containing varying concentrations of excipients. The results are the means of three replicates.

Excipients	Concn (% w/w)	Mean hardness (Kp)	Friability (%)	Disintegration time (min)
Sorbitol	1·00	10·57	1·00	0·61
	2·00	7·42	2·83	0·55
	4·00	5·53	3·15	0·43
	8·00	4·90	3·83	0·33
Sodium lauryl sulphate	0·25	10·56	2·64	0·60
	0·50	10·00	2·87	0·51
	1·00	9·75	2·18	0·47
	2·00	9·07	3·61	0·41
Aerosil (added internally)	1·00	9·72	2·70	1·96
	2·00	8·18	3·06	0·90
	4·00	7·74	3·49	0·70
	8·00	6·49	3·88	0·65
Aerosil (added externally)	1·00	11·52	2·00	2·43
	2·00	12·07	1·93	2·88
	4·00	14·24	1·70	3·29
	8·00	15·80	1·69	3·65

This result is also in agreement with those of Ragnarsson (1979) who reported that the addition of colloidal silica to a lubricated sodium chloride formulation increased the strength of the tablets. When the granules are compressed the Aerosil on the granule surface forms strong bonds between the granules and these are responsible for the increased hardness of the tablets (Pilpel 1970; York 1975).

Increasing the concentration of the excipients resulted in a decrease in the disintegration time and an increase in the dissolution rates of the tablets (Table 1 and Fig. 1).

The increased disintegration and dissolution rates of the tablets with increase in sorbitol concentration (Fig. 1) accord well with previous reports (Gwilt et al 1963; Walters 1968). These workers observed a better absorption of paracetamol from a paracetamol/sorbitol tablet formulation than from a paracetamol tablet formulation without sorbitol.

As expected from previous work on tablets (Stephenson 1961; Wurster & Taylor 1965; Bates et al 1966; Holzer & Sjogren 1981) and from the present results on paracetamol tablets (Table 1 and Fig. 1), the disintegration and dissolution rates increased with increase in sodium lauryl sulphate concentration.

The addition of Aerosil to the formulation before wet gramulation (i.e. added internally) resulted in a decrease in the disintegration times and an increase in the dissolution rates of the tablets (Table 1 and Fig. 1). In this instance, Aerosil may be behaving as a disintegrant by absorbing water. This behaviour of Aerosil may be complementing the disintegrant effect of the 5% starch. On the other hand, addition of the dry Aerosil powder to the granules (i.e. added externally) resulted in a fall

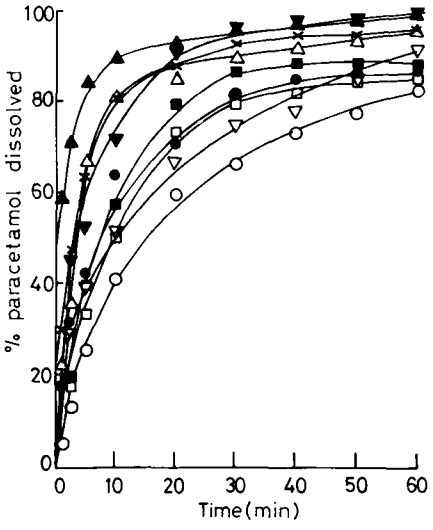

FIG. 1. Effect of the excipients concentrations on the dissolution profiles of paracetamol tablets. ○—○ 0% w/w excipients, □—□ 1% w/w sorbitol, ■—■ 2% w/w sorbitol, △—△ 0·5% w/w sodium lauryl sulphate, ▲—▲ 1·0% w/w sodium lauryl sulphate, ▽—▽ 2% w/w Aerosil (added internally), ▼—▼ 4% w/w Aerosil (added internally), ×—× 2% w/w Aerosil (added externally), ●—● 4% w/w Aerosil (added externally).

in their disintegration and dissolution rates (Table 1 and Fig. 1). This observation may be ascribed to the lubricant property of Aerosil (Sandell 1968; Pilpel 1970; York 1975; Lerk & Bolhuis 1977) or to its gel-forming ability (Sandell 1968). This latter mechanism is probably more significant since the gel would create a viscous barrier between the granules and the water. Increase in Aerosil concentration will produce thicker gel formation round the granules and hence would cause longer disintegration times and dissolution rates of the tablets (Esezobo & Pilpel 1976; Esezobo & Ambujam 1982).

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