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THE EFFECT OF PRECOMPRESSION IN A ROTARY MACHINE ON TABLET STRENGTH

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ABSTRACT

The effects of precompression on tablet strength/main compression pressure profiles have been studied with an instrumented rotary tabletting machine. The advantages of precompression are dependent upon individual formulation components and their behaviour under stress, tablet shape, and machine speed. Model systems and the mechanisms by which precompression may improve tablet strength, are discussed.

INTRODUCTION

Precompression describes the smaller preliminary compression force or forces which may be applied immediately prior to main compression on some rotary tablet machines. Some machines, e.g. Novapress (Manesty Machines, Liverpool, U.K.) provide the option of up to three district compression events per tabletting

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cycle. Although manufacturers have often claimed that precompression is capable of improving tablet strength, such claims are seldom supported with positive data. The mechanisms by which precompression may improve tablet strengths is not well documented, but an increase in total dwell and contact time could facilitate either time dependent plastic flow, relieving elastic stress or expulsion of air from the compact. These effects have been considered to determine freedom from lamination and capping on ejection in the context of single precompression (1,2).

In this study, the influence of precompression on tablet strength was determined using a number of excipients and formulations, by means of an instrumented rotary tablet machine. The influences of machine speed, dwell and contact times and tablet shape were also examined.

MATERIALS

Microcrystalline cellulose, Avicel pH 102 (Honeywill & Stein Ltd., Surrey, U.K.) Dicalcium phosphate dihydrate, Emcompress (K & K Greeff Limited, Surrey, U.K.). Sodium starch glycolate, Explotab (K. & K.Greeff Limited, Surrey, U.K.). Paracetamol fine powder and Paracetamol DC (Graesser Salicylates, Sandycroft, Clwyd, U.K.). Hydroxypropylmethylcellulose, Pharmacoat 615 (Shin-Etsu Chemical Co., Tokyo). Magnesium Stearate (Durham Raw Materials, Durham, U.K.).

METHODS

Direct compression mixes of microcrystalline cellulose (MCC) dicalcium phosphate dihydrate (DCP), 33%-67%w/w and MCC/DCP/paracetamol fine powder (23%: 47%:30%) were prepared by blending the ingredients in a planetary mixer (Hobart, U.K.) for five minutes.

Paracetamol granules were prepared by mixing paracetamol E.P. 95.5%, sodium starch glycolate 2.5% hydroxypropylmethylcellulose 2% with sufficient water to give a medium granulation which was rotorgranulated and screened to produce a sieve size range of 400-1400μ. MCC was compressed without lubricant. 0.5%w/w Magnesium stearate was incorporated into the DCP system, the blends of MCC/DCP, MCC/DCP/paracetamol and the paracetamol granules, by mixing for five minutes as described above. The MCC/DCP/paracetamol blend was compressed to form 450mg biconvex, and 450mg and 300mg flat tablets, and all other systems compressed to form 300mg flat tablets, on a rotary machine instrumented as previously described (3) using a single station. Flat faced punches of nominal diameter 10mm were used throughout and, in addition, concave punches of similar diameter but different radii of curvative (6.35 and 12.0mm) were used to compress the MCC/DCP/ paracetamol mix. All punches and dies used were machined to the same tolerances. Compression forces were measured with piezoelectric load washers attached to pre- and main compression roller bearings and/or strain gauged flat faced punches previously calibrated with an external load cell. Force data were processed via direct measurements from a storage oscilloscope (Tektronix, Maidenhead, U.K.). Forces, dwell and contact times were measured from recordings taken with a u.v. oscillograph (Type 6008, S.E. tabs., E.M.I. Limited). Tablet crushing strength, and hence tensile strengths (4) of flat faced tablets were obtained with a motorised hardness tester (G.B. Caleva Limited, Ascot, U.K.).

RESULTS AND DISCUSSION

Fig. 1 shows the tensile strength main compression pressure profiles of paracetamol DC tablets compressed

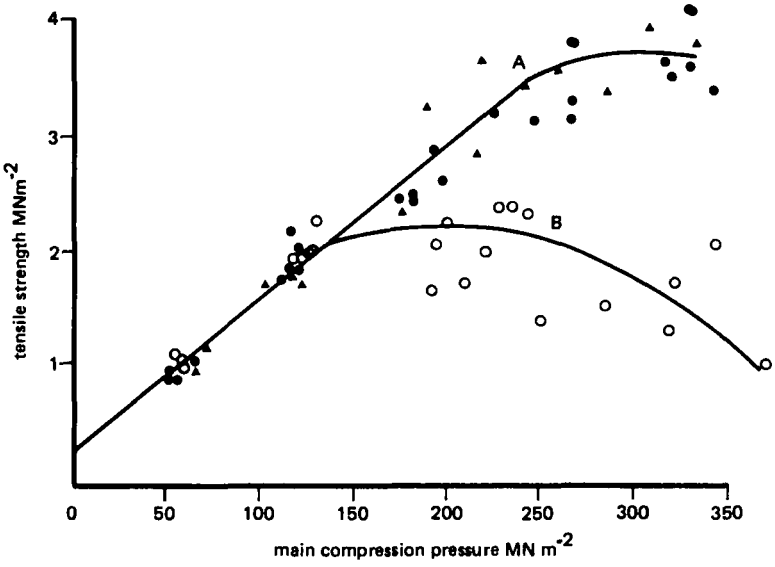

FIGURE 1

Dependence of tablet tensile strength on main and pre compression: 300mg flat paracetamol D.C. tablets: ○ without precompression; ● with 13MNm^{-2} precompression and ▲ with 26MNm^{-2} precompression. The shape and location of the upper curve A is invariant with precompression >13MNm^{-2}.

without precompression (B) and with precompression pressures of 13 and 26MNm^{-2} (A). The upper profiles appear to be invariant with precompression above 13MNm^{-2} the profiles of tablets made using the precompression pressures described are identical and even further doubling precompression has no effect on tablet strength (curve A). Profiles of tablets made with and without precompression are superposable up to main compression pressures of 140MNm^{-2}, above which a fall occurs in the tensile strengths of tablets prepared without precompression (B), such tablets showing increasing incidence of visible lamination with increase in main compression,incidence of lamination in unpre-compressed tablets corresponding to the separation of curves A and B. Capping occurred in unprecompressed

tablets during test fracture. At higher machine speeds (= 1200 to 1500 tablets/minute) tablets prepared with precompression, at main compression >200MNm^{-2} showed signs of lamination, but tensile strengths (curve A) appeared unaffected. Such behaviour may be more typical of tablet failure involving formation of strong integral laminae of individual tensile strengths approximating that of an intact tablet, - which is sometimes characteristic of elastic failure of a compressed mass (5), rather than of bonding failure of the mass which may occur with entrapped air (cf. Fig. 1 curve B).

Granulated paracetamol shows curves similar in shape to figure 1, A; these are not shown but tablets could not be prepared without capping in the absence of precompression. Edging, capping and lamination were strongly machine speed dependent, although unlike DC paracetamol there was no divergence of curves.

It has been proposed that precompression forces increase tablet tensile strength by increasing overall contact and dwell times: some authors, e.g. Jones (6) define dwell time as the interval during which maximum compression pressure is maintained by the punches during the compression cycle. However, the geometry of the majority of high speed rotary machines yield rounded pressure peaks, where the true time interval at peak pressure is infinitestimal. On such machines it is more practical to define dwell time in terms of compression pressure profile width at a given fixed fraction of peak height (e.g. 50%).

At the quoted speed, values of contact times measured with paracetamol DC tablets were typically

47ms and 63ms without and with precompression at 10% of main compression, respectively, although these figures depend slightly upon fill weight and main compression. Corresponding values of dwell times are 24.4ms (±0.4) and 17.0ms (±0.2) measured at 20% and 50% of peak height respectively, and, unlike total contact time, were invariant with precompression, when the latter is below the force at which dwell time is measured.

The hypothesis that tablet quality may be improved by precompression by increase in total contact time was examined by increasing (to = 1410 tablet min^{-1}) and decreasing (to = 783 tablets min^{-1}) machine speed with and without precompression respectively to equalise contact times. The deterioration, and improvement, respectively in the quality of the tablets, as measured by tensile strength and lamination vis a vis those plotted in Fig. 1 were negligible, the points continuing to fall on curves A and B of figure 1 respectively. Thus it appears that increases in dwell and contact times alone are insufficient to account for this significant improvements in tablet quality observed. Separation in time by relatively long intervals (0.2 seconds ~) of two distinct compression events at high machine speed appears to be of far greater importance.

Figure 2 shows tensile strength profiles of MCC, DCP and a 1:2 mix showing profile invariance with precompression. There were no signs of lamination or capping even on test fracture. Such curves may be typical of negligible elastic storage of compression work, or of the tabletting of compression aids where only a fraction of

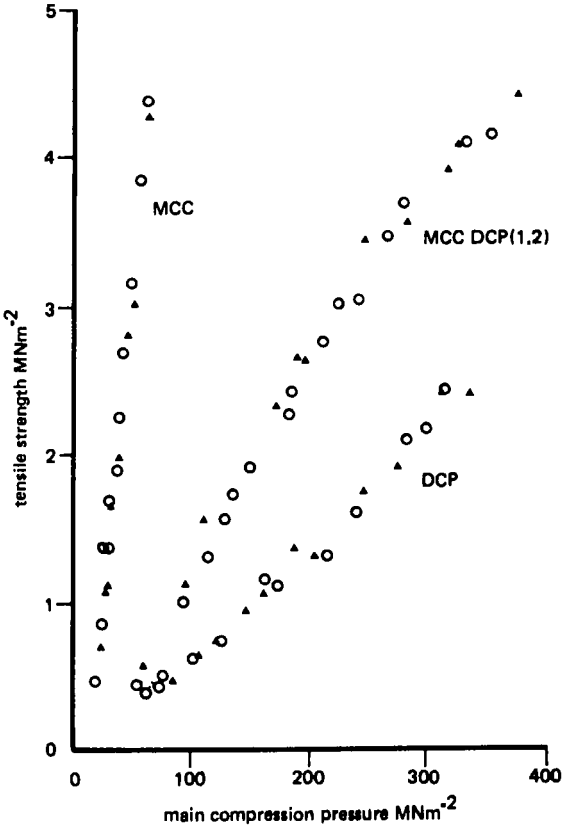

FIGURE 2

Tensile strength profiles of 300mg flat MCC tablets (A) MCC/DCP 1:2 (B) and DCP (C) ○ without and ▲ with precompression. Profiles are precompression invariant.

their capacities are filled. This state of affairs is frequently attained, especially in the tabletting of low-dose materials, and precompression is unnecessary.

Figure 3 shows crushing strength profiles off MCC/DCP/paracetamol mix. Good quality cylindrical tablets are produced under all conditions of main compression with unsignificant precompression dependence of tensile strength. Tensile strength/main compression pressure curves for 300mg and 450mg tablets (not shown) are nearly identical. Tabletting of this formulation

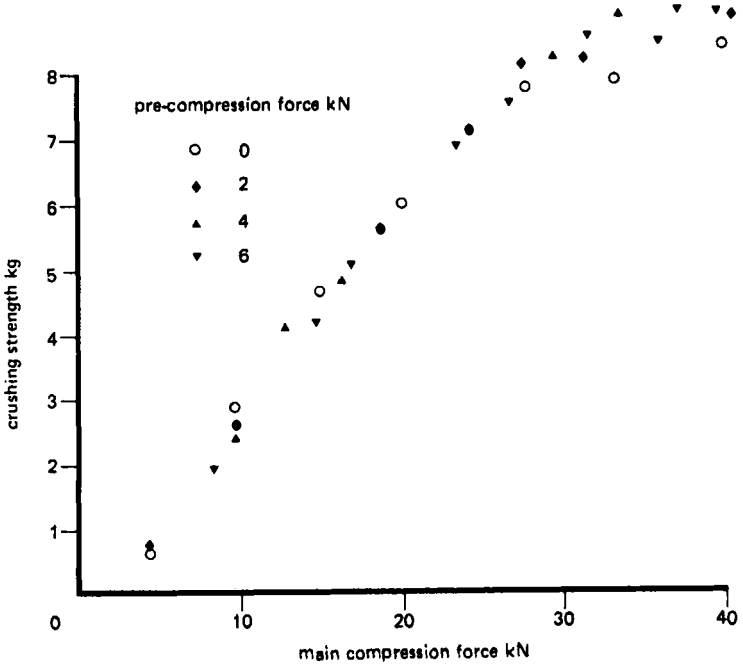

FIGURE 3

Diametral crushing strengths of 300mg flat tablets of MCC/DCP/paracetamol, 23%:47%:30%, showing precompression invariance.

became more critial with deep concave punches, however; tablet strengths depended significantly upon pre-compression (figure 4). This may arise from steeper stress gradients arising in noncylindrical tablets, or from air entrapment. Figure 4 shows diametral crushing strengths of MCC/DCP/paracetamol mix (cf. Fig. 3) tabletted with 9.525mm nominal diameter deep concave (r=6.35mm) punches, at tablet mass = 450mg. Punches of flatter concavity (r = 12.0mm) produce curves intermediate in shape between figure 3 and 4. The high scatter in the curve downturns in figure 4 is apparently due to significant internal lamination, visible only on test fracture, occurring specifically at low pre-compression, which may result in random orientation dependent resistance to external forces.

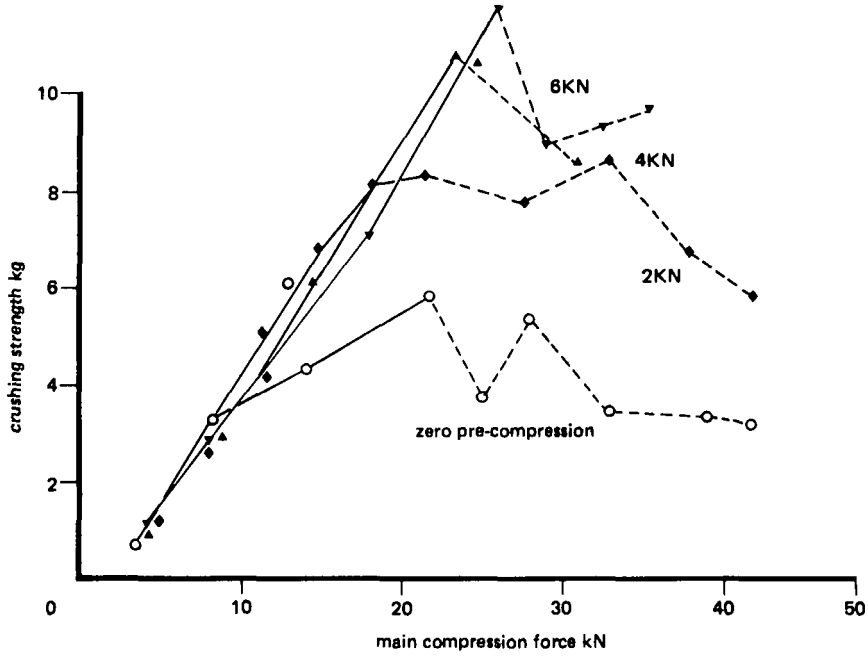

FIGURE 4

Diametral crushing strength profiles of MCC/DCP/ paracetamol 23%:47%:30% produced on deep concave punches, showing strong precompression dependence. Broken lines indicate the appearance of internal lamination and capping visible on test fracture.

CONCLUSIONS

Precompression may significantly improve tablet properties, although its advantages are highly dependent upon formulation and tablet shape. It appears that advantages of precompression arise more from separation of two distinct compression events by a relatively long interval of time, and not generally from increase in contact or dwell times, suggesting the involvement of relatively slow time dependent phenomena. Precompression also appears to become more important with biconvex tablets. Since only a minority of marketed products are in the form of flat tablets, the use of flat tablets as model systems for fundamental

studies may be questioned. It is suggested that simple compressional studies on an instrumented rotary machine, using tablets of the final proposed shape may be carried out to effectively optimise formulations and processes.

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