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Peak Offset Times as an Indication of Stress Relaxation During Tableting on a Rotary Tablet Press*

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Abstract—During powder compaction on a Manesty Betapress, peak pressures, P_{max}, are reached before the punches are vertically aligned with the centres of the upper and lower compression roll support pins. The interval between the time taken to reach this alignment and the time to reach P_{max} is defined as the peak offset time, t_{off}. The duration of t_{off} depends on the ability of the compacted powder to relieve stress and is an indication of the predominant mechanisms of particle deformation during consolidation. Thus, at a given P_{max}, short t_{off} values are characteristic of materials that consolidate mainly by brittle fracture while longer values indicate an increase in plastic flow. On the Betapress, the decrease in stress during t_{off} occurs under conditions approaching constant strain and t_{off} therefore, is an indirect measure of stress relaxation. Stress relaxation, and hence t_{off}, decreases with increase in P_{max} due to the reduction in the porosity of the compact and consequent restriction of plastic flow into the void spaces. In addition to P_{max}, the effects of variables such as punch head geometry, press speed and formulation on t_{off} are reported.

The success of powder compaction in producing strong, coherent tablets depends, at least in part, on the extent of deformation of the solid particles under stress. Deformation involves either fracture or plastic flow, or both (Train 1956). A characteristic feature of solids that exhibit plastic flow is their ability, over a period of time, to relieve the stress under conditions of constant strain. This phenomenon is called stress relaxation (Popov 1968).

During tableting, plastic flow occurs in a confined space over a time period which is determined by the type of compression equipment used. A powder bed will exhibit stress relaxation during some part of the compression cycle provided the dimensions of the confined space, i.e. the strain on the powder, remain more or less constant with time. Several reports in the literature allude to this. For example, Shlanta & Milosovich (1964) observed the stress relaxation of a number of pharmaceutical solids on an instrumented hydraulic press. Cole et al (1975) reported differences in the extent of stress relaxation of sodium chloride, potassium chloride, lactose and potassium citrate when these substances were compressed on a device specially developed to simulate a rotary tablet machine. Using a hydraulic press similar to the one used by Shlanta & Milosovich (1964), Hiestand et al (1977) found that materials that are known to cap showed slow stress relaxation. David & Augsburger (1977) quantitated stress relaxation on a Stokes RB-2 rotary tablet machine under static conditions. They recorded the drop in pressure over a period of several seconds for some direct compression excipients, applied the Maxwell model of linear viscoelasticity to these data and reported a characteristic viscoelastic constant for each material. Rees & Rue (1978) measured stress relaxation on a Wilkinson STD 1 reciprocating tablet machine and found an exponential decay of stress, contrary to the linear decay reported by David & Augsburger (1977). They argued that there could be more than one characteristic viscoelastic constant for the powders compressed. They also indicated that a rotary tablet machine, like the one used by David & Augsburger (1977), may not be a deflection-free system and therefore the strains during the period of stress relaxation may not be constant. More recently, using an Instron Physical Testing Instrument, Cutt et al (1987) demonstrated the effect of wet granulation on the stress relaxation of a model system consisting of glass bellotini granulated with different binders. The granulated glass showed significantly enhanced stress relaxation over a period of 6 min compared with non-granulated glass. Ho & Jones (1988a) studied the stress relaxation of a number of pharmaceutical materials on a modern compaction simulator.

These reports indicate both qualitative and quantitative differences in the stress relaxation behaviour of various substances. Relative to the operating conditions of a rotary press, the decrease in stress was followed over long periods of time ranging from a few seconds to several minutes. Only some of these studies provided evidence of constant strain.

To establish the relevance of stress relaxation in tableting on rotary presses, where compression normally occurs in less than 50 ms, evidence is required that stress relaxation indeed occurs at the speeds encountered on such machines and that the condition of constant strain is satisfied over the period of stress relaxation. To provide such evidence it is necessary to investigate the relationships between stress and strain (i.e. pressure and punch displacement) on a rotary tablet machine or on a compaction simulator.

Stress relaxation studies on a compaction simulator require an input of the punch displacement profile from the rotary tablet press in order to simulate its compression cycle. If the deflections of the press under stress are ignored, the resultant errors in the displacement profiles will lead to inaccuracies in the estimation of strain during the period of stress relaxation. The strain can be rigorously defined only if the machine deflections are taken into account (Oates & Mitchell 1989, 1990).

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Contrary to the assumption that the peak punch pressures occur at maximum punch displacement, Ho & Jones (1988b) reported the phenomenon of 'punch travel beyond peak force' on a compaction simulator and related it to the plastic flow of materials during compression. Experiments in our laboratory indicated that the peak punch pressures on a Manesty Betapress occur before the vertical alignment of the punches with the centres of the upper and lower pressure rolls. The time by which the peak pressures were set off from such an alignment was called the 'peak offset time' (t_{off}), the duration of which is related to the ability of a material to flow under stress (Oates & Mitchell 1989). Recently, Morehead & Rippie (1990) found that the punch stress profiles on a Colton 216 rotary tablet press were not symmetrical about the punch displacement profiles, and attributed this asymmetry to time-dependent viscoelastic processes occurring within the compact. For plastically deforming substances like Avicel, Klucel and Mannitol, they reported 'maxima lead times' analogous to the t_{off} on the Manesty Betapress.

Since the duration of t_{off} is related to time-dependent plastic flow, it is pertinent to investigate whether this occurs under conditions of constant strain. This paper shows that t_{off} occurs at approximately constant strain during high speed tableting on a Manesty Betapress and is therefore a valid measure of stress relaxation. Certain factors likely to affect the duration of t_{off} and hence stress relaxation are examined.

Materials and Methods

Materials

Tablets were made from Avicel PH102 (microcrystalline cellulose, FMC Corporation), Emcompress (dicalcium phosphate dihydrate, Edward Mendell), and spray-dried lactose (Foremost Whey Products), after mixing each material with 0·5% magnesium stearate. Tablets of crystalline paracetamol (acetaminophen) (Mallinckrodt Inc.), crystalline ibuprofen (Apotex) and direct compression formulations such as Rhodapap DC-P3 (directly compressible paracetamol containing 3% polyvinylpyrrolidone, PVP; Rhône-Poulenc), Compap CG (directly compressible paracetamol containing 10% starch; Mallinckrodt Inc.) and DCI-63 (directly compressible ibuprofen 63%, Mallinckrodt Inc.) were made with die wall and punch faces lubricated with a 5% solution of stearic acid in chloroform. Three different types of crystalline paracetamol were used, Acetaminophen USP Granular (95% particles larger than 45 μm), Acetaminophen USP Powder (60% particles larger than 38 μm) and Acetaminophen USP Fine Powder (20% particles larger than 38 μm).

Equipment

A Manesty Betapress was used for all experiments. One of the sixteen stations of the press was fitted with a die with 1/2″ (1·270 cm) flat faced upper and lower punches, and the remaining fifteen stations were blanked off. Two types of punch, namely IPT and Manesty, were used. Geometrical differences between these punches have been described by Oates & Mitchell (1990). No force was applied to the punches by the precompression pressure rolls. The hopper and feedframe were removed for easy access to the tooling.

The roll pin supporting the upper pressure roll and the cross beam supporting the lower pressure roll were instrumented to determine the upper and lower punch forces respectively as described previously (Oates & Mitchell 1989). The punch displacement for both IPT and Manesty punch types was determined according to the analysis procedure developed by Oates & Mitchell (1989, 1990).

Methods used for data collection, analysis and storage have been upgraded since these previous reports. After amplification and filtering, the analogue signals are converted to digital form using a 12-bit fast A/D converter (Metrabyte), and collected by an IBM compatible computer at a rate of 2500 readings s^{-1} for each of the two punch force channels. The raw data are analysed with the aid of a math coprocessor and software developed in this laboratory, which permit data analysis in two modes: one data file at a time in an individual analysis mode or several data files together in a bulk analysis mode. The total time taken for compression of a tablet and collection, storage and analysis of the corresponding data in the individual analysis mode is between 2 and 3 min. Appendix I lists some of the parameters routinely computed by the software.

Determination of peak offset time

Compression begins when the force on the upper and lower punches is first measurable and ends when the punches are vertically aligned with the axes of the two pressure rolls along an imaginary vertical line called the line of dead centre. In terms of time, t, this line is specified as $t=0$ (Fig. 1). Peak offset time is the interval between the time to reach peak pressure P_{max} and $t=0$ (Fig. 2). For an accurate determination of t_{off}, it is necessary to know when $t=0$ occurs following the triggering of data collection. Steel is virtually incompressible under the pressures used in this study and shows symmetrical pressure-time profiles with P_{max} at $t=0$ (Oates & Mitchell 1989). The position of P_{max} is given by the data analysis software as the point where the derivative of pressure with respect to time is 0. Thus, the position of $t=0$, on an experimental pressure-time profile at a given machine speed can be determined by compressing a steel tablet at that speed and finding the position of P_{max}. The machine speed is given in terms of 'turret time' which is defined as the time taken for one complete revolution of the turret.

When repeatedly compressed without ejection at pressures above 280 MPa, Emcompress showed pressure-time profiles almost identical with those of the steel tablet. Therefore, the position of $t=0$ at different speeds was found by determining

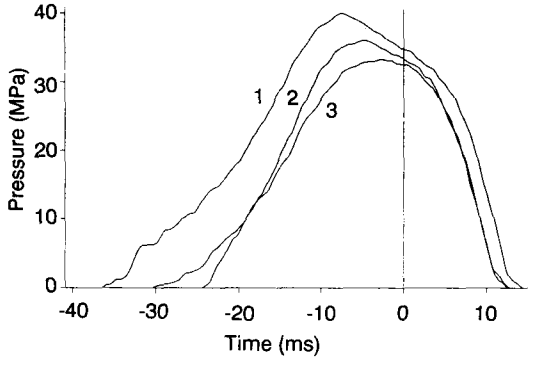

FIG. 1. Pressure-time curves for: (1) Avicel PH102, (2) spray-dried lactose, and (3) Emcompress. Turret time = 1s, IPT punches.

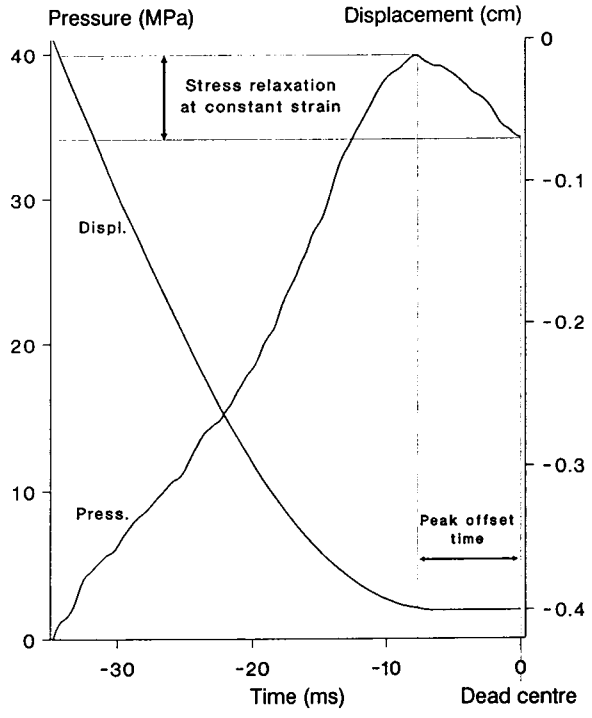

FIG. 2. Pressure and punch displacement-time curves showing stress relaxation at constant strain and peak offset time for Avicel PH102. Turret time = 1s, IPT punches.

the positions of P_{max} for Emcompress tablets made by repeated compression, without ejection, at pressures above 280 MPa. The average position of P_{max} for ten tablets at each turret time was used to give the average position of $t=0$ at that speed. The coefficient of variation of these averages was less than 0·4% at each turret time indicating high precision in the position of $t=0$. When provided with the turret time and the position of $t=0$, the data analysis software automatically determined the value of t_{off}.

Factors affecting t_{off}

The following experiments were performed to study various factors likely to affect t_{off}.

Experiment I. Using IPT punches at a turret time of 1 s, tablets were made from the three direct compression excipients over a range of P_{max} by (a) varying the mass of the tablet, with the tablet thickness setting on the machine fixed, and (b) fixing the mass of the tablet and varying the thickness setting.

Experiment II. Experiment I (a) was repeated at different turret times using Manesty punches in order to study the effect of machine speed on the t_{off} for Avicel PH102 and Emcompress.

Experiment III. To study the effect of different punch types on t_{off}, tablets of Avicell PH102 and Emcompress were made over a range of P_{max} at a turret time of 1 s using both IPT and Manesty punches.

Experiment IV. To study the effect of formulation on t_{off} for drugs with poor compression properties such as paracetamol and ibuprofen, tablets from crystalline samples and certain directly compressible commercial formulations of these drugs were made at a turret time of 1 s using IPT punches. The change in t_{off} with increasing P_{max} was recorded for each sample.

Determination of tablet strength

The strength of the compressed tablets was determined using a CT-40 tablet strength tester (Systems Engineering). The tablets were stored at about 21°C under ambient relative humidity for 24 h before the determination of the force of failure.

Results and Discussion

Some representative pressure-time profiles for Avicel PH102, spray-dried lactose, and Emcompress are shown in Fig. 1. All three materials show an offset of P_{max} with respect to the vertical alignment of the punches with the pressure rolls at $t=0$. However, the duration of t_{off} is different for each material. The net punch displacement profile (Fig. 2) shows that the displacement and therefore the distance between the upper and lower punch faces is approximately constant during t_{off}. It can be seen that the punch stress decreases during t_{off} while the strain remains essentially constant. Hence t_{off} is indicative of stress relaxation since the stress is decaying at constant strain albeit for a very short time.

Factors that can affect the degree of plastic flow during tableting are likely to affect the magnitude of t_{off}. At least three such machine-related factors can be readily identified, namely, P_{max}, turret time and punch type. A fourth factor is the addition of one or more plastically deforming components to the formulation. Each of these factors is discussed below.

Effect of P_{max} on t_{off}

Fig. 3 shows the changes in t_{off} for Avicel PH102, spray-dried lactose and Emcompress with changes in the P_{max} using IPT punches at a turret time of 1 s. Each of these excipients has excellent tableting properties, and the differences in t_{off} reflect differences in their deformation mechanisms.

Avicel PH102 had the longest t_{off} with values up to about 8 ms at the lowest P_{max} studied, suggesting that stress relief is achieved by plastic flow into the voids of the tablet.

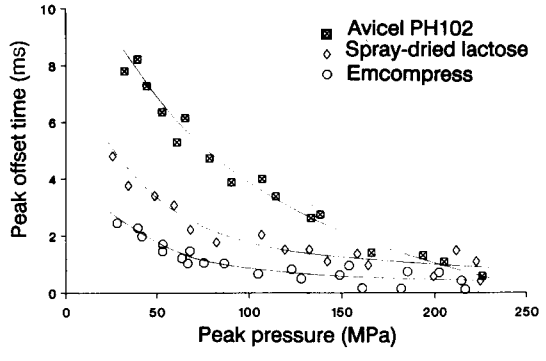

FIG. 3. Variation in peak offset times with peak pressure for three direct compression excipients. Turret time = 1s, IPT punches.

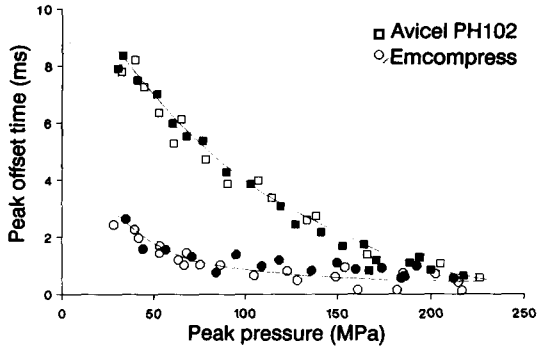

FIG. 4. Variation in peak offset time with peak pressure. Turret time = 1s, IPT punches. Open symbols, peak pressure varied by changing the mass at fixed thickness setting; closed symbols, peak pressure varied by changing the thickness setting keeping the mass constant.

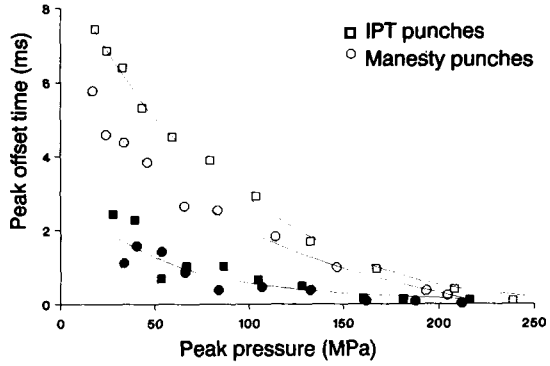

FIG. 6. Effect of punch type on peak offset times. Turret time = 1s. Open symbols, Avicel PH102; closed symbols, Emcompress.

Emcompress, which deforms predominantly by particle fracture, had much shorter t_{off} values than Avicel PH102 and spray-dried lactose. Spray-dried lactose is manufactured from a suspension of lactose crystals and consists of spherical aggregates of amorphous lactose with loose or embedded lactose crystals (Kussendrager et al 1981). Amorphous lactose shows plastic flow while crystalline lactose undergoes particle fracture (Morita et al 1984; Vromans et al 1986). Thus, spray-dried lactose exhibits deformation characteristics that are intermediate between those of Avicel PH102 and Emcompress, with t_{off} of up to about 5 ms at the lowest P_{max} studied.

The ability of particles to undergo stress relaxation within the confines of a die cavity will become increasingly restricted as the porosity of a powder bed decreases. This is illustrated by the results in Fig. 3 which, for each material, show that the duration of t_{off} decreased asymptotically towards a lower limit as P_{max} was increased.

The P_{max} on a rotary tablet press can be increased either by increasing the mass of the material in the die at a fixed thickness setting on the press, or by changing the thickness setting to reduce tablet thickness keeping the mass constant. Fig. 4 shows that the duration of t_{off} is independent of the method of increasing P_{max}. It was easier to change the mass of the material in the die at a fixed thickness setting, and this procedure for changing P_{max} was used in all further experiments.

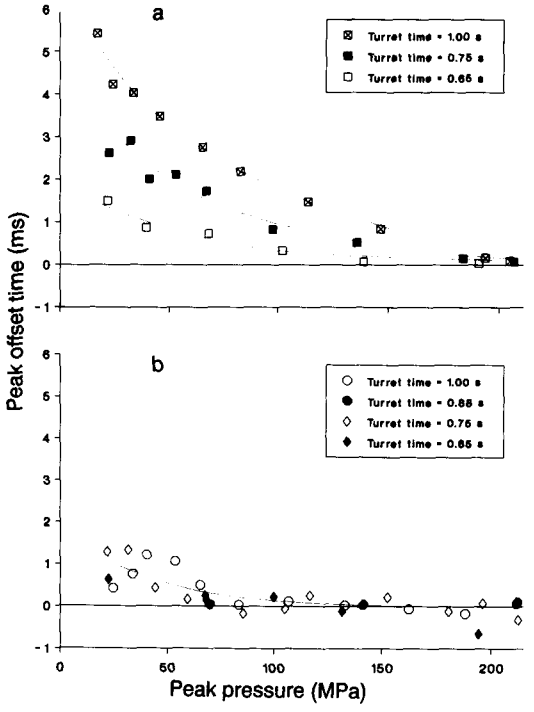

FIG. 5. Effect of turret time on peak offset times for (a) Avicel PH102, and (b) Emcompress. Manesty punches.

Effect of machine speed on t_{off}

The t_{off} for Avicel PH102 at different turret times is shown in Fig. 5a. Decreasing the turret time reduced t_{off} showing that at faster machine speeds Avicel PH102 has less time to undergo stress relief by plastic flow than at slower speeds. Situations can sometimes occur where a formulation produces good tablets on slow machines but fails when transferred to higher speed machines. One reason may be a decrease in the extent of plastic flow as indicated by a decrease in t_{off} at faster machine speeds. For Emcompress, t_{off} is independent of turret time (Fig. 5b) indicating that, for brittle materials, stress relief does not depend on the rate of application of stress.

Effect of punch type on t_{off}

The IPT punches have a flatter punch head profile than the Manesty punches (Oates & Mitchell 1990) thereby providing a longer dwell time for stress relaxation. Fig. 6 shows the t_{off} for Avicel PH102 and Emcompress compressed using the two punch types. At P_{max} below 110 MPa, the t_{off} for Avicel PH102 becomes progressively longer when compressed using IPT punches than with Manesty punches. For a brittle substance like Emcompress, differences in t_{off} due to punch type were not significant. These observations suggest that the tableting behaviour of plastically deforming substances is more likely to be affected than that of brittle materials on changing from IPT to Manesty tooling. Above about 110 MPa, equivalent to about 1·5 tons, there is little difference in t_{off} for Avicel PH102 between the two punch types suggesting that differences in dwell time are less significant than the decrease in porosity above this pressure.

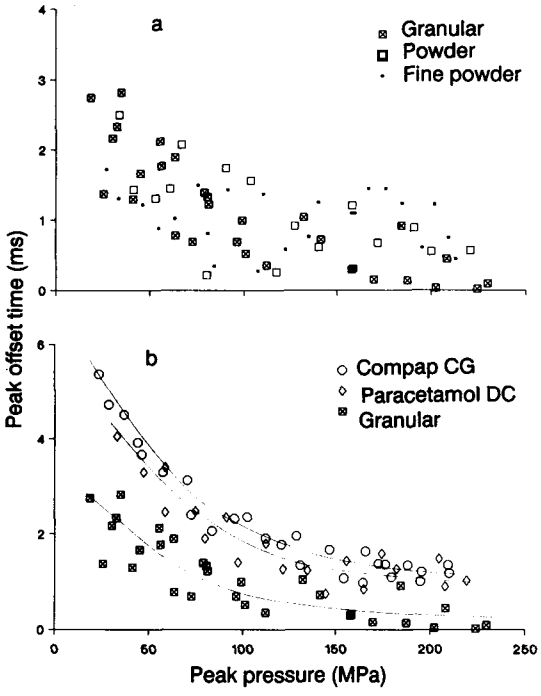

FIG. 7. Variation in peak offset times with peak pressure for paracetamol. Turret time = 1s, IPT punches. (a) effect of particle size, (b) effect of formulation.

Effect of formulation variables on t_{off}

Drugs such as paracetamol and ibuprofen which cap or laminate during or after decompression are modified commercially by formulating them with polymeric substances which deform plastically under stress. An examination of Rhodapap DC-P3 paracetamol by scanning electron microscopy indicated that it is made by spray drying a slurry of crystals in a solution of the polymer. Compap CG is containing 10% starch and appears to be made by a similar process.

Fig. 7a shows the relationship between t_{off} and P_{max} for three samples of crystalline paracetamol. The t_{off} values for the three samples were highly variable and were indistinguishable from one another despite major differences in their particle size distributions. The short t_{off} values indicate that crystalline paracetamol undergoes little plastic flow and,

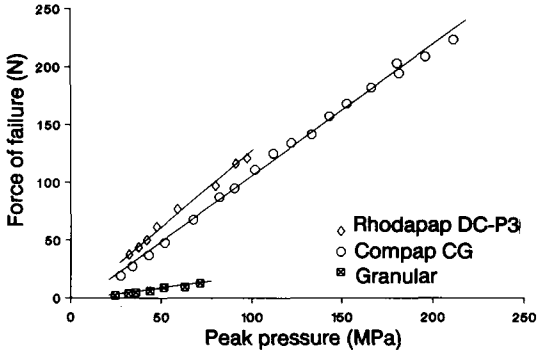

FIG. 8. Variation in force of failure with peak pressure for crystalline and direct compression forms of paracetamol. Turret time = 1s, IPT punches.

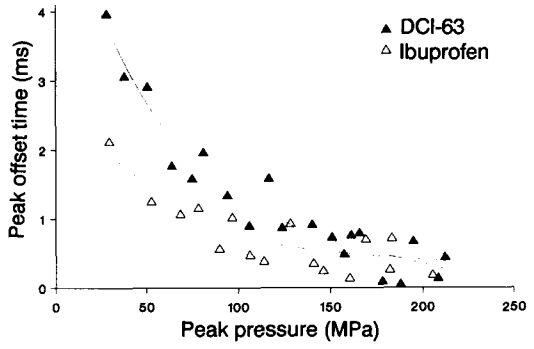

FIG. 9. Comparison of peak offset times for crystalline ibuprofen and a direct compression formulation. Turret time = 1s, IPT punches.

like Emcompress, deforms mainly by particle fracture. Acetaminophen Powder and Acetaminophen Fine Powder did not form tablets at any pressure. Acetaminophen Granular produced intact, but weak, tablets below about 80 MPa (Fig. 8), but capping occurred above this pressure. Below about 80 MPa, fracture of the large crystals of Acetaminophen Granular presumably exposes sufficient clean surfaces for the creation of interparticulate bonds. Above this pressure, it is suggested that elastic recovery of the tablets during decompression is sufficient to cause tablet failure.

It is evident from Fig. 7b that the addition of a small amount of PVP as in Acetaminophen DC increases plastic flow sufficiently to prolong t_{off} by about 2 ms for P_{max} up to about 90 MPa. Rhodapap DC-P3 forms strong tablets below this pressure but shows lamination at higher pressures where its t_{off} approaches that of crystalline paracetamol. Compap CG contains a greater amount of a plastically deforming substance (starch) and forms intact tablets up to P_{max} of about 210 MPa. The tablet strengths of Compap CG are comparable with those of the tablets of Rhodapap DC-P3 (Fig. 8).

Similar results were obtained for ibuprofen (Fig. 9). The directly compressible ibuprofen, DCI-63, has longer t_{off} relative to crystalline ibuprofen at P_{max} up to about 90 MPa. There are no differences in t_{off} above this pressure. Like the direct compression forms of paracetamol, DCI-63 forms tablets only below about 90 MPa, whereas above this pressure lamination occurs. Crystalline ibuprofen, on the other hand, does not form tablets at any pressure.

The increase in t_{off} for the direct compression formulations of paracetamol and ibuprofen suggests that these formulations permit a degree of plastic deformation which leads to interparticular bonding.

The duration of t_{off} is an indication of the extent of plastic deformation during compression. Using a Manesty Betapress it has been shown that the punch stress decreases and the punch displacement remains constant during t_{off}. This is direct experimental evidence of stress relaxation during high speed tableting. The ability of t_{off} to differentiate between the predominant mechanisms of deformation is illustrated by the t_{off} values of Avicel PH102, spray-dried lactose and Emcompress. Factors such as P_{max}, machine speed, punch type and formulation affect the duration of t_{off}. The tableting behaviour of poorly compressible drugs such as paracetamol

and ibuprofen is improved by formulation with plastically deforming excipients. This is reflected in the increased t_{off} values for various directly compressible forms of these drugs. Values of t_{off} give the time interval over which a material shows stress relief under conditions of constant strain. To further characterize the mechanical behaviour of pharmaceutical materials during high speed tableting, the rate and extent of decrease in the punch stress during t_{off} is currently being investigated.

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References

Cole, E. T., Rees, J. E., Hersey, J. A. (1975) Relations between compaction data for some crystalline pharmaceutical materials. Pharm. Acta Helv. 50: 28–32

Cutt, T., Fell, J. T., Rue, P. J., Spring, M. S. (1987) Granulation and compaction of a model system. II. Stress Relaxation. Int. J. Pharm. 39: 157–161

David, S. T., Augsburger, L. L. (1977) Plastic flow during compression of directly compressible fillers and its effect on tablet strength. J. Pharm. Sci. 66: 155–159

Hiestand, E. N., Wells, J. E., Peot, C. B., Ochs, J. F. (1977) Physical process of tableting. Ibid. 66: 510–519

Ho, A. Y. K., Jones, T. M. (1988a) Rise time: a new index of tablet compression. J. Pharm. Pharmacol. 40 (Suppl.): 74P

Ho, A. Y. K., Jones, T. M. (1988b) Punch travel beyond peak force during tablet compression. Ibid. 40 (Suppl.): 75P

Kussendrager, K., De Hoog, P., Van Leverink, J. (1981) Some physical properties of spray-dried lactose with respect to stability and compression. Acta Pharm. Suec. 18: 94–95

Morehead, W. T., Rippie, E. G. (1990) Timing relationships among maxima of punch and die-wall stress and punch displacement during compaction of viscoelastic solids. J. Pharm. Sci. 79: 1020–1022

Morita, M., Nakai, Y., Fukuoka, E., Nakajima, S. (1984) Physicochemical properties of crystalline lactose. II. Effect of crystallinity on mechanical and structural properties. Chem. Pharm. Bull. 32: 4076–4083

Oates, R. J., Mitchell, A. G. (1989) Calculation of punch displacement and work of powder compaction on a rotary tablet press. J. Pharm. Pharmacol. 41: 517–523

Oates, R. J., Mitchell, A. G. (1990) Comparison of calculated and experimentally determined punch displacement on a rotary tablet press using both Manesty and IPT punches. Ibid. 42: 388–396

Popov, E. P. (1968) Introduction to Mechanics of Solids. Prentice-Hall, Inc. Englewood Cliffs, NJ, pp 116–120

Rees, J. E., Rue, P. J. (1978) Time-dependent deformation of some direct compression excipients. J. Pharm. Pharmacol. 30: 601–607

Shlanta, S., Milosovich, G. (1964) Compression of pharmaceutical powders. I. Theory and instrumentation. J. Pharm. Sci. 53: 562–564

Train, D. (1956) An investigation into the compaction of powders. J. Pharm. Pharmacol. 8: 745–760

Vromans, H., Bolhuis, G. K., Lerk, C. F., Kussendrager, K. D., Bosch, H. (1986) Studies on tableting properties of lactose. VI. Consolidation and compaction of spray dried amorphous lactose. Acta Pharm. Suec. 23: 231–240

Appendix I

The data analysis software, called Beta Analysis Program, is menu-driven and requires the following information: name of the material, lubricant if used, information on particle size, punch head type, and turret time. The software recognizes the material name and automatically selects the corresponding true density from a previously defined database. The punch and die dimensions are also selected in a similar manner. The points specifying the onset of compression, $t=0$, and the end of decompression must be entered. This can be done through a menu or graphically and the three points can be saved with the data file. The software calculates the following parameters based on this information and the force vs time data obtained during tableting:

Force related parameters

Upper and lower punch force
Upper and lower punch pressure
Ratio of lower to upper force

Displacement related parameters

Total punch displacement
Tablet thickness at the onset of compression
Tablet thickness at peak pressure
Maximum and minimum relative density of the tablet
Heckel terms

Thermodynamic parameters

Work done to the powder bed during compression
Maximum power
Turret position where maximum power occurs

Machine speed related parameters

Compression time
Decompression time

Deformation related parameters

Peak offset time (t_{off})
Decrease in punch stress during t_{off}

The software also provides profiles of most of these parameters as a function of time. The individual values of these parameters, as well as their profiles, are saved as ASCII files and can be exported to various commercially available computer spreadsheets and graphical and statistical software.