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Review Article

Time-dependent factors involved in powder compression and tablet manufacture

N. Anthony Armstrong

Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff (U.K.)

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Introduction

Though for many years the tablet has been the most commonly used oral dosage form, it was not until the mid 1950s that a systematic study began of those factors which might affect tablet properties. The initiation of this work was stimulated by the invention of the so-called instrumented tablet press (Higuchi et al., 1954). In this, transducers capable of measuring the force exerted by the punch and also the position of the punch were fixed to the tablet press. Since many tablet properties are dependent on the applied force, a more fundamental investigation of those properties was now possible.

The output of these transducers is usually an electrical signal, and in the last decade, the introduction of relatively cheap computing facilities has aided the storage and manipulation of data received from instrumented tablet presses.

A considerable number of parameters have been introduced which attempt to describe the compaction process, both to elucidate underlying principles and also to predict the compressibility of solids. Some of these are summarised with selected references in Table 1 and this area has been comprehensively reviewed by Krycer et al. (1982) and Hiestand and Smith (1984).

With such a large number of varied methods available for the study of the compaction process, it is not surprising that discrepancies exist in the literature. Furthermore, interlaboratory collaborative studies have reported differing results for the same tablet property. See, for example, Jetzer et

TABLE 1

Experimental techniques used to characterise the compaction process with selected references

Technique	Reference
Brittle fracture propensity	Hiestand et al., 1977.
Elastic recovery	Huffine and Bonilla, 1962.
Force–displacement curves	DeBlaey and Polderman, 1971.
Multiple compression	Armstrong et al., 1982.
Pressure–density relationships	Kawakita and Ludde, 1970. Heckel, 1961.
Radial vs axial pressure cycles	Leigh et al., 1967. Huckle and Summers, 1985.
Strength–compression pressure profiles	Higuchi et al., 1953.
Surface hardness	Aulton, 1981.
Tensile strength–compression pressure profiles	Newton et al., 1971.
Work of tablet failure	Rees and Rue, 1978b.

Correspondence: N.A. Armstrong, Welsh School of Pharmacy, University of Wales Institute of Science and Technology, Cardiff, U.K.

al., 1985. These workers made the interesting suggestion that differences in procedures for making tablets in the various laboratories had a greater influence on the parameter of interest than interlaboratory differences in measuring that parameter.

A feature of all the techniques given in Table 1 is that none of them consider the time over which the compaction process occurs nor the speed of the punch when applying the compressing force. This is surprising since it has been known for many years that changing the rate of production of a tablet press, or changing from one type of press to another, can affect the quality of the resultant tablets. For example, Smith (1949) states that "with some intractable tablets, the trouble can be overcome at once by reducing the speed of the machine". Little and Mitchell (1963) point out that increased speed of production may necessitate modification to formulae such as increased amounts of lubricant or binder. However, Little and Mitchell also point out that many formulae can be compressed at higher speeds without any change in formulation being required. The perceptivity of these remarks will become apparent later in this article.

A further consequence of the speed-dependency of the compressibility of many formulations is that much research on powder compression is inapplicable to a practical situation as the times over which the force is applied are inordinately long. This point will be discussed in more detail later.

Duration of application of compressing force

References to compression time in the pharmaceutical literature are often confused, both in relation to the duration of the force application and also to the precise definition of the time involved.

Jones (1981) has divided the compression event into a series of time periods, and from this, proposed a number of useful definitions.

These are:

(1) Consolidation time: time to maximum force.
(2) Dwell time: time at maximum force.
(3) Contact time: time for compression and decompression, excluding ejection time.
(4) Ejection time: time during which ejection occurs.
(5) Residence time: time during which the formed compact is within the die.·

Fig. 1 is a diagrammatic representation of the lower punch force trace from an eccentric press, and shows Jones's definitions in this context. Dwell time cannot be shown in such a situation, since force reaches a maximum value and then immediately decreases. i.e. a peak is obtained with no plateau. However, in some studies, the maximum force is maintained for prolonged periods, and so "dwell time" has a meaning in such circumstances. Furthermore, in rotary presses, a definite though extremely short dwell time is encountered.

Punch speeds in the tablet compression process

Eccentric presses

The force–time profile shown in Fig. 1, and hence the duration of the times derived from them are dependent on the actual speed of the punch(es) involved. These in turn are governed by the rate of rotation of the drive shaft of the press and also the geometry of relevant parts of the press.

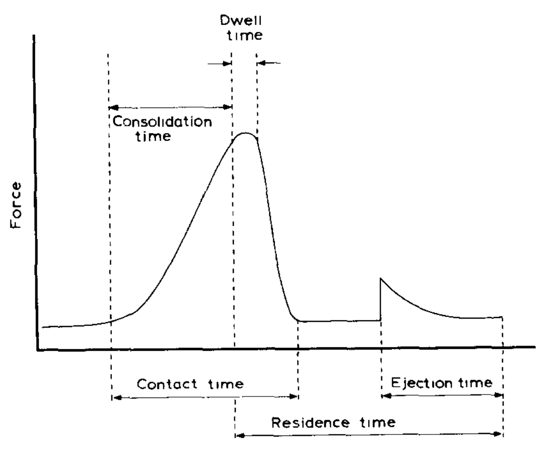

Fig. 1. Events during the compression process. (Reproduced from Jones (1981) with permission of the copyright owner, Childwall University Press.)

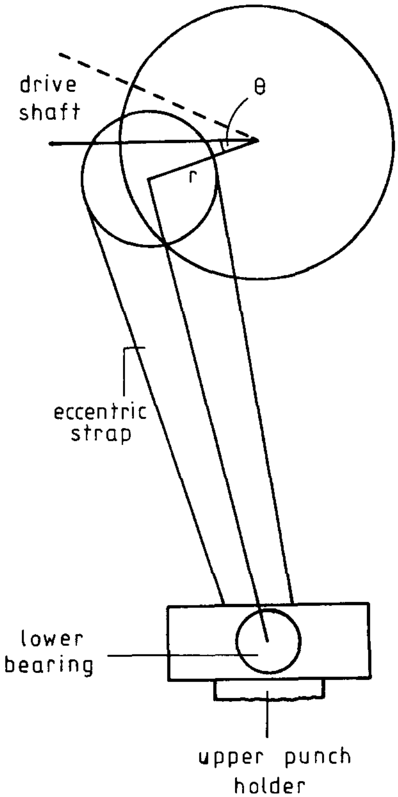

Fig. 2. Diagrammatic representation of drive shaft, eccentric strap and upper punch assembly of an eccentric tablet press. (Reproduced from Armstrong et al. (1983) with permission of the copyright owner, the Journal of Pharmacy and Pharmacology.)

In 1983, Armstrong et al. derived an equation relating the position of the tablet punch tip to the dimensions of an eccentric press and to its speed of rotation.

Fig. 2 represents the drive shaft, eccentric strap, eccentric sheave and upper punch holder of an eccentric tablet press. The position of any component below the lower bearing (for example the tip of the upper punch) is given by Eqn. 1:

$$y = a + \mathrm{r}\sin(90 + \omega t) + \sqrt{l^2 - r^2\cos^2(90 + \omega t)} \qquad (1)$$

where
ω = angular velocity of the shaft
t = time
a = position of that component when $\theta = 0°$
θ, l and r are defined in Fig. 2.

If t is arbitrarily set to zero when $\theta = 90°$, i.e. at maximum punch displacement, then by differentiation, the velocity of the punch tip at any value of θ is given by Eqn. 2.

$$\frac{\mathrm{d}y}{\mathrm{d}t} = \omega r \cos\theta\left(1 + \frac{r\sin\theta}{\sqrt{l^2 - r^2\cos^2\theta}}\right) \qquad (2)$$

Thus when $\theta = 90°$, the velocity is zero as the punch changes direction from downwards to upwards, whereas at $\theta = 0°$, maximum punch velocity is achieved.

An equivalent equation (Eqn. 3) was independently derived by Charlton and Newton (1984).

$$V_\mathrm{p} = D\sin\theta \cdot \omega \cdot (l - A) \cdot (l - A^2 \cdot \sin^2\theta)^{-1/2} \cdot \cos\theta \qquad (3)$$

In this derivation, V_p is the punch speed, D is the radius of the cam off-set, l is the length of the eccentric strap, and $A = D/l$.

Apparent differences between Eqns. 2 and 3 arise from the definition of θ, and when this is taken into account, the two are equivalent, and give the same values for punch speed when identical constants are substituted into them.

By substituting the relevant constants into Eqn. 1, the pattern of punch movement as a function of time can be calculated for any eccentric tablet press.

For example, the dimensions of r and l in a Manesty F3 press are 25 mm and 204 mm respectively. Thus the punch tip moves as a function of θ in the pattern shown in Fig. 3. A value of $\theta = 360°$ is equivalent to one complete revolution of the drive shaft of the press. Thus if the drive shaft rotates 60 times/min, then 360° represents a time of 1 s.

Similarly by use of Eqn. 2, the speed of the punch tip can be calculated. Using a Manesty F3 press rotating at 60 r.p.m., then the speed profile is shown in Fig. 4. It will be noted that the speed is essentially constant over a considerable time span. However, from the point of view of powder

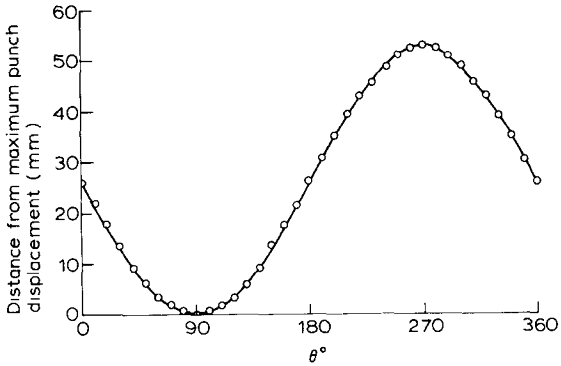

Fig. 3. Upper punch tip movement of a Manesty F3 press.

compression, this is misleading since the period at which a force is being applied to the powder mass is that very region where speed changes are greatest.

Table 2 gives the punch position and the corresponding speed of the punch as a function of θ.

As an example, consider the force being applied to a loose powder bed 10 mm thick, which results in a tablet 5 mm thick, i.e. the force is applied to the powder bed 5 mm before the maximum punch penetration of the die is achieved.

It will be seen that this point occurs when θ exceeds 55°, and between values of $\theta = 55°$ and $\theta = 90°$, the speed falls from 99.2 mm/s to zero. Hence in no way can speed be regarded as a constant over the time period when a compressing force is being applied. The consequences of assuming constant velocity over this period will be considered later.

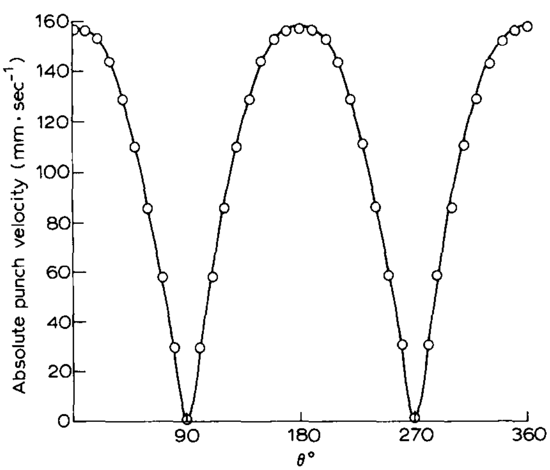

Fig. 4. Punch tip velocity of a Manesty F3 press.

TABLE 2

Punch tip position and punch velocity for a Manesty F3 press rotating at 60 rpm, calculated by the method of Armstrong et al. (1983)

θ (°)	Distance from maximum punch displacement (mm)	Velocity (mm/s)
0	26.54	157.6
10	22.16	157.1
20	17.81	153.8
30	13.66	144.4
40	9.83	129.8
50	6.48	110.4
55	5.00	99.2
60	3.73	86.9
70	1.70	59.9
80	0.43	30.6
90	0.00	0.0

A similar calculation also gives an indication of the time period over which the compression event occurs. If in the example shown above, a force is not applied until $\theta = 55°$, then the punch is only within the die for $2 \times (90 - 55)° = 70°$ and hence for $(360 - 70)°$, the punch is outside of the die. It follows therefore that the contact time is less than 70/360 of the total cycle time. If the latter is taken to be one second, this fraction = 194 ms, and the consolidation time is half this, namely 97 ms.

Increasing the speed of rotation of the drive shaft proportionally decreases the contact time.

Rotary presses

Punch movement and speed in rotary presses have been evaluated by Rippie and Danielson (1981) and Charlton and Newton (1984). As in the case of eccentric presses, equations derived by these two sets of workers appear dissimilar, but in fact the methods used in their derivation are almost identical.

Figs. 5 and 6 represent the relationship between punch, pressure roll and the die table of a rotary press, viewed from the side and from above respectively. As a particular set of punches and die

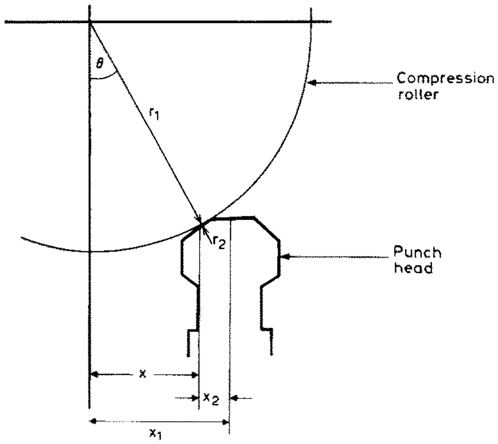

Fig. 5. Spatial relationship between punch head, pressure roll and die table of a rotary press; side view. (Reproduced from Rippie and Danielson (1981) with permission of the copyright owner, the American Pharmaceutical Association.)

rotate, the punch is lowered by contact with the cam track. The only force being exerted at this time is brought about by the mass of the punch and can be ignored. However, when angle θ becomes small enough, the punch head comes into contact with the pressure roll and active compression of the powder bed begins.

The factors which now control punch movement are the radius of the pressure rolls and the geometry of the punch head. The latter can be regarded as having a central flat area of radius x_2 with a curved periphery. A line joining the centre of the pressure roll with the centre of curvature of the punch periphery will always pass through the point of contact of roller and punch head, except when the flat part of the head touches the roller. Hence the vertical displacement of the punch (z) is given by Eqn. 4.

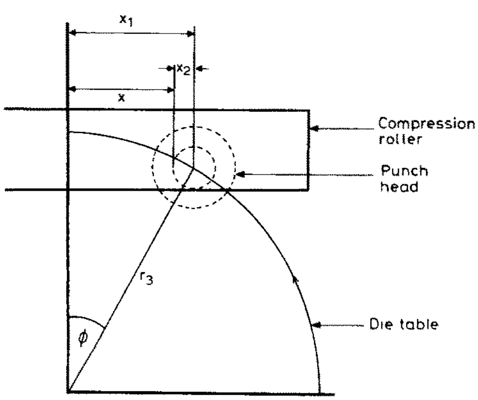

Fig. 6. Spatial relationship between punch head, pressure roll and die table of a rotary press; view from above. (Reproduced from Rippie and Danielson, 1981 with permission of the copyright owner, the American Pharmaceutical Association.)

$$z = \left[(r_1 + r_2)^2 - x^2\right]^{1/2} \quad (4)$$

where r_1 and r_2 are the radii of pressure roller and punch head curvature, respectively, and x is the horizontal distance between the centre line of the compression roller and the point of contact between roller and punch head.

In turn,

$$x_1 = r_3 \sin \phi \quad (5)$$

where r_3 is the radius of the circle in which the dies travel, x_1 is the horizontal distance between the centre line of the compression roller and the centre line of the punch, and ϕ is defined in Fig. 6.

$$\text{Hence } z = \left[(r_1 + r_2)^2 - (r_3 \sin \phi - x_2)^2\right]^{1/2} \quad (6)$$

Movement is described by this equation until the flat part of the punch head comes into contact with the pressure roll. This will occur when $r_3 \sin \phi$ equals the radius of the flat punch head. Displacement is now constant. This accounts for the dwell time in a rotary press referred to earlier.

Unlike the punch of an eccentric press, any given punch of a rotary press has both horizontal and vertical motion. The horizontal speed V_H is given by Eqn. 7

$$V_H = 2r_3 f \quad (7)$$

where f is the frequency of rotation of the turret.

The time interval represented by a change in ϕ of 1° is therefore $1/360f$.

The vertical velocity V_V at any particular value of ϕ can be calculated from Eqn. 6. The latter gives vertical displacement as a function of angle ϕ. However, the time interval represented by ϕ is

TABLE 3

Punch tip position and punch velocity for a Manesty B3B press operating at 44 rpm, calculated by the method of Rippie and Danielson (1981)

ϕ (°)	Distance from maximum displacement (mm)	vertical velocity (mm/s)
0	0	0
1	0	0
1.43	0	0
2	0.04	10.56
4	0.27	39.60
6	0.65	60.72
8	1.19	81.84
10	1.88	102.96
12	2.72	121.44
14	3.72	143.21
16	4.86	161.04
16.22	5.00	163.70
18	6.16	178.90
20	7.60	200.40

also a function of f in that the turret of the press will rotate through $\phi°$ in $\phi/360f$ s. As both displacement and time are known, the vertical velocity can be calculated.

Table 3 gives values of V_V for a Manesty B3B press. Values of ϕ up to 20° are given. At values much greater than this, the pressure roll is not in contact with the punch head, and so Eqn. 6 does not apply.

To repeat the example used earlier, consider a powder bed consolidated to a depth of 5 mm from an original depth of 10 mm, i.e., a significant force is applied when the punch is 5 mm above its maximum displacement. Let the geometry of the punch head be such that there is a central flat portion of diameter 6 mm and a radius of curvature of 12 mm. Hence vertical punch displacement will be constant when $r_3 \sin \phi$ is less than 3 mm.

In the case of a Manesty B3B, the pressure roll has radius 102 mm and the radius of the circle on which the punches are mounted (r_3) is 120 mm. Vertical punch displacement is therefore constant when $\phi = 1.43°$.

Similar calculations can be carried out for any type of press provided the necessary dimensions are known. Fig. 7A shows the punch movements plotted against time for a Manesty F3 eccentric press, a Manesty B3B rotary press and a Manesty Novapress rotary press, all operating at maximum speed. For comparative purposes, the minima of the displacement–time profiles are shown as coinciding in each case. Fig. 7B shows the punch displacements around the minima in greater detail. The dwell time obtained with the rotary presses is more clearly seen.

Punch speeds and the duration of events in the compaction process for some commonly used presses are given in Table 4, using the same hypothetical example of consolidation of a powder bed by 5 mm and a punch head of the same geometry

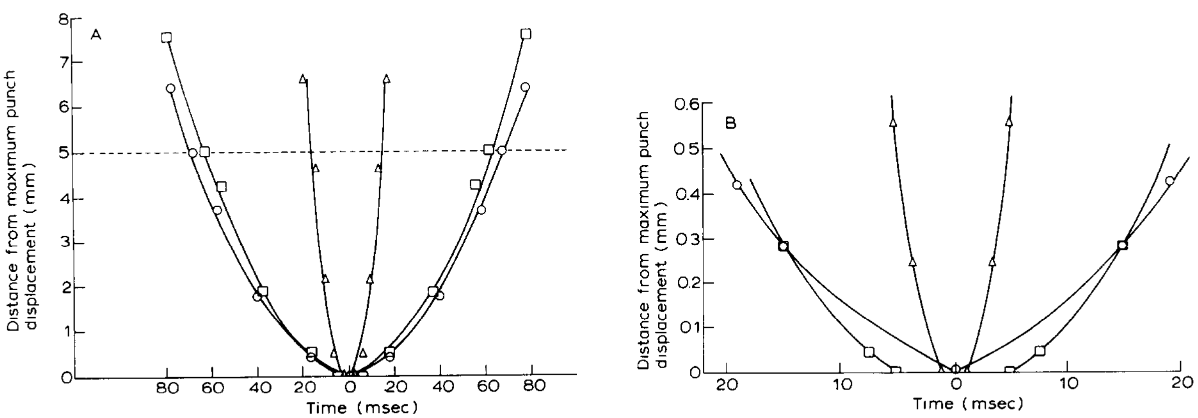

Fig. 7. Punch movement as a function of time for three types of press (○, Manesty F3; □, Manesty B3B; △, Manesty Novapress). A: general graph. B: detailed graph.

TABLE 4

Speed-related data for a number of commonly used tablet presses, all operating at their maximum production rate

Press	Max production rate per die (tablets/min)	Time for punch to descend last 5 mm (ms)	Punch speed at first contact (mm/s)	Dwell time (ms)
Manesty				
F3	85	68.6	139	0
B3B	44	61.4	163	10.84
Express	100	26.7	416	3.94
Unipress	121	19.1	485	3.16
Novapress	100	10.0	720	2.14
Kilian				
Tx	105	19.0	494	2.96
F1000	55	36.4	232	6.60
F1000	75	26.6	317	4.84
F2000	75	23.1	402	3.68
F2000	100	17.3	526	2.76
Korsch				
300	80	21.7	419	3.44
300	100	17.3	526	2.76

as used earlier. Fig. 7 and Table 4 illustrate the markedly different compressional environments to which a solid might be exposed when the type or speed of a press is altered. Also note that the punch speed can in no way be considered to be a constant over the time that a significant force is being applied. Consequently studies which utilise constant punch speeds, usually by means of a compaction simulator, are introducing circumstances into the compression process which do not apply in practice. Such "sawtooth" punch displacement profiles have been used by, among others, Bateman et al. (1987) and Pitt et al. (1987).

It is also worthy of note that the punch speed of the rotary Manesty B3B press is not much greater than that of the eccentric F3 press, and it might be expected that consolidation data obtained on these two presses would be comparable.

For any given type of press, speed is a function of the machine rotation rate, i.e., for the above presses operating at half their maximum rates, speeds shown in Table 4 are halved, and events last twice as long. The other factor which could be varied is the punch head geometry. This has a much smaller effect. For example, using punch heads with radii of curvature of 6, 12 and 24 mm on a Manesty Novapress, punch speeds of 727, 720 and 680 mm/s respectively are obtained at first contact with the powder bed.

Many rotary presses have some form of precompression mechanism, whereby a relatively low force is applied to the powder bed prior to the actual compression event. Whilst a number of advantages have been claimed for this, it is undoubtedly true that precompression will significantly lengthen the time over which a compressive force is exerted.

Studies on time and speed dependency of compaction parameters

Much work which has been carried out on time-dependent phenomena in compression has used punch speeds and consolidation times which bear little relation to those used in practice and the consequences of this will be discussed later. However considerable work does use realistic speeds and times, and a review of such work forms the concluding part of this article.

Punch speed can be derived from punch displacement data obtained from a displacement transducer fitted to the press. Signals from the transducer are displayed in analogue form, and punch speed determined from the slope of the displacement curve at any given point in time.

In recent years, the study of time-dependent compression events has been facilitated by the use of the digital computer. Transducers attached to the press produce electrical (analogue) signals which before storage and manipulation by computer must be converted into digital form. This is achieved by means of an analogue-digital converter which is set to take a signal from a particular transducer at a predetermined frequency. It follows therefore that the time interval between successive readings from that transducer is known to a high degree of accuracy. Hence the difference between two successive displacement values, divided by the time interval, gives the speed of the punch at that particular instant. Furthermore force and displacement data stored on computer can be readily manipulated to obtain the duration of the time periods in the compression event as defined by Jones (1981).

It is now generally recognised that consolidation of powders in a die by a compressing force can take place by two mechanisms. These are fragmentation and deformation, and most solids undergo consolidation by a mixture of these two, though the relative proportions may differ from solid to solid (Leuenberger and Rohera, 1986).

Rees (1980) stated that the strength of a perfectly elastic brittle particle shows no rate dependence. However, a viscoelastic particle may be expected to undergo deformation which is time-dependent. It follows from this that the more important role that deformation plays in the consolidation of a particular solid, the more likely it is to display time-dependent compressional properties.

Details of substances of pharmaceutical interest whose tabletting properties have been studied with respect to time are given in Table 5. Though this table is not exhaustive, it includes those papers which have made the greatest contribution to the understanding of this topic. Table 5 lists materials which have been studied in this respect and gives the tablet parameters used. The equipment on which the work was performed is indicated.

When using the references cited in the table, the speeds and times used in an individual study must be considered. As shown earlier, time and speed differences between eccentric and rotary presses can be considerable. In a number of the references cited, hand operated or hydraulic presses are used, in which punch speeds are very much lower than those used in practice. Furthermore, in some studies long consolidation times have been achieved by stopping the press when it is exerting a force. The difficulties of doing this, and subsequently maintaining constant punch positions, should not be underestimated. Due to the shape of the curve relating punch position and applied force, very slight changes in punch position can cause significant force changes and it is all too easy for these to be interpreted as being caused by changes in tablet dimensions. Consequently punch position must be controllable over long periods with a high degree of precision.

The study of time-dependent compressional properties has been revolutionised in recent years by the introduction of the compaction simulator. (See, for example, Hunter et al., 1976.) These are hydraulic presses in which movement of the plattens of the press (and hence anything attached to them) can be controlled extremely precisely. Platten position and the force exerted can be measured, and the plattens can be made to follow a predetermined path. Thus a punch fixed to the platten can be made to follow the punch movement of a particular tablet press operating at a predetermined speed.

A further feature of a simulator is that only small quantities of material are required, an obvious advantage during formulation studies on a new chemical entity. A survey of the use of simulators and studies involving them has been published by Bateman (1988).

Patterns of punch movement for use on a simulator can be derived theoretically, for example from equations such as 1–7, or from actual punch movements measured by displacement transducers. However, some care must be taken whichever method is chosen, since the actual punch movement may deviate from that predicted.

Armstrong and Palfrey (1987) compared actual punch speeds in an eccentric press with those predicted by Eqn. 2. It was found that the predicted and actual speeds were equal when an empty

TABLE 5

Substances whose time-dependent compression properties have been studied, and compressional and tablet properties used to study time-dependent phenomena

	Equipment [1]	References [2]
Substance		
Ascorbic acid	E	1
Aspirin	E	1
	S	2
	H	3
Calcium phosphate	E	4, 5, 6
	S	7
	H	8
Calcium carbonate	S	7
Compressible cellulose	E	1, 4, 5, 6
	R	9, 10, 11
	S	7, 12, 18, 19
	H	8
Ibuprofen	S	13, 20
Lactose	E	4, 5, 6, 14, 15
	R	1, 9, 10, 17
	S	7, 18, 19
	H	3, 15, 16
Magnesium carbonate	S	7, 19
Magnesium trisilicate	H	3
Maltose/dextrose	H	8
Mannitol	S	7
Paracetamol	S	7
	H	8
Sodium chloride	E	1, 5, 6
	S	7
	H	3
Starch	E	1, 4, 5, 6
	R	9
	S	7
	H	8
Sucrose	R	9
Property		
Axial recovery	S	20
Brittle fracture propensity	S	18
Capping tendency	R	11
Crushing strength	E	1, 14
	R	17
Density and consolidation	E	1,5, 6, 15
	S	7, 12, 13, 19
	H	15
Die-wall pressure	H	16
Friability	E	14
	R	17
Stress relaxation	E	5, 6
	R	9, 10
	H	3, 8
Tablet weight	E	14

TABLE 5 (continued)

	Equipment [1]	References [2]
Tensile strength	E	4, 5, 6
	R	9
	S	2
Work of failure	E	6

[1] E, eccentric press; R, rotary press; S, compaction simulator; H, hydraulic press.

[2]

Number	Reference
1	Baba and Nagafuji, 1965
2	Pitt et al., 1987
3	Shlanta and Milosovich, 1964
4	Armstrong and Blundell, 1985
5	Rees and Rue, 1978a
6	Rees and Rue, 1978b
7	Roberts and Rowe, 1985
8	Travers et al., 1983
9	David and Augsburger, 1977
10	Rippie and Danielson, 1981
11	Ritter and Sucker, 1980
12	Roberts and Rowe, 1987
13	Bateman et al., 1987
14	Fassihi et al., 1980
15	Fell and Newton, 1971
16	Hiestand et al., 1977
17	Seitz and Flessland, 1965
18	Roberts and Rowe, 1986a
19	Roberts and Rowe, 1986b
20	Marshall et al., 1986

die was used. However, if the die was not empty, deviations from the predicted speed occurred. For example. Fig. 8 shows data obtained when compressing directly compressible lactose up to a maximum force of 11.9 kN at a machine speed of 0.63 rev/s. As the punch applies the compressing force, punch movement is slower than theoretically predicted. This might be intuitively expected since as a progressively greater force is applied, the load on the driving motor is increased, causing it to slow down. After the maximum punch penetration has been achieved, the punch leaves the die at a greater speed than predicted. The authors found that deviations from predicted speed were dependent on machine speed, the material being compressed and the force being applied. They also suggested that the power of the driving motor of the press will be a major factor, in that the more

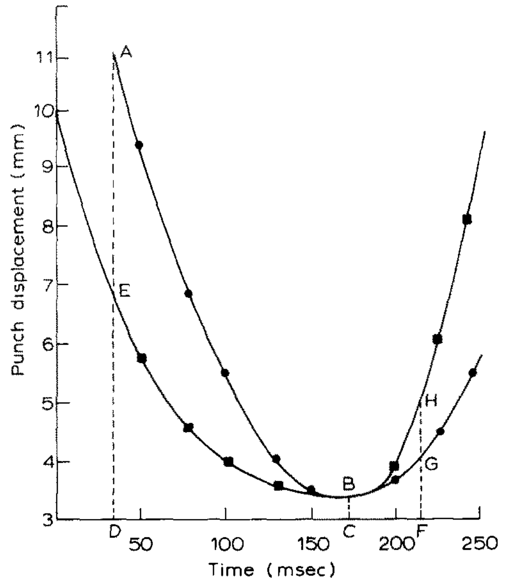

Fig. 8. Actual (■) and theoretical (●) punch displacements. (Reproduced from Armstrong and Palfrey (1987) with permission of the copyright owner, the Journal of Pharmacy and Pharmacology.)

powerful the motor, the better will it be able to accommodate changes in load as the applied force changes. However, if this is not the case, then any change in speed, force or substance may give rise to changes in the pattern of punch movement. Thus if a uniform pattern of punch movement is used in all circumstances, misleading data may result.

The great majority of studies in this area report the effect of speed and compression time changes on the strength of tablets or on strength-dependent properties.

Some of the earliest studies considered machine production rate rather than the punch speed itself. However, the two factors are directly related for any given press. For example, Baba and Nagafuji (1965) and Seitz and Flessland (1965) showed a decrease in breaking strength of tablets with increase in machine rate, and this has been confirmed in a number of subsequent studies. In this context, the finding by Fassihi et al. (1980) that increased production rate caused a rise in tablet strength is unusual.

Tablet strength is governed by 3 factors: (i) consolidation of the powder bed, resulting in increased particulate contact; (ii) the formation of interparticulate bonds, once consolidation has been achieved; (iii) changes in particle shape and structure which occur on removal of the compressing force.

Hence papers which attempt to differentiate between these 3 stages are particularly valuable. Of considerable interest is the work of Roberts and Rowe (1985).

These workers examined the effect of punch velocity on the consolidation of the powders involved. They used the Heckel equation (Heckel, 1961) as the basis of their study and calculated yield stress as the reciprocal of the slope of the linear portion of the Heckel plot.

They used a compaction simulator giving a "saw-tooth" displacement-time profile i.e. punch velocity was constant during the consolidation phase. They found that as punch speed was increased, then in general consolidation was reduced. Thus the powder showed an increased resistance to consolidation and the magnitude of the increase was substance-dependent. The authors suggested that this effect might be due to a reduction in the amount of plastic deformation due to its time-dependent nature. Hence bond formation is reduced or increasingly brittle behaviour is observed. Based on their findings, these authors drew

TABLE 6

Values of the strain rate sensitivity (SRS) of materials

Material	SRS (%)
Calcium phosphate	–
Calcium carbonate	–
Heavy magnesium carbonate	–
Paracetamol DC	1.8
Paracetamol	10.6
Lactose	16.2
Tablettose	19.2
Anhydrous lactose	20.3
Avicel PH101	38.9
Sodium chloride	39.9
Mannitol	46.4
Maize starch	49.3
Corvic	54.1

Reproduced from Roberts & Rowe, 1985 with permission of the author and the copyright owner, the Journal of Pharmacy and Pharmacology.

up a table showing the relative sensitivities of substances to strain rate changes (Table 6). Materials known to consolidate by fragmentation showed little change in yield pressure when velocity was increased.

Similar data were reported by Armstrong and Blundell (1985). These workers extended their study to include lactose particles divided into a number of size ranges. Whereas the tablet strength was reduced as compression speed was increased, the degree of reduction was not dependent on the size of the particles, i.e. the effect of speed was dependent on the substance and not its physical form.

From data presented by Roberts and Rowe (1985) and Armstrong and Palfrey (1988), it would appear that as the punch speed is increased, the particles of some materials consolidate to a reduced extent, i.e. they are unable to accommodate increased stress by changing their shape. Hence the descending punch meets what is in effect a more rigid body. Fragmentation, on the other hand, can be regarded as a virtually instantaneous process. No deformation is needed and hence accommodation to the increased stress is not time-dependent.

A number of grades of microcrystalline cellulose have recently been studied by Roberts and Rowe (1987). This work is of particular interest, in that close examination of the data would appear to indicate that an elevated water content magnifies the effect that strain rate increases have on consolidation. Though this point was not discussed by the authors, it could prove a useful indication of the role of water in the compaction process. It is known that many tablet formulations require an optimum water content, and though this has been linked to tablet porosity (Armstrong and Patel, 1987), its effect on strain rate sensitivity is worthy of investigation.

A considerable body of work exists which shows that the time over which the maximum force is applied can affect tablet quality. Some of the earliest work in this area was by David and Augsburger (1977). These workers studied a number of directly compressible fillers. Samples were compressed on a rotary tablet press, either in a normal mode of operation in which the compression force lasted 0.1 s, or by manual operation to obtain prolonged compression times. They noted that during the latter, the applied force was seen to decrease, and they attributed this to plastic flow causing stress relaxation. All materials showed both elastic and plastic behaviour and plastic flow was associated with an increase in tablet strength. Though such results are of interest, the long duration of force application may give rise to results not obtained in practice. This paper has been criticised by Rees and Rue (1978a). These workers pointed out that in a rotary press, springs are fitted to the compression wheel. Because of the buffering effect of these springs, stress will tend to be almost constant, but strain, the distance between the punch faces, will not be constant. For a study of stress relaxation to be valid, constant strain rather than constant stress is required.

Quantification of time-dependent effects

Progress in this area was made by Armstrong et al. (1983). These workers attempted to measure the power expended in the compaction process. The unit of power, the watt, is defined as the power dissipated when 1 joule is expended for 1 second. This can be derived in two ways, which are dimensionally equivalent.

(i) The area under the force-displacement curve is divided by the time over which the force is applied, i.e.

$$\left[\int_{D_1}^{D_2} \cdot F\,\mathrm{d}D - \int_{D_2}^{D_3} \cdot F\,\mathrm{d}D\right] \cdot t^{-1} \qquad (8)$$

where F is the applied force, t = time, D_1 the displacement when F deviates from zero, D_2 is maximum punch displacement and D_3 is punch displacement when F returns to zero.

(ii) The force applied by the punch is multiplied by the punch velocity at the time that force is being applied. Punch velocity can be calculated from Eqns. 2, 6 or 7, or from displacement data as described earlier.

The latter method was used by Armstrong and Palfrey (1987) to show the potential errors which might occur if theoretical punch velocities are used.

Calculation of power can also illustrate difficulties caused by inordinately long consolidation and compaction times. The paper by Malamataris et al. (1984) is a good example of this. In this paper, a load of up to 20 kN was applied at a rate of 0.667 kN/s. Hence the consolidation time was 30 s. The load was held for 30 s and then released over 30 s. If W is the work applied during the consolidation phase, then power expenditure will be $W/30$ W. If the same calculation is applied to the data given in Table 4, power expenditure for a Manesty F3, a Manesty B3B and a Manesty Novapress would be 14.6 W, 17.8 W and 111.9 W respectively, i.e. it would be increased by factors of 437, 536 and 3359.

Conclusion

It is becoming increasingly apparent that time-dependent properties are linked to the consolidation mechanism of the solid, in that the more important deformation is in a solid's consolidation mechanism, the more likely it is for that solid to show sensitivity to changes in the rate of application of the compressing force. Hence the importance when studying any aspect of tablet manufacture to use consolidation speeds which are related or are similar to those used in practice.

However, considerable work still needs to be done. For example virtually all the data so far reported are derived from single component systems. Yet commercial tablets are almost invariably multi-component systems, and the question must arise whether speed dependent properties of a mixture are the average of those of their components. This is particularly important if tablet manufacture by direct compression is to become more popular.

Time-dependency may also be involved in the alternative method of manufacture, wet granulation. One of the functions of the granulating agent is believed to be that of conferring increased plasticity on the solid and hence facilitating consolidation (Armstrong and Morton, 1979). However, plastically deforming materials are more sensitive to changes in consolidation speed, and it is interesting to speculate whether granulation may confer both beneficial and detrimental properties.

The study of time-dependent phenomena in the compression process has been facilitated by advances in instrumentation and data recording and manipulation by computer. It can be confidently expected that considerable progress will be made in this area over the next few years.

References

Armstrong N.A., Abourida, N.M.A.H. and Gough, A.M., A proposed consolidation parameter for powders. *J. Pharm. Pharmacol.*, 35 (1983) 320–321.

Armstrong, N.A., Abourida, N.M.A.H. and Krijgsman, L., Multiple compression of powders in a tablet press. *J. Pharm. Pharmacol.*, 34 (1982) 9–13.

Armstrong, N.A. and Blundell, L.P., The effect of machine speed on the compaction of some directly compressible tablet diluents. *J. Pharm. Pharmacol.*, 37 (1985) 28P.

Armstrong, N.A. and Morton, F.S.S., An evaluation of the compression characteristics of some magnesium carbonate granulations. *Pharm. Weekbl.*, 114 (1979) 1450–1458.

Armstrong, N.A. and Palfrey, L.P., Punch velocities during the compaction process. *J. Pharm. Pharmacol.*, 39 (1987) 497–501.

Armstrong, N.A. and Palfrey, L.P., The effect of machine speed on the consolidation of four directly compressible tablet diluents. *J. Pharm. Pharmacol.*, in press.

Armstrong, N.A. and Patel, A.N., The effect of water content on tablet porosity, *Proceedings, 6th Pharmaceutical Technology Conference, Canterbury*, 2 (1987) 329–334.

Aulton, M.E., Effect of compaction pressure and punch curvature on the indentation hardness profiles of some compressed tablets, *Pharm. Acta Helv.*, 56 (1981) 332–336.

Baba M. and Nagafuji, N., Studies in tablet compression, 1: compressibility of various powders. *Annu. Rep. Shionogi Res. Lab.*, 15 (1965) 138–146.

Bateman, S., High speed compression simulators in tabletting research, *Pharm. J.*, 240 (1988) 632–633.

Bateman, S.D., Rubinstein, M.H. and Wright, P., The effect of compression speed on the properties of ibuprofen tablets, *J. Pharm. Pharmacol.*, 39 (1987) 66P.

Charlton, B. and Newton, J.M., Theoretical estimation of punch velocities and displacements of single punch and rotary tablet machines, *J. Pharm. Pharmacol.*, 36 (1984) 645–651.

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

DeBlaey, C.J. and Polderman, J., The quantitative interpretation of force–displacement curves, *Pharm. Weekbl.*, 105 (1971) 241–250.

Fassihi, A.R., Falamarzian, M. and Parker, M.S., The influence of the rate of production of tablets at constant pressure upon their physical properties, *Drug Devel. Ind. Pharm.*, 6 (1980) 441–450.

Fell, J.T. and Newton, J.M., Effect of particle size and speed of compaction on density changes in tablets of crystalline and spray-dried lactose, *J. Pharm. Sci.*, 60 (1971) 1866–1869.

Heckel, R.W., An analysis of powder compaction phenomena, *Trans. Metall. Soc. AIME.*, 221 (1961) 671–675.

Hiestand, E.N. and Smith, J.F., Indices of tabletting performance, *Powder Technol.*, 38 (1984) 145–159.

Hiestand, E.N., Wells, J.E., Peot, C.B. and Ochs, J.F., Physical processes of tabletting, *J. Pharm. Sci.*, 66 (1977) 510—519.

Higuchi, T., Nelson, E. and Busse, L.W., The physics of tablet compression, 3; design and construction of an instrumented tabletting machine, *J. Am. Pharm. Assoc. Sci. Ed.*, 43 (1954) 344–348.

Higuchi, T., Rao, A.N., Busse, L.W. and Swintosky, J.V., The physics of tablet compression, 2; the influence of degree of compression on properties of tablets, *J. Am. Pharm. Assoc. Sci. Ed.*, 42 (1953) 194–200.

Huckle, P.D. and Summers, M.P., The use of strain gauges for radial stress measurement during tabletting, *J. Pharm. Pharmacol.*, 37 (1985) 722–725.

Huffine, C.L. and Bonilla, C.F., Particle size effects in the compression of powders, *A. I. Ch. E. Journal*, 8 (1962) 490–493.

Hunter, B.M., Fisher, D.G., Pratt, R.M. and Rowe, R.C., A high speed compression simulator, *J. Pharm. Pharmacol.*, 28 (1976) 65P.

Jetzer, W.E., Johnson, W.B. and Hiestand, E.N., Comparison of two different experimental procedures for determining compaction parameters, *Int. J. Pharm.*, 26 (1985) 329–337.

Jones, T.M., Physico-technical properties of starting materials used in tablet formulation, *Int. J. Pharm. Tech. Prod. Manuf.*, 2 (1981) 17–24.

Kawakita, K. and Ludde, K.-H., Some considerations on powder compression equations, *Powder Technol.*, 4 (1970/71) 61–68.

Krycer, I., Pope, D.G. and Hersey, J.A., The interpretation of powder compaction data, a critical review, *Drug Devel. Ind. Pharm.*, 8 (1982) 307–342.

Leigh, S., Carless, J.E. and Burt, B.W., The compression characteristics of some pharmaceutical materials, *J. Pharm. Sci.*, 56 (1967) 888–892.

Leuenberger, H. and Rohera, B.D., Fundamentals of powder compression, I. The compactibility and compressibility of pharmaceutical powders, *Pharm. Res.*, 3 (1986) 12–22.

Little, A. and Mitchell, K.A., *Tablet Making*, 2nd edn. Northern, Liverpool, 1963.

Malamataris, S., Bin Baie, S. and Pilpel, N., Plasto-elasticity and tabletting of paracetamol, Avicel and other powders, *J. Pharm. Pharmacol.*, 36 (1984) 616–617.

Marshall, P.V., York, P. and Richardson, R., The effect of duration of compression on the axial recovery properties of compacts of a crystalline drug substance, *J. Pharm. Pharmacol.*, 38 (1986) 47P.

Newton, J.M., Rowley, G., Fell, J.T., Peacock, D.G. and Ridgway, K., Computer analysis of the relation between tablet strength and compaction pressure, *J. Pharm. Pharmacol.*, 23 (1971) 195S–201S.

Pitt, K.G., Newton, J.M., Richardson, R. and Stanley, P., The effect of punch velocity on the tensile strength of aspirin tablets, *J. Pharm. Pharmacol.*, 39 (1987) 65P.

Rees, J.E., Postgraduate school on the theory and practice of solid dosage forms and manufacture, London, 1980.

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

Rees, J.E. and Rue, P.J., Work required to cause failure of tablets in diametral compression, *Drug Devel. Ind. Pharm.*, 4 (1978b) 131–156.

Rippie, E.G. and Danielson, D.W., Viscoelastic stress-strain behaviour of pharmaceutical tablets: analysis during unloading and postcompression periods, *J. Pharm. Sci.*, 70 (1981) 476–482.

Ritter, A. and Sucker, H.B., Studies of variables that affect tablet capping, *Pharm. Tech. Int.*, July (1980) 24–33.

Roberts, R.J. and Rowe, R.C., The effect of punch velocity on the compaction of a variety of materials, *J. Pharm. Pharmacol.*, 37 (1985) 377–384.

Roberts, R.J. and Rowe, R.C., Brittle fracture propensity measurements on tablet-sized cylindrical compacts, *J. Pharm. Pharmacol.*, 38 (1986a) 526–528.

Roberts, R.J. and Rowe, R.C., The effect of the relationship between punch velocity and particle size of the compaction behaviour of materials with varying deformation mechanisms, *J. Pharm. Pharmacol.*, 38 (1986b) 566–571.

Roberts, R.J. and Rowe, R.C., Source and batchwise variability in the compressibility of microcrystalline cellulose, *J. Pharm. Pharmacol.*, 39 (1987) 70P.

Seitz, J.A. and Flessland, G.M., Evaluation of physical properties of compressed tablets, 1: tablet hardness and friability, *J. Pharm. Sci.*, 54 (1965) 1353–1357.

Shlanta, S. and Milosovich, G., Compression of pharmaceutical powders, 1: Theory and instrumentation, *J. Pharm. Sci.*, 53 (1964) 562–564.

Smith, A.N., Compressed tablets, 1; resistance to wear and tear, *Pharm. J.*, 163 (1949) 194–195.

Travers, D.N., Celik, M. and Buttery, T.C., A computer-aided investigation on strain movements in compacts under constant stress in the die, *Drug Dev. Ind. Pharm.*, 9 (1983) 139–157.