Review Article

COMPRESSION PARAMETERS INVOLVED IN POWDER COMPRESSION AND MANUFACTURING OF TABLET

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Accepted on: 20-01-2011; **Finalized on:** 28-03-2011.

ABSTRACT

Tablet is the most acceptable oral dosage form. The properties of tablets depend upon the force of compression and also on the nature of powdered substance. The duration of compression involved consolidation time, dwell time, contact time, ejection time and residence time. The interactions between two particles are discussed and related to the compact properties. Compaction removes barriers to spontaneous attraction and strength. The attraction comes predominantly from dispersion forces, individual atom-to-atom bonds are believed to contribute very little to bonding. Plastic deformation is a universal component of producing tablets. Viscoelastic properties are observed in all organic materials studied, this provides additional plastic deformation. The magnitude of the elastic deformation constant has minimal influence on bonding. The contact is defined as a solid bridge other molecular processes that add to the strength are discussed.

Keywords: Tablets, Bonding, Solid bridges, Dispersion forces, Solid fraction, deformation.

INTRODUCTION

We know that the tablet has been most commonly used oral dosage form. The systemic study has carried out for those factors which affect tablet properties. The initiation of this work was stimulated by the invention of the so-called instrumented tablet press[1]. In this process the transducers are 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 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 summarized as follows[2,3]. With such a large number of varied methods available for the study. Furthermore, interlaboratory collaborative studies have reported differing results for the same tablet property[4].

EXPERIMENTAL TECHNIQUES USED FOR THE CHARACTERISATION OF COMPACTION PROCESS

Elastic recovery, surface hardness, multiple compression, work of tablet failure, brittle fracture propensity, force-displacement curves, pressure-density relationships, radial vs axial pressure cycles, strength-compression pressure profiles, tensile strength-compression pressure profiles.

It was stated that differences in procedures for making tablets in the various laboratories had a greater influence on the parameter. A feature of all the techniques 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[5]. Increased speed of production may necessitate to modify formulae such as increased amounts of lubricant or binder[6]. 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.

The discussion herein attempts to establish that: (1) Close range dispersion forces account for most interparticle attraction, the attraction is spontaneous. (2) Solid bridges, as often defined, have no common, unique features except adding strength to an existing contact. (3) Much of the increased strength from compaction is enabled by plastic deformation.

As with most products tabletting technology developed ahead of the theoretical understanding of the physical processes involved. For example, a capped tablet commonly is said to have poor bonding which was overwhelmed by entrapped air. Most often, the bonding is more than adequate, the capping was caused by brittleness. Comparison of compaction pressures in air and in vacuum was revealing[7], only very fine powders exhibited big differences. Very fine powder does impede the escape of air but such fineness introduces unacceptable flow problems and usually is avoid. For example: (a) Bonding with solid bridges contributes to the compact strength only for coarse plastically deforming materials that can melt during compaction. (b) It is suggested that most of the so called plastically deforming pharmaceutical materials often possess inadequate plasticity for the development of large zones that could take part in the interparticulate attraction by intermolecular forces and (c) the term intermolecular forces is used in this article as a collective term for all bonding forces that act between surfaces separated by some distance[8].

Duration of application in 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[9].

These are:

(1) Dwell time: Time at maximum force.

(2) Consolidation time: Time to maximum force.

(3) Ejection time: Time during which ejection occurs.

(4) Residence time: Time during which the formed compact is within the die.

(5) Contact time: Time for compression and decompression, excluding ejection time.

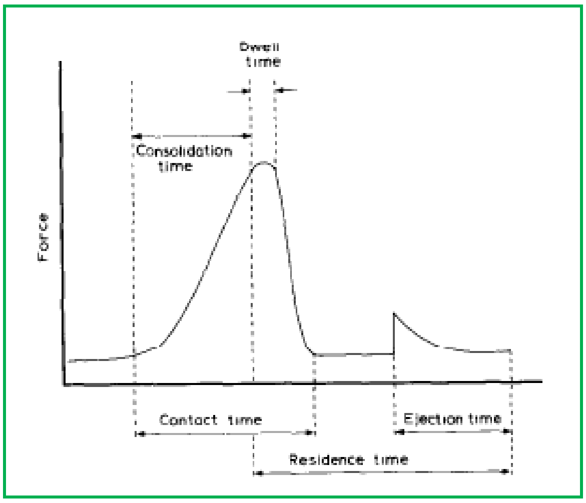

Figure 1: Events during the compression process.

PUNCH SPEED IN 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.

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. The position of any component below the lower bearing (for example the tip of the upper punch) is given by

$$y = a + r\sin(90 + wt) + \sqrt{l^2 - r^2\cos^2(90 + wt)} \quad .... \ (1)$$

Where w = angular velocity of the shaft

t = time

a = posi on of that component when θ = 0̊

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

$$dy/dt = wr\cos\theta\,(1 + r\sin\theta / \sqrt{l^2 - r^2\cos^2\theta}) \quad ......(2)$$

when θ = 90̊ , the velocity is zero as the punch changes direction from downwards to upward[10]. By substituting the relevant constants into Eq[n] 1, the pattern of punch movement as a function of time can be calculated for any eccentric tablet press.

Similarly by use of Eq[n] 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. 3. It will be noted that the speed is essentially constant over a considerable time span. However, from the point of view of powder 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.

Studies on time and time dependency of compaction parameter

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.

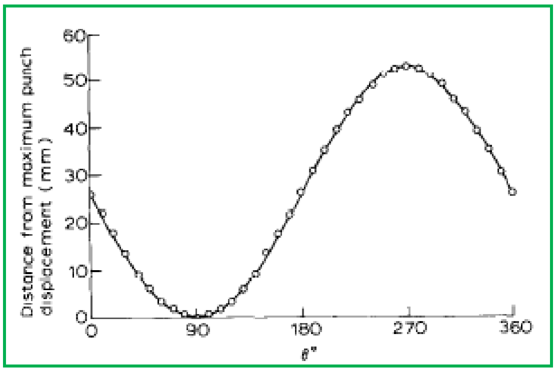

Figure 2: Upper punch tip movement of a Manesty F3 press.

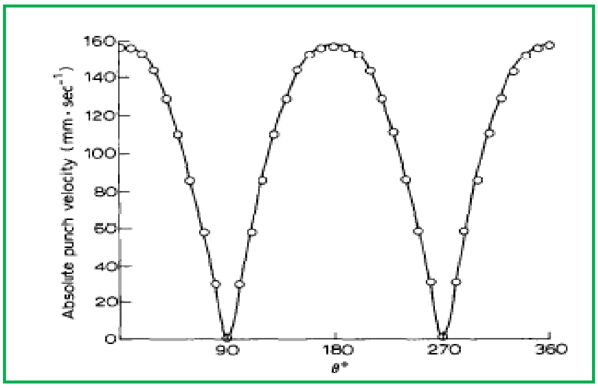

Figure 3: Punch tip velocity of a Manesty F3 press

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 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 events are defined[11]. 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[12]. 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[13]. 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. The equipment on which the work was performed is indicated. 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[14]. These are hydraulic presses in which movement of the platens of the press 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[15]. Patterns of punch movement for use on a simulator can be derived theoretically, for example from equations such as l-2, 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. Actual punch speeds in an eccentric press is compared with those predicted by Eq^n 2[16]. It was found that the predicted and actual speeds were equal when an empty die was used. However, if the die was not empty, deviations from the predicted speed occurred. For example. Fig. 4 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.

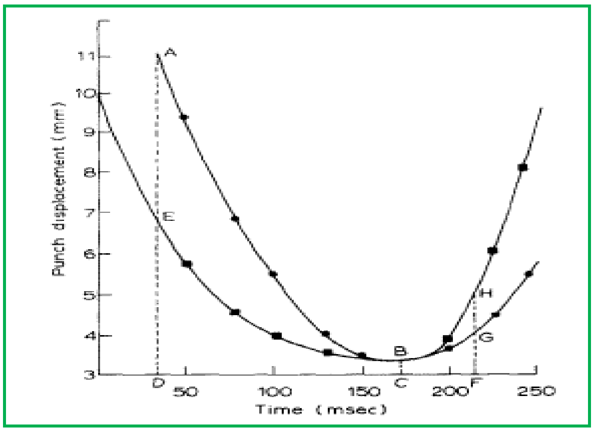

Figure 4: Actual (■) and theoretical (●) punch displacements.

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*, showed a decrease in breaking strength of tablets with increase in machine rate, and this has been confirmed in a number of subsequent studies[17,18]. In this context, the finding by that increased production rate caused a rise in tablet strength is unusual[19]. 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. These workers examined the effect of punch velocity on the consolidation of the powders involved[20]. They used the Heckel equation 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 up a table showing the relative sensitivities of substances to strain rate changes. Materials known to consolidate by fragmentation showed little change in yield pressure when velocity was increased[21]. 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 the data 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[22,23]. 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[24]. This work is of particular interest, in that close examination of the data would appear to indicate that 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[25], 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. 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 0.1s, 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[26]. Though such results are of interest, the long duration of force application may give rise to results not obtained in practice. 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[27].

INTERACTION AT/NEAR INTERPARTICLE CONTACT

Bonding strength

An arbitrary choice must be made for a mechanical property to represent the bonding strength of a compact of a given solid fraction. Compressibility is not used because in the fundamental sciences compressibility refers to volume change vs. pressure, not mechanical strength. Indentation hardness has been used for compactibility[28] and indeed is a useful mechanical strength parameter[29]. However, for this discussion, tensile strength is chosen to characterize bonding strength because an adequate tensile force assures fracture. The tensile strength has the units of stress, force per unit area over a cross section that includes the pores of the compact. It is the maximum stress, the stress that produces separation. This may lead to unrecognized, ambiguous conclusions. The strength differs from the interaction forces acting when at-rest, i.e. with no externally applied force (neglecting gravity). As compaction proceeded, both particle fracture and plastic deformation could be detected[30,31].

Rate dependent plastic deformation

Viscoelasticity is not required for compact formation. Because they deform plastically, significant 'green strength', before sintering, can be developed with many materials. While the hardness of metals is much higher than for organic pharmaceuticals, the adhesion forces also are much much higher. However additives may be useful. These technologies are different from pharmaceutics, success is defined as very dense, uniform packing in desired shape with sintering or firing providing needed strength. The following quotation[32] is most revealing, it has been demonstrated that a soft binder or more precisely, one with a glass transition temperature less than the room temperature results in better dimensional reproducibility than observed for a hard binder (i.e. Tg > room temperature). These differences are attributed to stress relaxation differences in the organic binders and their influence during pressing and ejection. Viscoelastic decay of stress occurring within the contact region changes both the unloaded geometry and the resultant tensile-critical radius of interparticle contacts. It is the combination of the applied stress plus the thermally induced random stress that induce the viscoelastic decay of stress. Since both are required, the decay proceeds only as long as the additive value of the two stresses is sufficiently large. The viscoelastic properties of compacts can be related to the viscoelastic properties of the particles[33]. This is reasonable, since time induced stress decay depends on random thermal fluctuations of localized energy. The total mass of the particle combined with bonding energies at contacts of a particle may be so large that whole particle response to random thermal fluctuations are extremely rare with viscoelasticity, the time of compaction plus the time to make a measurement allows the stress distribution in the contact region to change dramatically[34,35] and results in a different tensile-critical radius of contact and tensile strength. To obtain reproducible experimental results, a rigid time schedule must be followed for making compacts and testing them.

The solid bridge between particles

Processes that happen at an existing contact, sintering, melting, crystallization, chemical reactions, and hardened binders[36] have been grouped as solid bridges. Solid bridges so defined have no universal feature, except for being strengthening mechanisms unburdened by the inherent stresses induced by compaction. However, the kinds of attraction forces acting always include close range molecular forces. At normal compaction rates, none of those processes are common or frequent participants during the compaction. The nomenclature choices are: (a) All contacts are solid bridges, i.e. any solid-to-solid contact (b) a chasm isn't spanned, a bridge doesn't exist or (c) solid bridges refer to post compression processes. The first is chosen by the author to emphasize that contacts are solid-to-solid. Since viscoelasticity, also, is a post compaction process, choice (c) would need refinement. Solid bridges that contribute to the overall compact strength can be defined as areas of real contact, i.e. contact at the atomic level between adjacent surfaces in the compact. Viscoelastic decay of stresses within the contacting particles results in changes of contact radius and produces stress distribution changes[37]. One concludes that modest plastic deformation at contacts dramatically increases the strength, large zones of plastic deformation are not needed. Clearly plastic deformation is a major factor in determining the size of a contact and strength of bonding. A common observation in tableting is that two lots of the same material have very different tableting characteristics, lot-to-lot variation.

MECHANICAL PROPERTIES OF COMPACTS

Elastic and plastic deformation

There is little evidence that the magnitude of the elastic constant is an important parameter for tablet strength. When plastic deformation occurs, it distorts the stress field so that the reversible elastic recovery process leaves residual elastic stresses, i.e. internal offsetting tensile and compression stressed regions. Consequently, the at-rest volume reduction from elastic deformation is essentially zero. Volume reduction, consolidation, during the compaction cycle may include particle fracture, plastic deformation and particle rearrangement. Unloading is not event free. Too often, it is stated that elastic recovery may rupture weak particle-particle bond. This breaking of bonds interpretation depends on both atom-to-atom bonds and separation. Even if that contact is ruptured, attraction continues, i.e. attraction diminishes gradually but continues until separation by compact fracture. Compact fracture occurs when the cumulative attraction in the compact either has reached a maximum or a more local region produces catastrophic crack propagation, i.e. the strength becomes a compact property; the sum of all attractions at fracture. Since most commercial tabletting machines use uniaxial compression-decompression cycles, plastic deformation occurs in both parts of the cycle. At a specific site, shear displacement may either increase or decrease the local attraction by changing the cumulative proximity of atoms. Increased strength has been observed[38] from multiple compactions to the same pressure within the same die. Due to destructive failure of the transducers, this could not be resolved. Some may remain to weaken the strength[39]. Since the combined shear-hydrostatic stress condition produces competing processes, strengthening by increasing the contact area of existing contacts and weakening micro-fracture regions, the net effect will depend on the mechanical properties of the compact[40,41]. Only for brittle materials does fracture dominate.

CONCLUSION

The time dependent properties are linked to the consolidation mechanism of the solid, 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. 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.

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