Tablets Under Pressure

The hardness of a tablet has traditionally been used as a measure of quality; however, tensile strength is more appropriate when comparing tablets of different composition, shape and size, and compressed on different pieces of equipment.

The modern tablet is a complex drug delivery system in which the drug substance is combined with a number of excipients to aid formulation of the desired product; these include bulking agents, binders, disintegrants and coatings, all of which have some function to aid processing of the drug substance into the end-product. The excipients and drug substance are processed through a number of unit operations such as mixing, blending, granulation, tabletting and often coating to form the final product.

The final tablet has to fulfil a number of characteristics, including the ability to deliver the correct amount of drug substance into the patient’s system at the required rate, as well as physicochemical properties that make it easy to handle, administer and store. For dispensable products, these include a suitable size, hardness, texture and stability, as well as taste and smell.

Process and formulation development of the desired tablet form is time-consuming and complex because knowledge of excipient/drug substance material properties and their relationship to processing parameters is limited – preventing a priori prediction of quality.

This causes manufacturers particular problems in developing and producing the ideal tablet that fulfils its therapeutic purpose, and can be manufactured both efficiently and economically. Even small variations in material properties or process parameters can have profound effects on final tablet quality.

Measuring the Correct Tablet Properties

To assess the impact of starting material properties and manufacturing conditions on tablet properties, it is important to ensure that the correct characteristics are used when making comparisons between tablets comprising different formulations or made on different pieces of equipment. In fact, it is actually very difficult to make scientifically robust comparisons between formulations and processes for a number of reasons.

Tablet hardness, or breaking strength, is an important and widely used parameter to control the tablet manufacturing process. In many cases, it is used as a surrogate measure for compression force during manufacture – often because the tablet machine is unable to measure compression force. It is a very important control parameter because compression affects every tablet property, including disintegration, dissolution and friability. In some cases stability is also affected. However, tablet hardness (or breaking force) comparisons are applicable to one tablet size and shape only. If the size, shape or thickness of a tablet is materially changed, then all tablet hardness comparisons will become incorrect. It is obvious that it is more difficult for a small tablet to withstand a given fracture load than a larger tablet. Simple hardness measurements are thus not a valid basis for comparison in this situation.

In fact, there are two factors at work here. One is the area across which a tablet breaking force is applied, as clearly the strength of the tablet will be proportional to the area across which the force is distributed.

The second factor is that, if the same compaction force is applied to (say) a 6mm circular tablet and a 3mm circular tablet, the force per unit area on the small tablet will be four times that on the large tablet (because area is proportional to the square of the diameter of a circle). So the material in the 3mm tablet will experience a compaction pressure four times that of the 6mm tablet at the same load.
It is essential that these factors are taken into account when making comparisons between tablets.

Instead of comparing breaking loads (measured in Newtons or kg), tablets should be compared using breaking stress ('pressure'), which in engineering terms is called the tensile fracture stress (TFS) (1). Rather than comparing compaction force, we should compare fracture stress based on the work of Newton et al (2). When we do this, the results make much more sense.

In Figure 1, 3mm and 6mm tablets appear to have a similar hardness (measured by breaking force); however, this takes no account of the differences in tablet thickness, or the effect of differences in compaction pressure (see Figure 2). Only the applied compression force is quoted, which does not take into account the punch diameter, and hence the area over which the compaction force is applied.

### Making Valid Comparisons

Comparing formulations using only compression force and hardness does not reveal all of the information available in the data. To make the proper comparison, the tablet punch diameter, thickness of the tablet and compression force must also be taken into account so that a graph of TFS versus compaction pressure can be prepared. The differences in tablet thickness, diameter and compression force for circular tablets can then easily be accounted for by calculating the tablet tensile fracture strength and tablet compaction pressure.

### Tablet Tensile Fracture Stress

For cylindrical tablets, TFS can be calculated from the breaking force according to the following equation, first used by Fell and Newton in 1970 (1):

$$\sigma_t = \frac{2P}{Dt}\text{,}$$

where $\sigma_t$ is the tensile fracture strength of the tablet, $P$ is the fracture force (N), $D$ is the tablet diameter and $t$ is the overall thickness. The equation takes account of the breaking load, thickness and diameter of the tablet, and effectively divides the breaking load by the area of the fracture surface.
The appropriate formula must be used to calculate the TFS for the comparison to be valid.

**Compaction Pressure**

For a flat-faced tablet, compaction pressure is calculated simply by dividing the force applied by the die area:

\[
P = \frac{C_p}{A}
\]

where \( C_p \) is the compaction pressure and \( A \) is the area of the die.

As mentioned earlier, at the same compression force, punch diameter has an exponential effect on compaction pressure. For example, 400kg of compression force on a 3mm punch produces four times the pressure as 400kg on a 6mm punch.

This formula is only correct for flat-faced cylindrical tablets; for convex-faced round tablets, the formula becomes:

\[
\sigma_t = \frac{10P}{\left(\frac{t}{D} - \frac{t}{W} + \frac{W}{D} + 0.01\right)}
\]

where \( \sigma_t \) is the tensile strength, \( P \) is the fracture load, \( D \) is the tablet diameter, \( t \) is the overall thickness and \( W \) is the wall height of the tablet.

Both of these equations are also listed in monograph 1217 of the United States Pharmacopoeia. Similarly, an equation for a wide range of elongated tablets has been derived by Pitt et al (3). Hence if tablets of different shape are to be compared, the

For tablets that are not flat-faced, the cross-sectional area of the die is still normally used.

**TFS/Compaction Pressure Comparisons**

When TFS and compaction pressure are reviewed, the data reveals its full value. By using the tensile strength for tablets and normalising the applied force with the punch diameter to give the compaction pressure, we can see the impact of tablet size and compaction pressure on TFS, and the effect of tablet size on compressibility.

The effect of increasing compaction pressure on tablet tensile strength is shown in Figure 3. There is an area of overlap of around 150MPa of compaction pressure where the tensile strength of a 6mm tablet is similar to that of a 3mm tablet. Normalising the data in this way provides an objective way to measure tablet physical properties over a wide range of compaction pressures and using a small amount of material. The data shows that the behaviour of Avicel PH-102, when compressed into a 30mg tablet of 3mm diameter, is completely scalable to the behaviour of a 100mg tablet of 6mm diameter. Similar results have been obtained for other materials (2).
TFS Measurement in Formulation Development

Tensile fracture stress measurement is an important material property independent of tablet size. Any statement requiring a specific hardness to pass a friability test or survive a coating operation is not universally applicable as it would apply to one specific size only. Normalising the data would remove that barrier and help in comparing formulations of different tablet sizes and shapes, or compressed on different equipment.

Comparison of tablet TFS is relatively straightforward if tablets are made at a controlled compaction pressure. At Gamlen, we have developed a bench-top, computer-controlled tablet press (the GTP-1, Figure 4) that is well-suited for this purpose as it is both a tablet press and a tablet fracture tester. For the measurement of tablet breaking load, the press records both force and displacement during both compression and fracture, and also provides the ejection force profile associated with tablet ejection (see Figure 5).

In the scale-up of tablet production, the press can be used to determine the relationship between tablets developed at the bench-top scale using a few grams of material (often at the early development stage) and the final tablet manufactured on a rotary tablet press. The latter uses hundreds of kilograms of material, making process development difficult because of practical difficulties in experimentation; smaller and different shaped tablets can, however, be scaled to the final desired tablet design if TFS is used as the basis for comparison.

Conclusion

While tablet development has traditionally used tablet hardness as a measure of the physical attribute of a tablet, tensile strength is in fact more appropriate when comparing different formulations and tablets compressed on different pieces of equipment and at different scales.

References

1. Fell JT and Newton JM, Determination of tablet strength by the diametral compression test, J Pharm Sci 59, pp688-691, 1970