QUALITY CONTROL

Key factors influencing measured tablet hardness

Measuring tablet hardness (breaking force) plays a vital role in defining dosage form with optimum physical characteristics and testing whether produced dosage form meets the defined specifications in manufacturing. Testing tablet hardness is more than ensuring the mechanical integrity of produced tablets during subsequent processes. Because the hardness of a tabletdirectly relates to all other physical parameters, it is a fast and efficient test that indicates whether specifications such as disintegration time and friability will be met. It is therefore essential, that hardness measurement is done correctly – and that the equipment used to test tablet hardness guarantees repeatable results.

As mentioned in both US and European Pharmacopeia, the term "hardness" is actually misleading in a scientific sense, but commonly used as a synonym for breaking force or resistance to crushing strength. In simple terms, tablet hardness is the force (load) required to break a tablet. Pharmacopeia also gives some requirements as to how the tablet should be tested including basic design specifications for the tester. Key specifications are:

- The tablet is placed between two platens (= jaws)
- One platen (= jaw) moves to apply sufficient force to the tablet to cause fracture
- The mechanism should be free of any bending or torsion displacement as the load is applied
- Rate and uniformity of loading (= rate of the platen movement or the rate at which the compressive force is applied)
- A calibrated load cell measures the force applied
- Results are expressed in Newton (N) or Kilopond (kp)

To ensure comparability of results, testing must occur under identical conditions. This proves to be particularly difficult when it comes to comparing results from different type of testers. Whereas tablet geometry and correct tablet orientation during testing are relatively straightforward to verify, some of the tester-specific influencing factors during hardness testing require an in-depth understanding of hardness measuring technology.

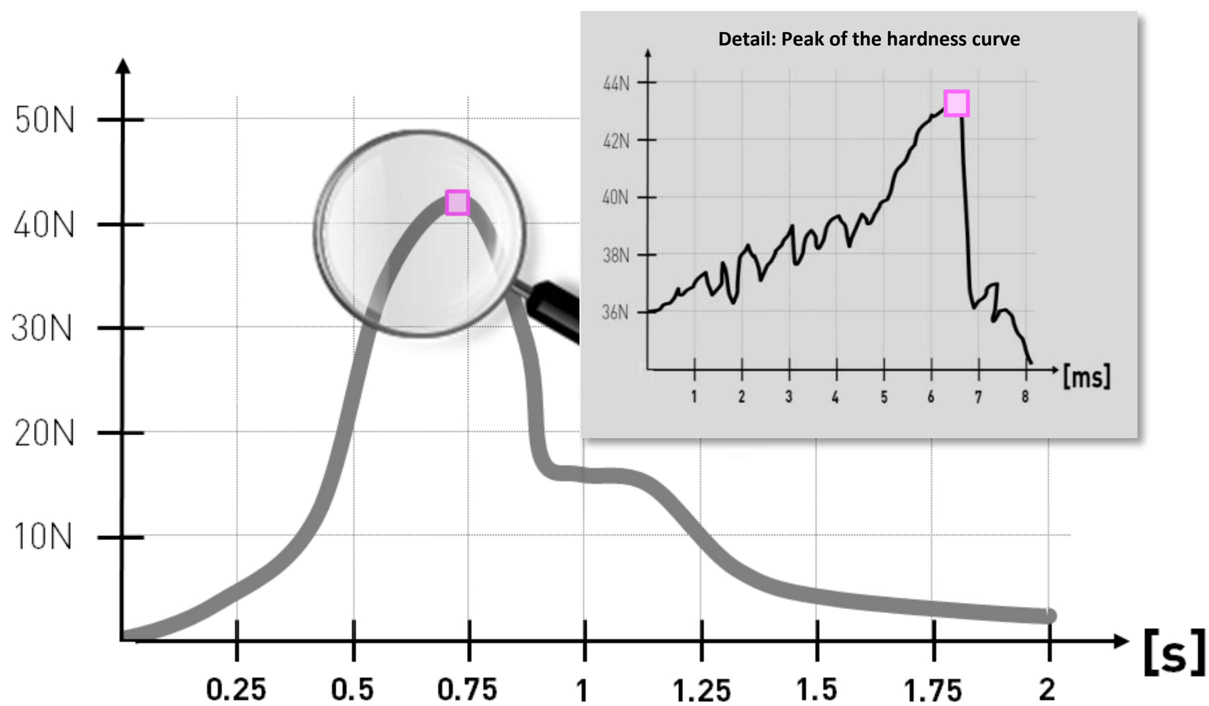
The following paragraphs give an overview of the most important factors that influence any tablet hardness measurement, including tester-specific factors.

Not tester-specific	Tester-specific
• Tablet breaking characteristics • Correct tablet orientation	• Precision & linearity of load cell • Sampling rate of tester • Measuring principle used • Mechanical construction of tester

→ Main factors influencing measured hardness results

TABLET BREAKING CHARACTERISTICS

How a tablet fractures when an increasing force is applied varies significantly depending on various product characteristics (e.g. physical dimensions / tablet geometry, carrier material for the active drug, compression force during production, etc.). Although individual "breaking characteristics" are very different, basically all tablet types – regardless of their shape – will fracture partially irregular. A close look at a tablet's breaking characteristics in a force / time diagram shows that the breaking process occurs in a series of small fractures (see Diagram 1).



→ Diagram 1: A close look at the peak of a hardness curve

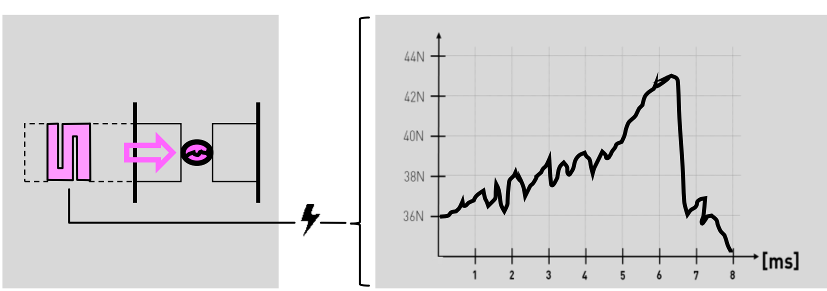
CORRECT TABLET ORIENTATION

If the tablet is oriented in a different way than when the product specification for hardness has been defined, measured results will usually differ significantly. It is therefore important to orient the tablet sample to be measured in exactly the same way for all tests. Pharmacopeia gives some general instructions as to how position common tablet shapes, but also mentions that tablets with a unique or complex shape may have no obvious orientation. In any case it is best to settle on a standard orientation, preferably one that can be most readily and easily reproduced by operators or automatic tablet testing systems.

→ Tablet sample oriented in hardness measuring station of MultiTest 50

PRECISION & LINEARITY OF LOAD CELL

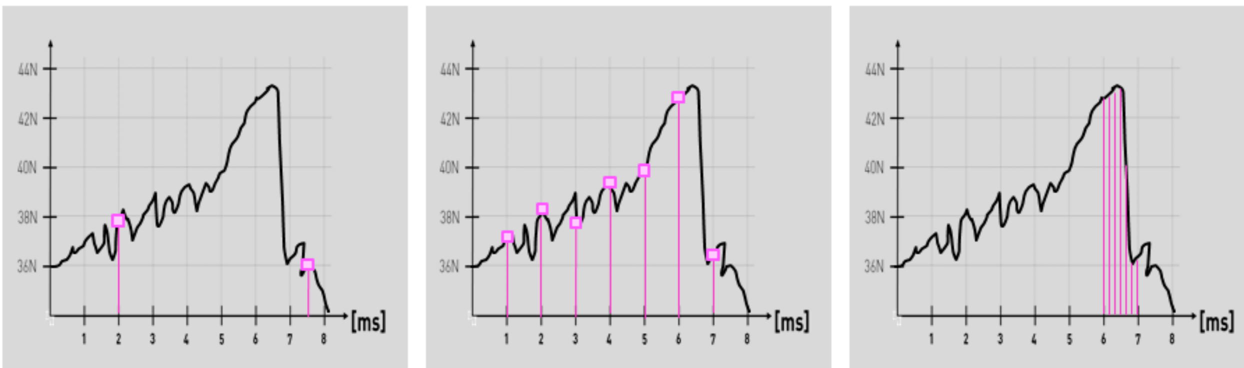
A load cell is a transducer that converts force into an electrical signal. This electric (analog) signal created when force is applied on a tablet during testing is the basis for all hardness measurements (see Diagram 2). It is therefore essential that the load cell is very sensitive to even the smallest force changes. Once calibrated,the load cell must be able to transducethe applied force over the entire measuring range (e.g. up to 400N) with a guaranteed linearity of minimum 99.95%. A higher non-linearity will not allow for precision results. This is true no matter whether the load cell inside the tester is calibrated using reference weights or another load cell is used to calibrate the load cell inside the tester (= dynamic calibration). In case of dynamic calibration, the reference load cell has also been calibrated using static weights and therefore will only calibrate the load cell inside the tester correctly if it has a guaranteed minimum linearity of 99.95%.Dr. Schleuniger® Pharmatron S-beam type load cells with multiple strain gauges have been proven and certified to fulfill all requirements – particularly those pertaining to sensitivity, linearity and accuracy.



→ Diagram 2: Electric (analog) signal created by a S-beam type load cell

SAMPLING RATE OF TESTER

Having a high-precision S-beam load cell doesn't automatically guarantee that the peak of a hardness curve (= the breaking point) is detected correctly. The (continuous) analog electrical signal produced by the load cell must be sampled in short time intervals to calculate measuring points – otherwise the actual peak may be "missed" (see Diagram 3). Especially when the hardness curve has a very "steep peak", testers with a low sampling rate may produce different results than testers that have state-of-the-art electronics.



→ Diagram 3: Measured hardness (peak) at different sampling rates

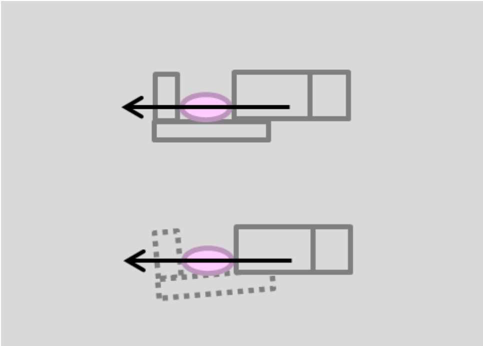
MEASURING PRINCIPLE USED

The term "measuring principle" refers to the rate and uniformity at which force is applied to the tablet during testing – either by defining the speed at which the platen moves or by determining how much force is applied per second. According to Pharmacopeia, both constant speed and constant force (= linear force increase) can be used, because there is no basis to declare an absolute preference for one system over the other. Interesting is, however, that the maximum value specified for constant force (20N/s) is very low, whereas the maximum speed specification allows for very fast testing (up to 3.5mm/s). At maximum specified constant force a common tablet with a nominal value of 160N will take approximately 8 seconds to break, whereas the same tablet will break in a fraction of that time when a speed of 3.5 mm/s is being used.

Measured hardness values may differ significantly depending on the measuring principle used. Results can also be higher/lower if different settings for speed or linear force increase are being used. Even if a tester allows programming e.g. the speed of platen movement, for some testers it may be questionable whether the platen is effectively moving at that speed. Using constant force is technically even more difficult, because the tester must be able to "translate" the currently measured force directly into platen movement – requiring sophisticated electronics for extremely fast motor speed adjustments.

MECHANICAL CONSTRUCTION OF TESTER

One factor that should not be underestimated is how the tester itself responds to forces applied. A solid overall design prevents bending and torsion displacement – ensuring accurate and repeatable results. If parts of the tester bend during measuring, the hardness result will be incorrect. Any displacement occurring in the mechanics of the tester should only be caused by the load cell's strain gauge and therefore should not exceed 0.15mm at 300N.



→ Example of falsified measuring: platen assembly bends when force is applied

CONCLUSION

Tablet hardness testers only provide accurate and reliable results if the mechanical components and electronics of the tester fulfilla whole set of design requirements. When comparing results from different testers, it is important to look at how the testers meet these requirements in order to identify possible reasons for variations.