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Indices for the brittleness of pharmaceutical tablets: A reassessment

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ABSTRACT

Brittleness is an important mechanical property. In the classical sense, a material is considered brittle if, during loading, it behaves elastically until failure. Nevertheless, it is also sometimes understood as the fact to be resistant to breakage. In the case of pharmaceutical tablets, three different indices have been defined to measure brittleness: the brittle fracture index (BFI), the brittle/ductile index (BDI) and the tablet brittleness index (TBI). The aim of this work was to reassess the meaning of the different indices that are known to give contradictory results. Using theoretical considerations, numerical modelling and experiments, it was possible to show that the only index that unequivocally measures the brittleness of the tablet understood as elastic until failure is the BFI. If the other two indices can be useful, for example to assess the friability of the tablet in the case of the TBI, they do not make it possible to measure tablet brittleness in the classical sense, i.e. as opposed to ductility.

1. Introduction

Brittleness is an important property in the mechanics of materials like rocks, ceramics, metals or concrete, but also for pharmaceutical tablets. Despite the large use of the term, the definition of brittleness is not always very clear. Hucka and Das, among others, reviewed different definitions that can be found in the literature (Hucka and Das, 1974). Even if all the given definitions are not strictly the same, they all points toward the same direction which is that a solid is considered as brittle if, before failure, it does not present significant plastic deformation. As such, brittleness is considered as the opposite of ductility. In mechanical terms, brittle materials can be treated using the concepts of linear fracture mechanics, whereas ductile solids will be studied using the tools of plasticity and yielding. In the following text, we will refer to this definition of brittleness as “Elastic Until Failure”.

Generally, in the literature, brittleness is considered as a material property. Nevertheless, the problem is in fact more complex. Materials like rocks or pharmaceutical tablets are in fact quasi-brittle materials (Bažant, 2002; Girardot et al., 2023). This means that during a failure test, a fracture process zone (FPZ) develops ahead of a crack (micro-cracking, etc.) before the development of a macroscopic crack (Bažant, 2002). Depending on the material, the size of the FPZ can be very different. For example, FPZ in concretes are in general considered to have a size around some 100 mm (Hillerborg, 1985) whereas in a pharmaceutical tablet it can be only of a few mm (Girardot et al., 2023). The impact of the FPZ on the failure behavior in fact depends on the size of the structure. If the FPZ is very small compared to the typical size of the sample, the sample will behave like a brittle material whereas if the size of the FPZ is larger than the sample size, it will behave in a ductile way (Bažant, 2002; Morel and Dourado, 2011). Considering this definition, brittleness is the conjunction between a material property and the geometrical features of the test used.

One of the way to quantify this size effect, is to compare a characteristic length of the fracture process of the material to the actual size of the material. Hillerborg et al. proposed that the characteristic length of the fracture process of the material (l_c) can be expressed using the material properties as (Hillerborg et al., 1976):

$$l_c = \frac{EG_c}{\sigma_t^2} \quad (1)$$

With E the Young modulus of the material, G_c its fracture energy (i.e. the energy required to generate a unit area of a crack) and σ_t its tensile strength. The shorter l_c compared to the size of the structure, the more brittle the material will be. Equation 1 can be rewritten using the critical stress intensity factor K_c, which can be written as:

$$K_c = \sqrt{EG_c} \quad (2)$$

Equation 1 thus becomes:

$$l_c = \left(\frac{K_c}{\sigma_t}\right)^2 \quad (3)$$

In the present paper, we will only discuss cases where the failure occurs in mode I (tension), so we will consider G_{Ic} for the fracture energy and K_{Ic} for the critical stress intensity factor.

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Beside this definition based on the opposition to ductility, Brittleness is sometimes defined based on the strength of the material. For example Rosato and al. stated that (Rosato and Rosato, 2003): "Brittleness identifies material easily broken, damaged, disrupted, cracked, and/or snapped". This definition in fact relies more on the sense of brittle in the everyday life. From a fundamental point of view, it is completely different from the other definition. A perfectly brittle solid in the previous sense (i.e. a solid that can be treated with the tools of linear fracture mechanics) would resist more or less to a crack propagation depending on its fracture toughness. In the second sense (of the second definition i.e. solid easily broken) a more brittle solid would thus have a lower fracture toughness.

Even if fundamentally different, these two definitions can have things in common. For example, plastic deformation might help a solid to hindered a crack propagation, making it apparently more tough or resistant. It is also interesting that even authors who rely on the first definition sometimes refers also to the second sense. For Example, Hillerborg, who defined the characteristic length presented above, stated in another article that (Hillerborg, 1985): "If concrete were a perfectly brittle material any small crack or flaw in a region with tensile stresses would cause a running crack, which might lead to a catastrophical failure." This would only be true if a perfectly brittle solid is considered: 1) to be a material that can be treated with linear fracture mechanics (i.e. no plastic deformation) and 2) to have a fracture toughness equal to zero. This hence is a mix of the two definitions.

The consequence of brittleness being not always a well-defined concept is that a lot of different indices have been proposed to quantify it. In this paper we will focus on those used in the case of pharmaceutical tablets. Three main indices can be found in the literature that are supposed to quantify the brittleness of pharmaceutical tablets.

The first one was proposed by Hiestand *et al.* and is called the Brittle fracture index (BFI)(Hiestand et al., 1977; Hiestand and Smith, 1984). It is defined as follows:

$$BFI = \frac{1}{2}\left(\frac{\sigma_t}{\sigma_{th}} - 1\right) \quad (4)$$

where σ_t is the tensile strength of a normal tablet and σ_{th} is the apparent tensile strength of a tablet with the same characteristics than the previous one but with a hole inserted in the middle.

An extension of the BFI was recently proposed as it was demonstrated that the value of the BFI was influenced by the size of the hole (Croquelois et al., 2020, 2017). This extension was based on the use of a failure criterion called "average-stress criterion"(Whitney and Nuismer, 1974) and made it possible to define a characteristic length a_0 which can be used to quantify brittleness (i.e. the larger a_0, the less brittle). This length can be defined as using the following equation:

$$\frac{\sigma_t}{\sigma_{th}} = \frac{0.145}{\frac{1}{a_0}\int_a^{a_0} f\left(\frac{a}{x}\right)dx} \quad (5)$$

where a is the radius of the hole at the center of the tablet, x is the distance to the hole center and f is the stress distribution at hole edge. If a_0 was previously determined using different hole sizes to lower the uncertainties, it can also be calculated with a single hole size using equation 5.

The second index, called the Brittle/Ductile index (BDI), was introduced by Sönnergard and is defined as (Sonnergaard, 2013):

$$BDI = 100 \times \frac{2 \times WOF}{F \times D} \quad (6)$$

where WOF is the work of failure of a tablet during the diametral compression test, F is the failure force during the same test and D is the original diameter of the tested tablet. Note that in a recent publication, Sonnergaard presented also closely related indices but showed that the BDI was the most efficient (Sonnergaard, 2023). We will thus focus on the BDI.

Finally, the more recent index was proposed by Gong and Sun (Gong and Sun, 2015). It is called the tablet brittleness index (TBI) and is defined as:

$$TBI = \frac{1}{\varepsilon_F} \quad (7)$$

where ε_F is the elastic strain at fracture during the diametral compression test.

As it can be seen from their definition, these index are based on very different premises, and they can give contradictory results. The aim of the present article is to try to understand, from a fundamental point of view, what exactly do these indices measure and how is this related to the definitions of brittleness presented above. For this, the reasoning will rely on the equations of the mechanics but also on the use of numerical modelling especially in the case of Hiestand's BFI. An experimental case study will also be presented to illustrate the findings.

2. Material and method

2.1. Experimental part

2.1.1. Powders used

Three classical pharmaceutical excipients were used: Microcristalline cellulose (MCC)(Vivapur 200, JRS Pharma, Rosenberg, Germany), Lactose Monohydrate (LAC) (SuperTab 30GR, DFE Pharma, Goch, Germany) and starch (StarTab, Colorcon, West Point, USA). Magnesium stearate (MgSt) (Ligamed MF-2-V, Peter Greven, Bad Münstereifel, Germany) was used for external lubrication.

Starch was used as a pure product. MCC and LAC were used as a mixture. The mixture was 50/50 (%w/w) and the blending was performed using the T2F turbula mixer (Willy A. Bachofen, Muttenz, Switzerland) at 49 rpm for 5 min. The mixture will be referred to as MCC/LAC in the following text.

2.1.2. Tablet manufacturing

All the tablets were manufactured on a Styl'One Evolution compaction simulator (Medelpharm, Beynost, France). This device is a single station instrumented tableting machine equipped with strain gauge force sensors to measure the force on both punches. The default compaction cycle was used at 25% of the maximum speed of the machine. An example of a force–time profile obtained with this cycle can be found in the supplementary material. The punches used were Euro B punches with a flattened disc geometry, with a diameter of D = 11 mm and two parallel chords defined by a circular angle of $\alpha = 30°$(Mazel et al., 2016).

The filling heights were adapted for each product to obtain a final tablet thickness of 2.5 mm (after ejection) under the chosen compaction force. The compaction forces used were chosen for the sake of the demonstration and were 12.5 kN for MCC/LAC (130 MPa) and 29.5 kN for Starch (315 MPa). These compaction pressures were chosen to have, for both products, a similar breaking force (around 100 N) to ease the comparison.

An external device was used to lubricate the punches and the die. This system used a pulsed air blow cabinet to spray the Magnesium Stearate powder on the punches and die.

2.1.3. Tablet testing

Diametral compression tests (Brazilian tests) were performed, immediately after compression, using a TA.HDplus texture analyzer (Stable microsystems, United Kingdom). Compacts were compressed between two flat surfaces at a constant speed of 0.10 mm/s with an acquisition rate of 500 Hz. During the test, the tablet could be positioned with the platens in contact with the flat parts of the tablet band. This test will be referred as the flattened Brazilian test (FBT). The other possibility was to rotate the tablet of an angle of 90° and to apply the stress on the round part of the band. This is equivalent to the classical test used in the pharmaceutical field and will be called classical Brazilian test (CBT). Fig. 1 summarizes the two test configurations.

To measure the BFI, tablets with a hole at the center were prepared by inserting holes of 1 mm of diameter using a drill Micromot 50 E/EF (PROXXON S.A., Luxembourg). Machining speed was adapted for each formulation. The tablets were maintained using a specially designed polymeric holder obtained by 3D printing. To avoid defects at the back of the tablet during machining, two tablets were placed together and only the upper one was finally used for experiments. Tablets with holes were broken using both the FBT and the CBT. These tests will be referred to as HFBT and HCBT. For every test configuration, 5 tablets were broken.

2.2. Numerical method

2.2.1. General frame work

For the interpretation of the BFI, FBT and HFBT were simulated using FEM simulation on Abaqus® 6.13 (Dassault Systèmes, Vélizy-Villacoublay,France). In each case, the tablet was represented by an elastic isotropic body. Using the symmetries of the system, it was possible to represent only a quarter of the whole tablet. The geometry of the tablet was fixed and inspired by the tablets used in the experiments with a diameter of 11 mm, a thickness of 2.5 mm and an angle of 30° for the two flat-ends. For the case of tablets with a hole, a hole with a diameter of 1 mm was inserted at the center.

2.2.2. Cohesive zone model

The tablet was considered as a quasi-brittle solid (Girardot et al., 2023) and its failure behavior was modelled using a cohesive zone model (Hillerborg et al., 1976). The model used was the same than in a previous work where it was shown to be well suited to represent the failure behavior of pharmaceutical tablets (Mazel et al., 2023). In the simulation, the tablet was initially cut into two halves along the plan which corresponds to the final failure surface. Then the two obtained surfaces were connected using a triangular traction-displacement curve (Fig. 2). This model is the simplest of the cohesive zone models. The initial slope k_i was set in Abaqus using the default contact enforcement method, which means that the value of k_i was based on the underlaying element stiffness (Vervloet et al., 2019).

The parameters σ_t, which represents the tensile strength of the tablet, and G, which represents the fracture energy ($J.m^{-2}$) where varied in order to understand the influence of these parameters on the BFI. As elastic properties have also a role in l_c, they were also varied. The values for the simulation are presented in Table 1. For each variable, 2 values were considered, and a full factorial design of experiment (DOE) was performed for each test (FBT and HFBT) leading to 16 simulations for each test. A central point was added to the design (E = 6 GPa, $\nu = 0.195$, G = 3 $J.m^{-2}$ and $\sigma_t = 3.5$ MPa).

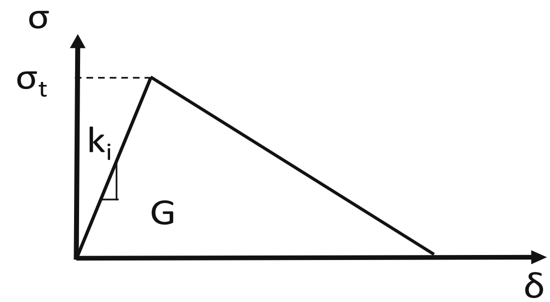

Fig. 2. Triangular model for a traction separation curve. σ represent the stress and δ represent the displacement.

It can be noted that the values of the tensile strength used are on the high side for pharmaceutical tablets for which 2 MPa is generally considered to be a good value (Pitt and Heasley, 2013). This choice was made in order to ensure that during the simulation, using the fracture energies chosen, a clear force drop would be obtained at the breakage that made it possible to identify clearly the breaking force. This is not always possible using the flattened Brazilian disk depending on the values used. This point will be further discussed in the result section.

2.2.3. Statistical analysis

The analysis was performed using the software MODDE (Umetrics, Malmö, Sweden). The relationship between the factors and each response was obtained by fitting with MLR (multiple linear regressions). First, the complete equation was used in order to identify the significant terms. The model parameters were considered as significant if their p

Table 1
Parameters used for the numerical study.

Parameter	Values
E	4–8 GPa
ν	0.13–0.26
σ_t	2–5 MPa
G	2–4 $J.m^{-2}$

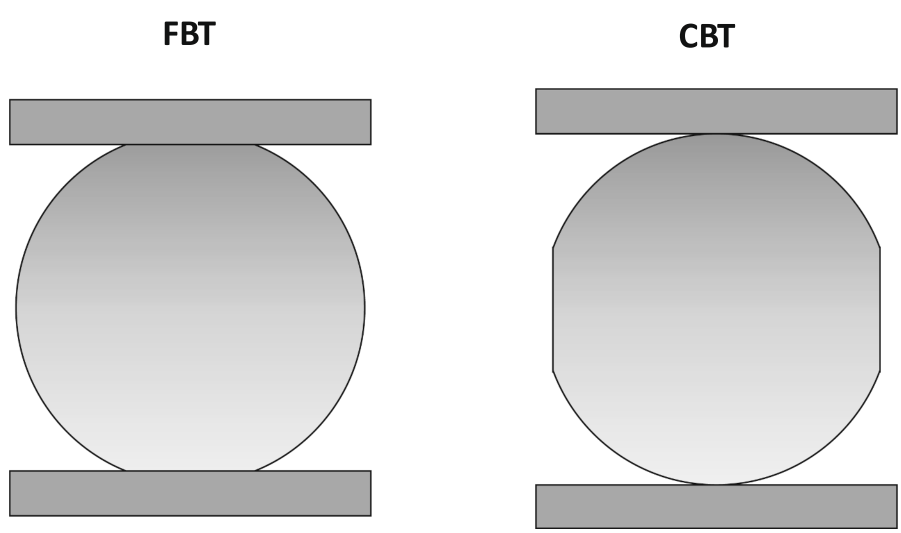

Fig. 1. Schematic representation of the failure tests used: Flattened brazilian test (FBT, Left) and Classical Brazilian test (CBT, right).

value was lower than 0.05 (confidence level of 95%). Then, the insignificant parameters were removed and the final model was built. The quality of the final model was evaluated with a summary of the fit method which included the goodness of fit(R^2) and the goodness of prediction (Q^2). A model is considered good (goodness of fit and goodness of prediction) if the difference R^2-Q^2 was lower than 0.2, Q^2 was higher than 0.5 (Eriksson et al., 2013).

3. Results and discussion

3.1. Hiestand's BFI

As explained above, Hiestand's BFI is based on the ratio between the force needed to break a tablet without a hole and the force to break the same tablet with a hole at its center (if the geometrical dimensions are kept the same, the breaking forces do not need to be transformed into stresses). In the article that introduced the BFI, the authors explain that the hole in the middle promote a stress concentration of around 3 at the hole edge (Hiestand et al., 1977). Note that the correct value is in fact 6 as demonstrated elsewhere(Croquelois et al., 2017), but that does not change the logic of the test. Hiestand *et al.* supposed that a perfectly brittle solid would thus break at a force which would be 1/3 (i.e. in fact 1/6) of the force needed to break the tablet without the hole and that any deviation from this value means that plastic deformation occurs at the hole edge. This reasoning supposes that a perfectly brittle solid can be treated with the maximum stress failure criterion (i.e. the failure happens when, at one point of the solid, the maximum stress reaches the tensile strength). But this would mean that the material has no toughness (i.e. any stress on a sharp crack would break the solid) which is not true if we consider the first definition considered in the introduction (Mazel et al., 2023). In fact, the ratio should be influenced by both the toughness of the sample and the fact that plastic deformation could occur, which are two different concepts from a fundamental point of view.

It can be noted that several articles challenged the concept of BFI itself. Especially, several authors referred to the paper written in 2003 by Podczeck and Newton (Podczeck and Newton, 2003). This paper is for example cited by Sonnergaard and by Gong and Sun, in their article introducing the BDI and the TBI to justify the need of new indices(Gong and Sun, 2015; Sonnergaard, 2013). Nevertheless, the critics raised by Podczeck and Newton were in fact incorrect. Their first error was to use the equation from Durelli and Lin (Durelli and Lin, 1986) in the wrong direction (confusion between x and y axis) which led to a stress concentration factor of 10 instead of 6. But the most important mistake was that they misunderstood the concept of BFI. To calculate the BFI, Podczeck and Newton considered that the actual value of the stress at the hole edge should be considered. This reasoning misses completely the point of the BFI. When the compact with a hole is considered, the fact to use the apparent tensile strength (i.e. the tensile strength calculated with same equation used without a hole) is the mean to understand the effect of the hole. If the hole has no effect (perfectly ductile product, i.e. no influence of stress concentration) both tensile strengths would be the same. If not, this means that the hole has an influence, the apparent tensile strength will be lower. The BFI is meant to quantify this difference. It would have been possible to define BFI using the stress at the hole edge but the equation would have to be modified. Using the actual stress at the hole edge to calculate the BFI using Hiestand's equation is not correct (and obviously leads to negative values). Note that another point in the paper of Podczeck and Newton, is that they found, in the case of lactose, a higher breaking force for tablets with a hole than for tablets without a hole. But the tablets are not obtained at the same pressure, so it is not really surprising that such effect can arise. Authors claimed, that they have the same porosity, but it is not clear why the hole in the tablet would affect so much the compressibility. So, all this indicates that this article is to be taken with caution and does not invalidate the Hiestand's approach as claimed elsewhere by the same authors (Podczeck and Newton, 2005).

Nevertheless, as explained above, the original reasoning of Hiestand does not seem completly correct. It is thus interesting to try to reinterpret the BFI for a fundamental point of view. Note that originally, the BFI was calculated by Hiestand using square tablets and transversal loading. It was then applied to round tablet by other authors (Roberts and Rowe, 1986), using the CBT, leading to similar trends. Due to the problem of interpretation of the CBT in terms of tensile strength(Fell and Newton, 1970; Mazel et al., 2016), it was then further adapted to the FBT(Croquelois et al., 2017). This last geometry will thus be considered in the following text.

First of all, the stress needed to break the tablet without a hole is intrinsically connected to the material's tensile strength. This dependency would be exclusive if the test was a pure tensile test resulting in a uniform stress across the specimen. This is not exactly true for the flattened Brazilian test. Nevertheless as the stress is fairly homogeneous at the center(Mazel et al., 2016), we can suppose that the tensile stress will drive the value of the obtained failure stress with low influence of the other parameters (Mazel et al., 2023).

The case of the tablet with a hole is more complex. If instead of a hole a thin sharp crack at the center would be used (a sharp crack gives a stress that theoretically goes to infinity at the crack edge), the breaking force/stress would be directly influenced by the critical stress intensity factor. In the case of the hole, the stress is less concentrated so we can suppose that both the critical stress intensity factor and the tensile stress might play a role. According to this reasoning, the ratio between the breaking forces/stresses should thus depend on both σ_t and K_{Ic}. The BFI could thus be linked to the l_c as defined in equation 3.

To test this reasoning, a numerical DOE was performed as explained above. For each set of parameter, FBT and HFBT were simulated. In each simulation, the maximum force before breakage was considered to be the breaking force. Note that, as explained above, the set of values chosen for the simulation shows a clear force drop when the crack starts to propagate which makes it possible to determine a clear value for the breaking force.

The values obtained for the whole design of experiment are presented in Table 2. The first remark is that the set of parameters used makes it possible to obtain BFI values between 0.15 and 1.7 (theoretical limits are between 0 and 2.5) which covers most of the values published in the literature for the BFI except the very low values obtained for MCC for example. Nevertheless BFI values calculated with this kind of products are to be taken with caution as, for very ductile products, the maximum force during the test might not correspond to the crack formation (Jonsén et al., 2007). This point will be further discussed below.

Even if the fracture energy is the input parameter of the numerical model, the reasoning made above seemed to indicate that the stress intensity factor might be a more interesting factor to study the influence of the parameters on the different values.

The results of the parameters for the statistical analysis of FBT and HFBT are presented in Fig. 3. In both cases, excellent correlation and prediction can be obtained by using only σ_t and K_{Ic}. In the case of FBT, as expected, the value of the breaking force is mainly driven by the tensile strength and K_{IC} has only a minimal influence. For the case of HFBT, the correlation is more complex. K_{Ic} has the major influence but the influence of σ_t is also important, with the presence of cross effects. The presence of square terms indicates also that the effects are not linear.

The results presented in Fig. 3 confirm the trends that were expected for the breaking force in FBT and HFBT. The BFI contains the ratio between the force in the FBT (which is mainly influenced by σ_t) and the force in the HFBT (which is mainly influenced by K_{Ic} and also by σ_t). So considering the previous results it was logical to look if there was a correlation between the BFI and the ratio σ_t/K_{IC}.

Fig. 4 shows the evolution of BFI as a function of this ratio. The curve indicates that BFI increases with increasing σ_t/K_{IC} which is coherent with the results found above. The ratio σ_t/K_{IC} is equal to the square root of the inverse of l_c as defined in equation 3. This means that when BFI

Table 2
Results of the numerical design of experiment. Fr is the breaking force.

E (GPa)	ν	G ($J.m^2$)	σ_t (MPa)	Fr (FBT) (N)	Fr (HFBT) (N)	BFI	K_{Ic} ($MPa.m^{(1/2)}$)	l_c (m)
4	0.13	2	2	107.0	57.1	0.44	0.089	2.00E-03
8	0.13	2	2	109.4	73.1	0.25	0.126	4.00E-03
4	0.26	2	2	107.1	57.2	0.44	0.089	2.00E-03
8	0.26	2	2	109.7	73.3	0.25	0.126	4.00E-03
4	0.13	4	2	109.5	73.1	0.25	0.126	4.00E-03
8	0.13	4	2	117.0	90.1	0.15	0.179	8.00E-03
4	0.26	4	2	109.7	73.3	0.25	0.126	4.00E-03
8	0.26	4	2	117.3	90.6	0.15	0.179	8.00E-03
4	0.13	2	5	262.0	59.3	1.71	0.089	3.20E-04
8	0.13	2	5	263.5	84.4	1.06	0.126	6.40E-04
4	0.26	2	5	259.9	60.0	1.67	0.089	3.20E-04
8	0.26	2	5	262.0	84.4	1.05	0.126	6.40E-04
4	0.13	4	5	263.2	84.2	1.06	0.126	6.40E-04
8	0.13	4	5	265.8	117.1	0.63	0.179	1.28E-03
4	0.26	4	5	261.8	84.4	1.05	0.126	6.40E-04
8	0.26	4	5	265.6	117.2	0.63	0.179	1.28E-03
6	0.195	3	3.5	186.9	87.3	0.57	0.134	1.47E-03

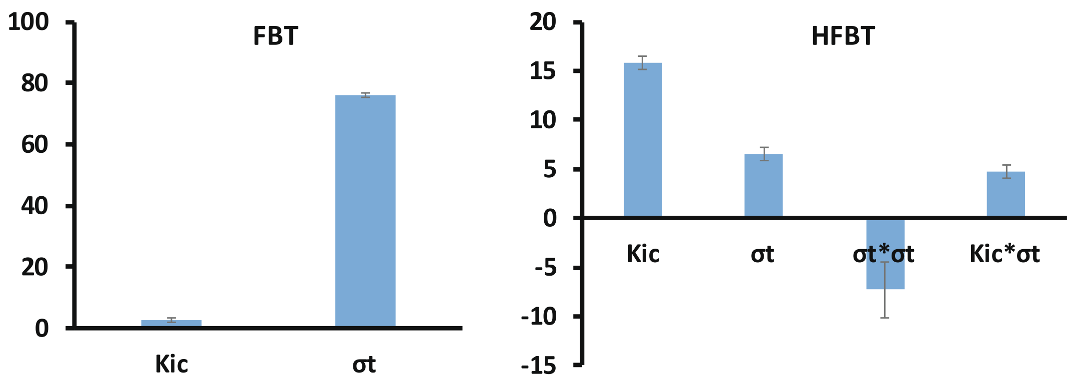

Fig. 3. Results of the statistical analysis for fbt (r^2 = 0.999, Q^2 = 0.991) and HFBT (R^2 = 0.996 and Q^2 = 0.962).

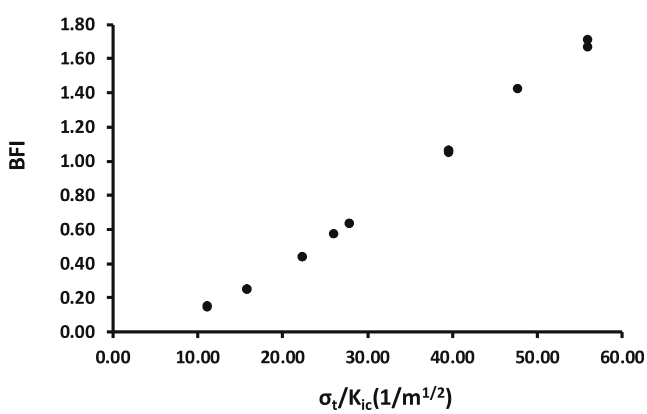

Fig. 4. Evolution of BFI as a function of σ_t/K_{IC}.

increases, l_c decreases. And as said above the brittleness of a sample can be characterized by comparing l_c to the sample size. So for samples of comparable size, as are pharmaceutical tablets, the higher BFI, the lower l_c, i.e. the more brittle the sample.

The numerical results thus make it possible to have a more complete view of the meaning of Hiestand's BFI in the case of pharmaceutical tablets. A high BFI means that l_c is small, i.e. that the tablet is more prone to behave in a brittle manner, with brittle taken in the sense of elastic until failure.

The values of l_c for the different cases can be found in Table 2 and range from 0.32 mm to 8 mm. In the present case the sample size was typically 11 mm. If larger l_c are considered, tablets should behave in a more and more ductile manner during the simulations. To show this effect, new simulations were performed. They were based on the case E = 8 GPa, ν = 0.13 and σ_t = 2 MPa. Different fracture energies were used: 2, 4, 8 and 12 $J.m^{-2}$, which leads to lc values of 4, 8, 16 and 24 mm respectively. As described elsewhere in the literature (Wang and Xing, 1999), the fracture of the tablet during the FBT does lead to a complete ruin of the sample, and after failure, the tablet can be further loaded. So the fracture corresponds to a drop of force during the loading. Fig. 5, shows the numerical results obtained for the different values of l_c. For the two smallest values (which correspond to the values used in the DOE

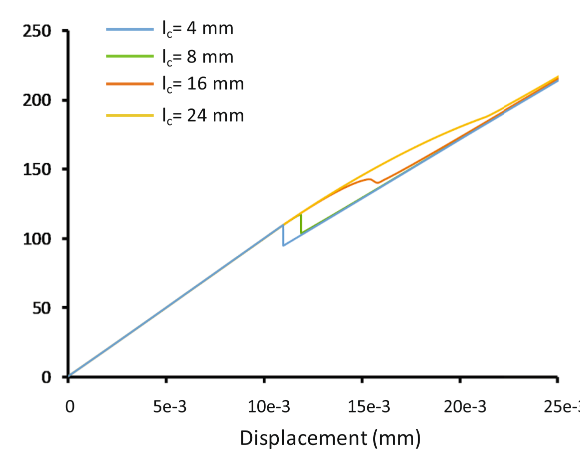

Fig. 5. Force/displacement curves obtained for the numerical simulation of the FBT using different values of l_c.

presented above) a sharp decrease is obtained. But as l_c continues to increase, the force drop becomes less sharp. For $l_c = 24$ mm, there is no more force drop on the curve. So in this last case, it is impossible to measure a breaking force. This is why, this kind of values were excluded in the DOE presented above. This means that for the products that are very ductile, FBT is difficult to use to assess the mechanical properties as the failure force is not detected. The breaking force that will be detected will thus correspond to the final failure of the tablet which will not correspond to the development of the central crack but rather to a shear failure at the edge of the flat surface of the band. This limitation has to be kept in mind, and will be further developed below.

Despite this limitation, these curves show how the FBT could be used as a way to qualitatively assess the brittleness/ductility of tablets. Sharp drops in the loading curve indicate brittle products whereas shallow drops or absence of drop indicate ductile products. BFI can afterward be calculated, in the case of sufficiently brittle product, to classify them.

3.2. Average stress extension of the BFI (Croquelois et al., 2020, 2017)

As said in the introduction, it was demonstrated that the BFI was in fact impacted by the size of the hole used. So comparison should only be made between tablets made with the same hole size. To avoid this problem, a characteristic length a_0 was introduced by using the “average stress” failure criterion. Using the results of Table 2 and Equation 5, it is possible to calculate a_0 for each case of the DOE presented above. The obtained values are plotted as a function of l_c for the whole DOE in Fig. 6.

The parameter a_0 monotonically increases with the value of l_c. This means that a_0 can, as the BFI, be used as an indicator of brittleness. It presents the advantage of being insensitive to the size of the hole and as such, to make easier the comparison between tablets obtained under different conditions. The two parameters a_0 and l_c are characteristic lengths that are defined differently. They don’t have the same numerical value but they are in the same order of magnitude and follow the same trend. The parameter a_0 is easier to obtain than l_c as it can be directly calculated with the results of FBT and HFBT without the use of numerical modelling. Knowing that its value is around 1/2 or 1/3 of l_c it can be directly compared to the size of the sample to assess the brittleness of the tablet.

3.3. Sonnergaard’s BDI (Sonnergaard, 2013, 2023)

The roots of the BDI are to be found in the work of Hucka and Das cited above (Hucka and Das, 1974). But rather than using the definition of brittleness given in the article, the approach developed is based on the facts that are generally observed along with brittleness. Hucka and Das cited several facts that are supposed to be associated with high brittleness:

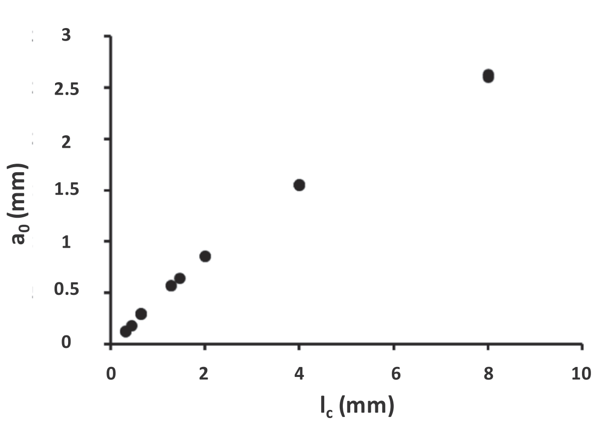

Fig. 6. Evolution of a_0 as a function of l_c.

- Low values of elongation
- Fracture Failure
- Formation of fines
- Higher ratio of compressive to tensile strength
- Higher resilience
- Higher angle of internal friction
- Formation of cracks in indentation

First of all, it must be noted that it is not straight forward that these facts could be derived from the definition of brittleness being defined as failure in the elastic domain. Nevertheless, in his approach, Sonnergaard tried to find which of these facts could be used to obtain a quantitative view of brittleness. He made the choice of the first point, i.e. that brittleness generally leads to small strain at failure. Based on this idea, he proposed an index that could quantify the brittleness using the force displacement curve during the diametral compression test. For this purpose, instead of using directly the displacement, the index calculates a normalized displacement by dividing the work of failure (WOF) by the fracture force over 2. In the case of a purely elastic case this would be equal to the total displacement during the test. This displacement is then divided by the tablet diameter to obtain a dimensionless index which is equivalent to a strain. Note that, contrary to BFI, a high BDI means low brittleness or high ductility.

The idea behind this index is that ductile materials should lead to larger deformation during the test. Nevertheless this assertion is questionable. If plasticity occurs before breakage, the displacement to reach a certain force will be higher than the value that would have been found for a purely elastic process, if everything else is kept constant. Plasticity can also occur at the contact between the tablet and the platen. This would also tend to increase the displacement during the test. Nevertheless, the total deformation is strongly influenced by the value of the Young modulus of the tablet but also by its tensile strength. It is thus not easy to understand exactly what is measured by this index. In the original article, this index is used to differentiate Microcrystalline cellulose (MCC), Anhydrous Lactose and their mixtures. It shows that BDI increases with the percentage of MCC in the mixture, meaning that a greater percentage of MCC render the mixture more ductile. Nevertheless, these two products have also different Young’s modulus, so it is possible that in fact, in this case, the BDI also contains information on the elasticity of the system. And even if E is used in the expression of l_c (equation 1) other parameters are also to be taken into account that are not present in the BDI.

Finally, it is also shown that BDI does not change with the pressure used to make the tablet. Indeed, the representation of the work of failure as a function of the breaking force seems to be a straight line. This was confirm in the more recent paper on the subject (Sonnergaard, 2023) showing that “no general systematic relation is present” between BDI and breaking force for a single product. This means that the brittleness would be the same for all the tablets made for the same product regardless of the compression pressure. This is in contradiction with the results known for the BFI which increases with increasing pressure used to make the tablet (Croquelois et al., 2020; Roberts and Rowe, 1986). This point is one of the facts that were used to justify the use of the third index studied in this paper, the TBI.

3.4. Gong and Sun’s TBI (Gong and Sun, 2015)

The TBI is based on the same premises than the BDI, i.e. that the brittleness can be quantified by using the strain at the fracture point, and the authors stated that: “A smaller strain at the fracture point corresponds to a more brittle specimen”. To illustrate their point, the authors consider a schematic representation of the strain–stress evolution during a failure test. This representation was adapted and is presented in Fig. 7a. In their paper, Gong and Sun considered that ductility increases from curve 1 to 3. This is coherent with brittleness in the sense “elastic until failure” because the more ductility and the more non-linearity on

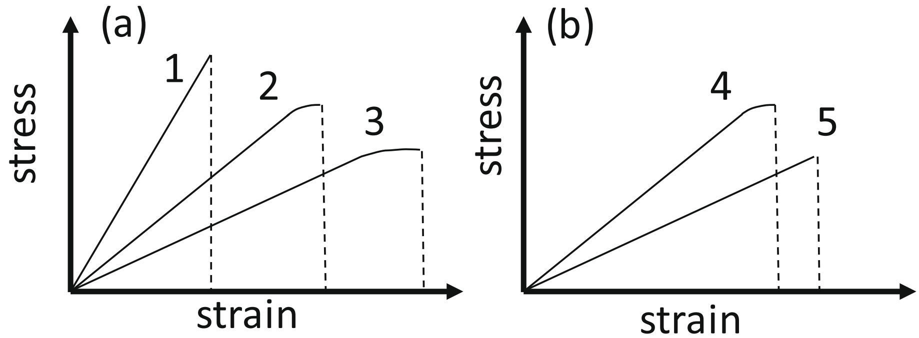

Fig. 7. Schematic representation of the evolution of stress and strain during failures tests. (a) adaptation from (Gong and Sun, 2015) (b) other cases.

the curve. Nevertheless, there is also a change in Young's modulus from 1 to 3 (the slope of the elastic part decreases going from 1 to 3). And it is not clear why a high ductility would be linked with a lower Young's modulus. For example, most of the metals are very ductile but have high Young's moduli. It is thus perfectly possible to imagine the cases 4 and 5 presented in Fig. 7b. In this cases, 4 is more ductile than 5, but 5 has a lower Young's modulus and finally a higher strain until failure. From a fundamental point of view, there is nothing that would render such a case impossible.

The main difference between BDI and TBI is the way the strain is calculated. In the BDI, the WOF was considered which means that both the linear and non-linear part of the curve are taken into account. In the TBI, only the linear part is considered i.e. the index is not influenced by the non-linearity in the curve. As such, TBI is directly linked to the breaking force and the Young modulus. The other difference is that the TBI is defined by the inverse of the strain, meaning that, as the BFI, a high value of the TBI means a high brittleness. A complete comparison between the two indices can be found elsewhere(Sonnergaard, 2023).

Based on the definition, the TBI should increase when Young's modulus increases (steeper slope) and when the tensile strength decreases. This last point was confirmed in a further publication where the correlation between TBI and tensile strength was studied (Gong et al., 2015). If Young's modulus and tensile strength are indeed in the definition of l_c (equation 1), the other parameter (G_c) is absent from the definition of the TBI.

Even if the brittleness definition considered by the authors seems to be "elastic until failure" as shown in Fig. 7a, this definition is not used to test the index. In fact, the validation of the index is based on the idea that brittleness means high friability. This idea was developed earlier in another article that dealt specifically with friability (Osei-Yeboah and Sun, 2015). According to the authors, when a material is very brittle, as it is less capable to reduce the effect of local stresses, it will be more prone to fracture during deformation and will present a higher friability. This reasoning would be perfectly correct if we consider two products with the same strength. But the friability is also strongly influenced by the strength itself. It is well-known that friability increases when the strength decreases. So considering friability as an indicator of brittleness could mean a change in the brittleness definition from "elastic until failure" to "easy to break" which is different as mentioned above.

Using this definition changes the trend that we can expect. For example, usually for a product, friability decreases when the porosity decreases (i.e. when the compaction pressure used to make the tablet increases). So with this definition, it means that, for the same product, a tablet made at higher pressure is considered less brittle than a tablet made at low pressure as assumed and presented by Gong and Sun (Gong and Sun, 2015). This is in contradiction with the results obtained for the BFI which generally increases with the pressure (Croquelois et al., 2020; Roberts and Rowe, 1986). This also means for example that a tablet of MCC obtained at very low pressure, can be considered as more brittle than a tablet of Lactose made at high pressure. It is thus clear that the TBI gives an information which is different from the one given by the BFI.

3.5. *Experimental case study*

To emphasize the different points developed above, two products were chosen for the sake of the presentation. One was the mixture MCC/LAC, which was already studied by Sonnergaard and by Gong and Sun (Gong and Sun, 2015; Sonnergaard, 2013). The other was starch. The idea was to compare the brittleness prediction using the different indices presented above. The comparison of force displacement curves during the CBT for the two products is presented in Fig. 8. To ease the comparison, we chose two curves with approximately the same maximum force (115 N in this case) and straight lines were added to visualize the linear part.

The shape of the curves makes it directly possible to see which of the two tablets is the more brittle in the sense "Elastic until failure". Clearly starch is much more linear until failure and a sharp decrease of the force is seen when the failure starts. The MCC/LAC mixture departs more early from linearity and present a round peak at failure. So visually, considering the brittleness definition "elastic until failure", the starch tablet is the most brittle.

If the BDI is calculated for both products, it gives 1.7% for the MCC/LAC and 2.2% for Starch, meaning that starch is more ductile. It is obvious from the graph that the length of the linear portion is larger for Starch than for MCC/LAC. The TBI will thus be smaller for Starch. Calculations give a TBI around 120 for MCC/LAC and 60 for Starch. So according to both indices, Starch is more ductile, which is clearly not the case according to the shape of the curves on Fig. 8.

The idea was then to test the BFI. For this, we first tried to use the FBT configuration as performed before (Croquelois et al., 2020, 2017). Fig. 9 shows typical force displacement curves for the two products in the FBT

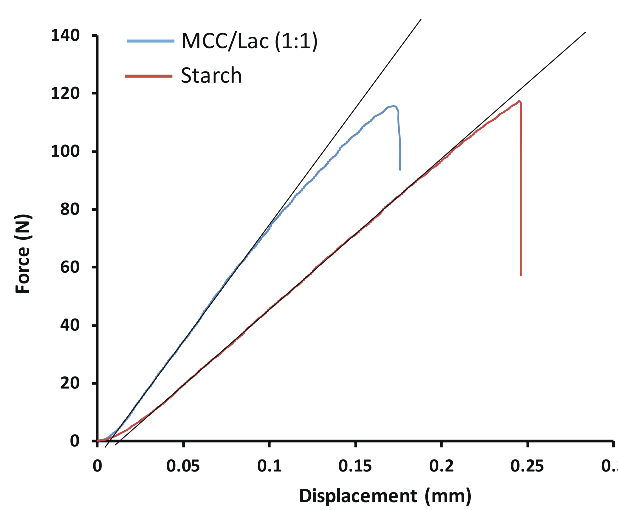

Fig. 8. Comparison of the force/displacement curves during diametral compression for mcc/lac (1:1) and starch.

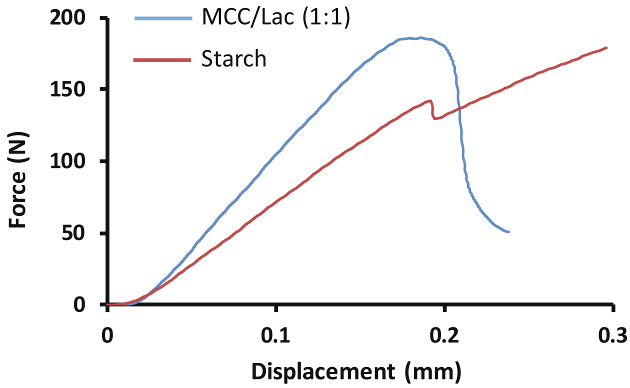

Fig. 9. Examples of force/displacement curves during the FBT for Starch and MCC/LAC.

configuration (i.e. without holes). If the force drop is clearly visible for starch, it is completely absent for MCC/LAC. For this product, only a force drop after a large rounding is seen which experimentally corresponded to the final shear failure of the tablet at the edge of the flat part. This corresponds to the phenomena explained in part 3.1, i.e. when a tablet is too ductile, the force drop becomes impossible to detect. The graph itself is a confirmation of the fact that the starch tablets are indeed more brittle than the MCC/LAC tablets, contrary to what is found by BDI and TBI. It also shows that the FBT cannot be used correctly to calculate the BFI in the case of MCC/LAC.

In the case of the CBT, the central breakage of the tablet leads to the ruin of the tablet. The value of the force detected, even if influenced by the contact, should at least be in relation with the failure pattern. We thus decided to use the CBT to calculate the BFI value of the MCC/LAC tablets even if this way of calculating is also to be taken with caution. The value found was 0.12. Note that in his work, Sonnergaard gave a value around 0.1 for a similar mixture(Sonnergaard, 2013). For starch tablets, the FBT was usable as the failure force was easily detected. Nevertheless, for the sake of the comparison with the other product, BFI was calculated using both CBT and FBT. The values found were 0.24 and 0.28 for CBT and FBT respectively. Both values are above the one calculated for MCC/LAC. So BFI indicates that, in accordance with the curves presented in Fig. 8 and Fig. 9, the starch tablets are more brittle than the tablets made of MCC/LAC. This is in accordance with the numerical results presented above.

4. Conclusion

Brittleness, is a common concept in the mechanics in material. Nevertheless, some contradictions can be found. It is generally defined as opposed to ductility, i.e. the material behaves elastically until failure. Nevertheless, sometimes another definition is also used, derived from the common sense of the word, that links brittleness to the fact that a material is easy to break.

Among the three indices for brittleness used in the case of pharmaceutical tablets, the results presented above showed that the BFI is the only one which is unequivocally related with brittleness in the sense of "elastic until failure". Numerical simulation results showed that the BFI is related with the characteristic length l_c which can be used to predict the brittle/ductile behavior when compared to the actual size of the sample.

BDI and TBI give results that are in contradiction with the BFI, especially considering the evolution with porosity. On a case study, we also showed that their prediction can be in contradiction with experimental findings. So these indices should not be used to quantify brittleness in the sense of elastic until failure. Nevertheless, Gong and Sun showed that TBI seems to be related with friability, which is an important property of pharmaceutical tablets. As such TBI is a useful index. But friability is not really linked with brittleness except if brittleness is understood as easy to break.

To conclude, the different indices are not in contradiction one with the other, they just don't characterize the same material property. In the case of brittleness being understood as "elastic until failure", which is the more common sense of brittleness in the mechanics of materials, the BFI is the most adapted index among those which have been published.

CRediT authorship contribution statement

Vincent Mazel: Methodology, Investigation, Conceptualization, Writing – original draft. **Pierre Tchoreloff:** Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpharm.2023.123364.

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