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Research Paper

A new tablet brittleness index

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ABSTRACT

Brittleness is one of the important material properties that influences the success or failure of powder compaction. We have discovered that the reciprocal of diametrical elastic strain at fracture is the most suitable tablet brittleness indices (TBIs) for quantifying brittleness of pharmaceutical tablets. The new strain based TBI is supported by both theoretical considerations and a systematic statistical analysis of friability data. It is sufficiently sensitive to changes in both tablet compositions and compaction parameters. For all tested materials, it correctly shows that tablet brittleness increases with increasing tablet porosity for the same powder. In addition, TBI increases with increasing content of a brittle excipient, lactose monohydrate, in the mixtures with a plastic excipient, microcrystalline cellulose. A probability map for achieving less than 1% tablet friability at various combinations of tablet tensile strength and TBI was constructed. Data from marketed tablets validate this probability map and a TBI value of 150 is recommended as the upper limit for pharmaceutical tablets. This TBI can be calculated from the data routinely obtained during tablet diametrical breaking test, which is commonly performed for assessing tablet mechanical strength. Therefore, it is ready for adoption for quantifying tablet brittleness to guide tablet formulation development since it does not require additional experimental work.

1. Introduction

Brittleness is one of the important material properties that determines the deformation and fracture of tablets under stress. Tablets of highly brittle materials tend to have more defects because of their lower ability to accommodate stress during tablet production, storage, transportation, and handling. This is shown as the propensity of these tablets to easy chipping, high friability, and generation of hidden defects [1]. On the other hand, tablets from very plastic materials tend to loss tabletability after dry or wet granulation processes [2–5]. When a bilayer tablet consisting of two layers with very different brittleness is diametrically compressed, the more brittle layer tends to fracture more easily leading to a unique breakage mode [6]. These problems can be minimized or even eliminated by maintaining a balanced tablet brittleness through appropriate choice of excipients in the formulation [7]. However, the effective design of a formulation with balanced brittleness and ductility requires a reliable method for quantifying tablet brittleness.

Outside of the pharmaceutical arena, material brittleness is usually quantified using an empirical index that correlates with performance of importance. In geotechnical engineering, brittleness of rocks is usually assessed by penetration rate index or drilling rate index [8,9], because they correlate well with the brittle fracture propensity of rocks. This approach, although empirical, has been widely adopted in the geoengineering field because of its practicality and effectiveness in assessing brittleness of rocks. A similar approach has also been used to quantify brittleness of dental ceramics using a chipping factor, which quantifies the propensity to chipping at the edges [10]. Hucka and Das [11] comprehensively summarized methods for measuring brittleness. Five common approaches to obtain brittleness of rocks are based on strain, reversible energy, Mohr's envelope, strength ratio, and special tests [12]. The special tests include impact test [13], indentation test [14,15], and punch penetration test [8]. Because of the unique specimen shape requirement for performing test, approaches based on Mohr's envelope and strength ratio are not applicable for tablets. However, the approaches based on strain, reversible energy, and special tests can possibly be adopted for determining tablet brittleness. These have been explored in this work.

In an effort to quantify brittleness of pharmaceutical materials, a brittle fracture index (BFI) was proposed by comparing tensile strength of tablets with and without a central hole [16–18]. Despite the initial promise and enthusiastic adoption of BFI in pharmaceutical research [19,20], its usefulness was questioned in

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light of the finding that BFI did not vary in a systematic manner with composition [21]. This is related, at least partially, to the fact that BFI does not sufficiently discriminate among materials with brittleness in the middle range of the 0 – 1 scale where most materials lie. BFI was further challenged on the basis that the tensile strength of a compact with a central hole cannot be calculated using the same equation for an intact tablet because of the different stress distributions in the two types of tablets [22]. Practically speaking, making tablets with a central hole is challenging because it requires either the use of special punches when making the tablets or drilling post tablet compression.

In a recent effort to improve the technique for quantifying brittleness, Sönnergaard proposed a new brittle-ductile index (BDI) for compacted cylindrical tablets based on the work of failure (WOF) and maximum breaking force (F_{max}) [23], as shown in Eq. (1):

$$BDI = 100 \times \frac{WOF \times 2}{F_{max} \times D} \quad (1)$$

where D is the diameter of the tablet. The term, $2WOF/F_{max}$, in Eq. (1) is used to approximate the displacement required to fracture the tablet because of the experimental difficulty in directly determining the initial point of contact between the platen and tablet [23]. Unlike BFI, BDI values do vary in a more systematic manner with changes in composition of a mixture consisting of plastic and brittle materials [23]. This approach yields a reasonable estimate of the maximum diametrical strain in a tablet for brittle materials, such as lactose. However, errors are expected for pharmaceutical tablets that exhibit substantial plastic deformation leading to the tablet fracture because of work due to irreversible plastic deformation that should have not been included for characterizing brittle fracture behavior, which is, elastic by definition. For this reason, the relationship between WOF and force is actually not strictly linear [23]. To alleviate this problem, WOF was plotted against F_{max} of tablets prepared under different pressures [23] and the slope of the line, α, is used to calculate BDI using Eq. (2):

$$BDI = 100 \times \frac{2\alpha}{D} \quad (2)$$

The application of Eq. (2) implies that tablet fracture behavior is independent of tablet porosity, which varies when the compaction pressure changes. This assumption is, however, inconsistent with both theoretical expectations and practical observations. Qualitative observations suggest that tablets with high porosity or made from brittle materials are usually more brittle. For example, porous tablets (prepared at a low pressure) of relatively plastic hydroxypropyl cellulose (HPC) fracture during diametrical compression but a denser HPC tablet (prepared under a high pressure) yields without fracture during the same test. Therefore, a measurement of brittleness of a tablet should not be assumed to be a reliable descriptor of the brittleness of the material and a clear distinction between brittleness of a material and that of a tablet needs to be made. In addition to the problems discussed above, both BFI and BDI were developed without being validated against a tablet property known to correlate with brittleness. In absence of such validation, the application of BFI and BDI requires caution.

Inspired by the successful approaches in quantifying the brittleness of the rocks and dental ceramics, we set out to identify a new tablet brittleness index (TBI) that most strongly correlates to tablet friability, a tablet property with recognized linkage to tablet brittleness. Unlike BFI and BDI, TBI quantifies brittleness of individual tablets; regardless, they are made from the same powder or not.

1.1. Theoretical considerations

In the most rigorous sense, brittleness determination is suitable only for an elastically deforming body, which is represented by the line **oa** in Fig. 1. In this case, the strain at the fracture point is used to quantify brittleness of the specimen. A smaller strain at the fracture point corresponds to a more brittle specimen. However, most pharmaceutical materials have some degree of ductility. Hence, the specimen undergoes some degree of plastic deformation before it fractures (curve **obcd** in Fig. 1). The non-linear strain immediately before the peak force corresponds to the buildup of stress that is required for the crack to grow within the specimen to eventually split it. For more ductile materials, such as those shown in **oe**, the non-linear strain before breakage is longer. In the situations similar to **obcd** and **oe**, the strain that should be used to quantify brittleness of the specimen is difficult to define. In this work, we adopt the more conservative approach by using the strain at the elastic limit, i.e., the point of initial deviation from linearity instead of the point of maximum force, to quantify brittleness.

Curves shown in Fig. 1 are usually obtained using specimens with a standard shape, e.g., dumb bell shaped bar, in the strength test (either compressive or tensile). However, such a specimen is rarely relevant to pharmaceutical tablets. On the other hand, cylindrical tablets studied by the Brazilian test [24–26], or diametrical breaking test, are commonly used for calculating tablet tensile strength. It will be very efficient if we can calculate TBI using data collected in this test. Under this test configuration, a generic force–displacement curve, as shown in Fig. 2, is usually obtained. This curve differs from those in Fig. 1 mainly in the appearance of a brief non-linear part of the curve, OA, before linear segment AB. This non-linear portion is because of the initially very high local stress due to the line contact (very small contact area) between the tablet and the platens despite the small loading force. The high local stress exceeds the elastic limit of the specimen and induces local plastic deformation. At this stage, the elastic deformation of the entire tablet is negligible since the overall force is still low. However, the plastic deformation increases contact area between the tablet and platens, which quickly lowers the stress at the contact to below the elastic limit. Beyond point A, the tablet undergoes mainly elastic deformation, which is shown as the linear portion, AB, in the curve. The part BC is due to the birth and propagation of cracks in the tablet until sufficient elastic energy is built up to eventually split the tablet.

In this work, we have considered as many brittleness indices as we can find in a literature search. In the strain based approach, 4 possible brittleness indices (B_1 to B_4) can be defined from data shown in Fig. 2 (Appendix 1). Here, B_1 is the same form as the index defined by Sönnergaard [23]. The adoption of Yagiz's brittleness index [8], F_{max}/displacement, generates four more possible brittleness indices, denoted by B_5 to B_8.

In the energy based approach, compression force was applied diametrically without breaking the tablet so that both the loading (OABC) and the unloading (CD) curves can be obtained (Fig. 3). From the force–displacement curves shown in Fig. 3, one can

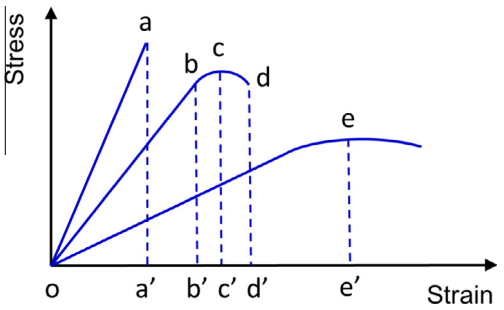

Fig. 1. Stress–strain curve of materials using specimens with uniform width. (**oa**: brittle material; **obcd**: brittle-ductile material; **oe**: ductile material).