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The powder flow and compact mechanical properties of sucrose and three high-intensity sweeteners used in chewable tablets

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Abstract

The physical, flow, and mechanical properties of four common pharmaceutical sweeteners were measured to assess their relative manufacturability in solid dosage formulations. Sucrose, acesulfame potassium (Sunett®), saccharin sodium, and aspartame were evaluated to determine significant differences in particle shape, size distribution, and true density. Powder flow and cohesivity as well as compact mechanical properties such as ductility, elasticity, and tensile strength were measured and found to be noticeably different. Among these sweeteners, sucrose and acesulfame potassium demonstrated excellent flowability and marginal mechanical property performance relative to over 100 commonly used pharmaceutical excipients evaluated in the authors' laboratory. Saccharin sodium and aspartame demonstrated poor flowability and superior compact strength relative to sucrose and acesulfame, despite their noticeably higher brittleness. These data suggest that careful selection of an appropriate sweetener is warranted in obtaining desirable process and tableting robustness, particularly if sweetener loading is high. Detailed descriptions of each material property and recommendations for sweetener selection in formulation development are included.

Keywords: Pharmaceutical sweeteners; Tableting indices; Flow; Mechanical; Tensile strength; Indentation hardness

1. Introduction

Successful tablet formulation development involves the careful selection of ingredients in order to manufacture a robust solid dosage form. Choosing the appropriate excipient to perform a specific function in a tablet formulation, such as disintegration or lubrication, can be critical to achieving acceptable manufacturing performance. Sweeteners, both naturally occurring and synthetic, are one type of functional excipient commonly used in chewable tablet formulations to mask unpleasant tastes and facilitate pediatric dosing. Several types and grades of powdered sweeteners are available for use in the pharmaceutical industry (Kibbe, 2000a; O'brien Nabors and Gelardi, 1986). However, the rational selection of a sweetener can be challenging since one must consider drug–excipient compatability, patient acceptability, and manufacturability.

Current literature contains data such as chemical and physical stability on powdered sweeteners (Askar, 1988; O'brien Nabors and Gelardi, 1986). However, limited data are available on the relative manufacturability of these materials. Therefore, it is difficult to logically select the appropriate sweetener to use in a tablet

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formulation. Recently, quantitative methods have been developed that attempt to identify key mechanical and flow properties that are important to manufacturing a robust tablet form (Alderborn and Nystrom, 1996). Specifically, the research of Hiestand offers a systematic approach to identifying attributes and deficiencies of a material, but very little of this type of data have been published to date in the scientific literature (Hiestand, 1989; Hiestand, 2002; Kibbe, 2000a).

Hiestand noted that successful tableting operations require the selection of excipients that balance desirable physical, flow, and mechanical properties for tablet manufacturing (Hiestand, 1989; Hiestand, 2002). The quantification of these properties using a unified approach is essential to the design and optimization of solid dosage formulations (Kibbe, 2000b). This manuscript describes the physical, flow, and mechanical properties of four sweetening materials—sucrose, acesulfame potassium, saccharin sodium, and aspartame—and uses these data to evaluate their suitability for use in solid dosage formulations.

2. Materials and methods

2.1. Materials

Sucrose (extra fine granular), acesulfame potassium (Sunett®), aspartame, and saccharin sodium were selected as common sweetening agents and were evaluated as received from their vendors (Table 1). These materials were typical of lots previously received from these vendors and were selected because they had a diverse range of physical properties such as true density, particle size, particle shape, and sweetening intensity. Sucrose typically comprises 2–20% of dry granulated formulations and 50–67% of wet granulated formulations. Acesulfame potassium, saccharin sodium, and aspartame are considered to be high-intensity sweeteners and can be used in much lower proportions (<5%) to achieve the same degree of sweetening intensity (Kibbe, 2000a). In some instances, such as the manufacture of fast dissolving tablets, these materials may be incorporated at significantly higher levels (Lefevre and Dupas, 2003). The samples were stored at environmentally controlled laboratory conditions of $20 \pm 2\,^{\circ}C$ and $40 \pm 10\%$ relative humidity.

2.2. Powder characterization methods

Photomicrographs of each material were taken with a Jeol JSM-5800 scanning electron microscope (Jeol USA Inc., Peabody, MA). The photographs were taken at a working distance of 10 mm with an accelerating voltage of 5–10 kV.

The true densities of the samples were determined with a helium pycnometer (Quantachrome Inc., Boynton Beach, FL) operated at $20 \pm 2\,^{\circ}C$ according to the instrument manufacturer's recommended methods. Calibration was performed using standard stainless steel spheres, and the mean value of triplicate determinations is reported.

The particle size distribution of each powder was determined using a Sympatec Helos/Rodos laser diffraction particle size analyzer (Sympatec Inc., Princeton, NJ) with dry powder dispersion capability. The powder dispersion pressure was varied between 0.5 and 2.0 bar (depending on the tendency for agglomeration) with direct feed into the dispersion funnel. The optical concentration was maintained in the range of 5–20%. The mean value of duplicate determinations is reported.

Bulk and terminal tapped densities were determined using a VanKel tapping device fitted with a 100 ml glass measuring cylinder (VanKel, Cary, NC). The bulk and tapped solid fraction (2000 taps) was calcu-

Table 1
Description of sweetener materials

Material	Supplier	Sweetening intensity (relative to sucrose)[a]	Particle shape
Sucrose (extra fine granular)	North American Sugars, Inc., Brooklyn, NY	1	Equant square
Acesulfame potassium (*Sunett*)	Nutrinova, Inc., Somerset, NJ	200	Equant round
Aspartame	Spectrum Quality Products, Gardena, CA	180–200	Needles
Saccharin sodium	Spectrum Quality Products, Gardena, CA	300	Equant square

[a] Kibbe, 2000a.

lated by dividing the bulk or tapped density by its corresponding true density. The Carr index was calculated as the relative change in apparent density (tapped minus bulk) divided by the tapped density (Carr, 1970).

Powder flow was assessed using a custom-built plate-type shear cell that has previously been described (Hiestand and Wilcox, 1968). A two-point determination of the effective angle of internal friction (EAIF) was performed at $20 \pm 2\,^{\circ}C$ and 50% RH using normal stresses of 75.6 and 104.9 g/cm^2. The mean of two replicates is reported.

Powder cohesivity was determined under ambient conditions (20–25 °C; 30–50% RH) using a commercial powder avalanche tester (Aeroflow from TSI Instruments, Amherst, MA). A 50 ml bulk powder sample was rotated in a 5-in. diameter hollow plastic disk at a speed of 0.41 revolutions per minute for 20 min and the resulting avalanche events were monitored using a sensitive photocell. The mean time to avalanche (MTA) was determined from the measured frequency distribution of avalanches using methods previously published (Kaye et al., 1995). Powders that demonstrated a higher MTA were considered to be more cohesive in the dilated state. All determinations were made in duplicate and the mean values are reported.

2.3. Mechanical property testing of compacted samples

Samples for mechanical testing were ∼5 g rectangular compacts measuring 1.9 cm × 1.9 cm × 1.0 cm. They were formed by uni-axial compression (∼1 mm/s compression speed) using a custom-built hydraulic press that permitted gradual tri-axial decompression of the samples (Hiestand and Smith, 1984). Dwell time for the compression was 1.5 min and tri-axial decompression time was 2 min. The punch and die surfaces were sparingly lubricated with magnesium stearate suspended in methanol (∼5%). Each sweetener powder was compressed to the same porosity (15%) in order to directly compare the mechanical properties of the compacts. This laboratory has successfully prepared over 1000 excipients, drugs, and formulations at 15% porosity, and this condition has proven to be ideally suited for the type of indentation hardness and tensile strength tests described in this work. This porosity is also typical of commercial tablets measured in this laboratory.

Indentation hardness determinations were performed in ‘dynamic’ mode (∼1500 mm/s impact speed) using a pendulum impact device and in ‘quasi-static’ mode (∼0.008 mm/s impact speed) with a custom-built indentation tester (Hiestand and Smith, 1984). The spherical indentors were of 2.54 cm diameter and 65.6 g mass, and the pendulum length was 92.3 cm with a release angle of 30°. Quasi-static indentation forces were selected to produce indentations of a similar size to the dynamic indentation test (1.5–2.0 mm radius). The compact indentations were measured using a white light interferometer (Zygo Corporation, Middlefield, CT) and the dent depth, dent diameter, apparent radius of curvature and pendulum initial and rebound heights were used to calculate the indentation hardness and elastic modulus of the compacts (Hiestand and Smith, 1984).

The tensile strength of the compacted samples was determined by transverse compression with a custom-built tensile tester (Hiestand and Smith, 1984). Tensile failure was observed for all the rectangular compacts when compressed between flat-faced platens at a speed ranging between 0.006 and 0.016 mm/s. Specially modified punch and die sets permitted the formation of square compacts with a centrally located hole (0.11 cm diameter) that acted as a stress concentrator during tensile testing. This capability permitted the determination of a ‘compromised’ compact tensile strength and thus facilitated an assessment of the defect sensitivity of each compacted material. At least two replicate determinations were performed for each mechanical testing procedure and mean values are reported.

3. Results and discussion

3.1. Powder physical properties

Scanning electron micrographs (SEMs) showed that the sweeteners have distinct particle morphologies and sizes (Fig. 1). Acesulfame potassium and sucrose particles were relatively large and equant shaped while saccharin sodium and aspartame particles were much smaller and plate and needle-shaped, respectively. The laser diffraction particle size distribution statistics (Table 2) were largely supportive of the particle sizes from the SEMs. The laser diffraction technique

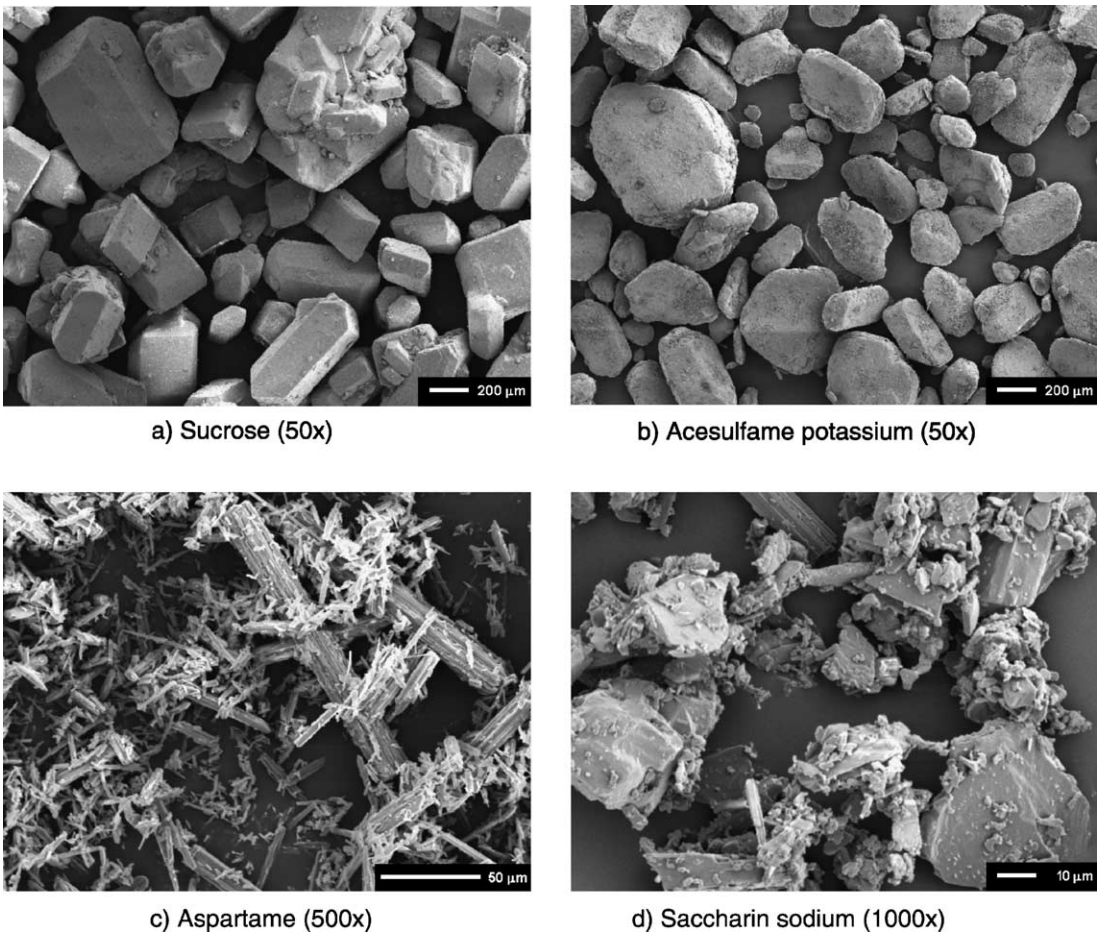

Fig. 1. Scanning electron micrographs of sweeteners samples.

assumed a spherical morphology and, therefore, the particle size data for aspartame (needle-like particles) were considered cautiously. In general, smaller particle size materials, like aspartame and saccharin, have a larger true contact area between particles that can contribute to an increase in the friction coefficient or decrease the flowability of the material (Hiestand and Wilcox, 1968).

The true densities of pharmaceutical materials generally range from 1.0 to 3.0 g/cm^3, and are typically ~1.5 g/cm^3 in the authors' laboratory. The true densities of the sweeteners tested were between 1.35 and

Table 2
Mean particle size distribution statistics for sweetener samples

Material	Mean volume diameter (μm)	10th % size (μm)	50th % size (μm)	90th % size (μm)
Sucrose	632	424	629	851
Acesulfame potassium	338	61	294	683
Aspartame	12	1	6	26
Saccharin sodium	20	2	11	49

Table 3
Mean densities and solid fractions of sweetener samples

Material	True density (g/cm^3)	Bulk density (g/cm^3)[a]	Tapped density (g/cm^3)[b]	Bulk solid fraction[a]	Tapped solid fraction[b]
Sucrose	1.58	0.83	0.95	0.53	0.60
Acesulfame potassium	1.83	1.04	1.28	0.57	0.70
Aspartame	1.35	0.17	0.29	0.12	0.22
Saccharin sodium	1.69	0.37	0.68	0.22	0.40

[a] Bulk conditions were measured on the untapped powder.
[b] Tapped conditions were measured after 2000 taps.

$1.83\,g/cm^3$ as shown in Table 3. Calculations have shown that the attractive forces between the particles are orders of magnitude greater than the gravitational force, which suggests that these small differences in density are not likely to incite significant segregation in typical blends (Hiestand, 2002).

Powder densification behavior was determined by performing bulk and tapped density measurements. The bulk and tapped solid fractions are also reported (Table 3). Although there was no change in ranking by converting from density to solid fraction, (acesulfame > sucrose ≫ saccharin > aspartame), the tapped solid fraction profile in Fig. 2 shows a more significant difference between the sucrose/acesulfame and saccharin/aspartame powders than in Fig. 3. The directly comparable solid fraction measurements show that the larger more equant shaped particles (sucrose and acesulfame) can be tapped to a much higher solid fraction than the smaller more irregularly shaped particles (saccharin and aspartame). Therefore, if used in the same proportions, one would generally select the sucrose or acesulfame to maintain a lower specific volume formulation and promote efficient material storage and tablet press die filling.

3.2. Powder flow properties

The Carr index, EAIF, and MTA of the powder were used to evaluate the overall flow properties of each material. Each test subjected the powder samples to a different type of flow condition. The Carr index was measured under low frequency vibration, the angle of internal friction was measured under compressive shear flow, and MTA was measured under dilated flow.

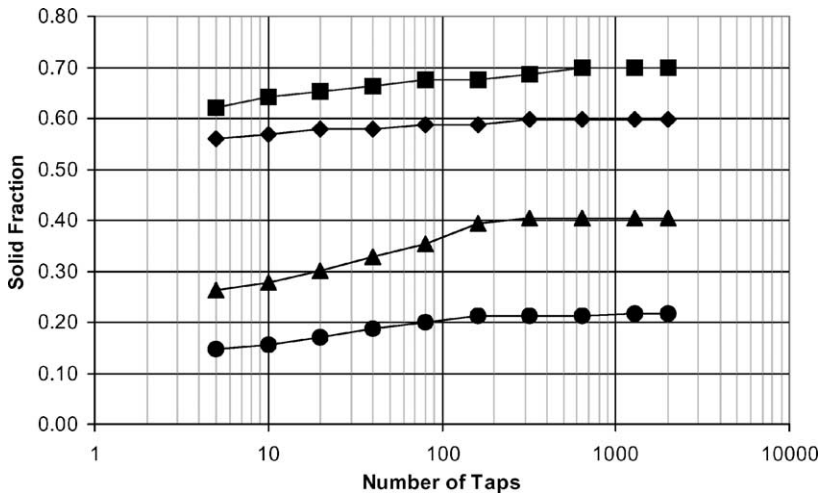

Fig. 2. Tapping profiles for sweetener samples (solid fraction). Saccharin sodium (▲); acesulfame potassium (■); aspartame (●); sucrose (◆).

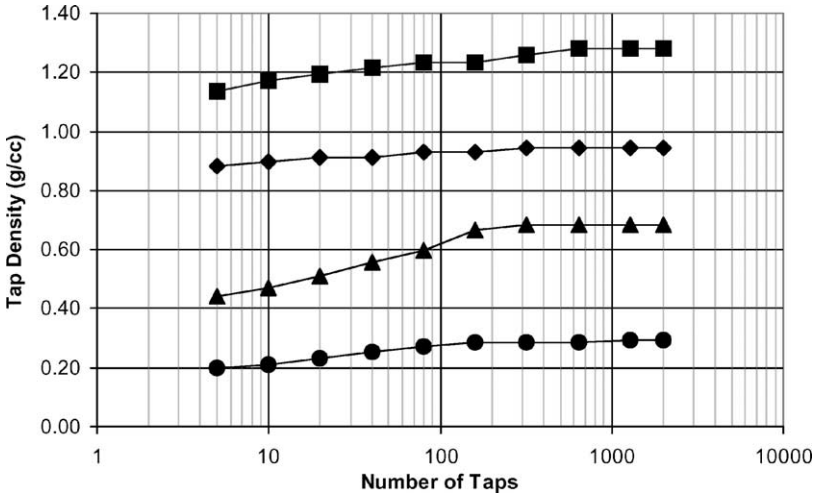

Fig. 3. Tapping profiles for sweetener samples (tap density). Saccharin sodium (▲); acesulfame potassium (■); aspartame (●); sucrose (◆).

In some cases, all of these tests are required to properly evaluate the overall flow properties of a powder. For reference purposes, the 10th and 90th percentiles and mean values of the flow parameters collected in the authors' laboratory for over 100 excipients are reported in Table 4 (previously unpublished data).

In general, a lower Carr index, EAIF, and MTA are desirable for acceptable powder flow. The data in Table 4 suggests that aspartame and saccharin had poor flow characteristics because they rank in the top 2% (EAIF) of poor flowing and top 40% (MTA) of highly cohesive powders. This result is consistent with the particle size analysis and photomicrograph data. Their elongated particle shape and small particle size could cause high tablet weight variation, unacceptable blend uniformity, and difficulty in filling containers and dies if these sweeteners were used in significant quantities (>10%) such that their properties would influence the performance of the formulation. Acesulfame and sucrose were considered to exhibit rather good flow characteristics because they ranked in the top 25% of good flowing and low cohesive powders based on EAIF and MTA data. Their relatively large particle sizes would contribute to good bulk powder handling in any proportion.

The physical and flow properties of powders can have a significant effect on product content uniformity. At low levels, the probability of achieving a uniform distribution of large particles, such as those of the acesulfame and sucrose, in a small tablet can reach unacceptable limits. Statistical models can be helpful for these types of determinations (Zhang and Johnson, 1997). Smaller particle size and poorer flowing sweeteners, such as saccharin and aspartame, may also be difficult to disperse uniformly if proper blending and material handling techniques are not employed.

Table 4
Flow parameters of sweetener samples (mean and standard deviation)

Material	Carr index (%)	Effective angle of internal friction (°)	Mean time to avalanche (s)
Sucrose XFG	12 ($n = 1$)	31.1 (0.1)	3.9 (<0.1)
Acesulfame potassium	19 ($n = 1$)	28.1 (0.1)	3.2 (<0.1)
Aspartame	44 ($n = 1$)	43.0 (0.0)	6.3 (0.5)
Saccharin sodium	45 ($n = 1$)	40.5 (0.5)	8.5 (<0.1)
Typical range[a]	NA	29–38	3–11
Mean[a]	NA	33	7

[a] Unpublished data generated in the authors' laboratory. The 10th to 90th percentile and mean of over 100 excipients evaluated. A higher value indicates poorer flowability.

Table 5
Mechanical properties of sweetener compacts (at a compact porosity of 15%) (mean and standard deviation)

Material	Dynamic indentation hardness (H_0; MPa)	Quasi-static indentation hardness (H_{10}; MPa)	Elastic modulus (E; GPa)	Tensile strength (TS; MPa)	Compromised tensile strength (TS_0; MPa)
Sucrose XFG	212 (14)	32 ($n = 1$)	5 ($n = 1$)	0.7 (<0.1)	0.6 (<0.1)
Acesulfame potassium	70 (2)	27 ($n = 1$)	4 ($n = 1$)	0.5 (<0.1)	0.4 (<0.1)
Aspartame	450 (73)	66 (1)	5 (1)	3.5 (0.1)	1.1 (0.0)
Saccharin sodium	182 (40)	34 (1)	3 (<1)	1.4 (0.1)	0.7 (<0.1)
Typical range[a]	53–461	12–81	1–8	0.5–6.2	0.4–4.8
Mean[a]	225	43	4	3.0	2.1

[a] Unpublished data generated in the authors' laboratory. The 10th to 90th percentile and mean of over 100 excipients evaluated.

3.3. Compact mechanical properties

Compacts of each sweetener were evaluated for dynamic indentation hardness, quasi-static indentation hardness, elastic modulus, tensile strength, and compromised tensile strength. These mechanical property data are summarized in Table 5. The 10th and 90th percentiles and mean values of excipient mechanical properties as collected in the authors' laboratory are also presented.

The dynamic indentation hardness (H_0) is defined as the pressure (force/area) required to plastically deform a compact during a very fast compression operation using a pendulum impact device (Hiestand, 2002). The subscript on the indentation hardness symbol, e.g. H_t, indicates the approximate dwell time (t) of the indenter in minutes. Table 5 summarizes the compact H_0 values for each sweetener. Intuitively, this measurement is inversely proportional to ductility. The acesulfame compacts demonstrated a relatively low H_0, while the aspartame compacts demonstrated a relatively high H_0. This indicates that acesulfame compacts (which were in the lower 20% of the excipient population) deformed rather easily, suggesting that interparticulate bonding surfaces formed relatively easy. Acesulfame presumably could have a tendency to demonstrate high die wall friction or extrude past the punch tip and cause crowning due to its high ductility. In contrast, aspartame compacts were relatively hard (in the upper 20% of the excipient population), suggesting that bonding surfaces did not form easily which could contribute to lower tablet crushing strength. One would typically prefer to select materials with moderate H_0, say within the interquartile range ($H_0 \approx 100$–250 MPa), such as sucrose and saccharin, whose particles deform well under rapid compression to form bonding surfaces without the likelihood of causing excessive die wall friction. This range was empirically established in the authors' laboratory for materials that demonstrate acceptable performance during tablet manufacturing.

In general, the quasi-static indentation hardness (H_{10}) of a compact was approximately 20% of the H_0 under these test conditions as shown in Table 5. This measurement is defined as the pressure required to plastically deform a compact during extremely slow indentation. The large difference between H_0 and H_{10} of each material was due to significant difference in dwell time (0 min versus 10 min) and a 10^6 order of magnitude difference between indentation strain rates. The two indentation hardness measurements for each material followed a similar trend, aspartame > saccharin $\cong$ sucrose > acesulfame. The relationship between the results of the two indentation hardness measurements will be discussed later. Except for aspartame, each H_{10} value was in the interquartile range (27–56 MPa). The high H_{10} value for aspartame reaffirms the H_0 data that indicated that the aspartame compacts are very hard and its particles do not form bonding surfaces as well as the other sweeteners. Only one quasi-static indentation hardness data point was achievable with the sucrose and acesulfame samples because successful replicates could not be produced without cracking the surface of the compact. This phenomenon is not uncommon with materials that have relatively low tensile strength (see later) and suggests that these materials do not promote good tablet strength.

The elastic moduli of the sweeteners were determined by measurement of the dent recovery during quasi-static indentation hardness testing. The values observed for each sweetener were within the interquartile range relative to other excipient materials tested in

this laboratory and, therefore, these materials are considered to demonstrate moderate elasticity. The moderate elasticity values measured suggest that the elastic properties of the compact are not sufficient to rupture the particle–particle bonds and incite compact fracture (Hiestand, 1997).

The experimental results showed that most of the tensile strengths of the sweetener compacts were notably different (aspartame $\gg$ saccharin $>$ sucrose $\cong$ acesulfame). Since tensile strength is proportional to the tablet crushing strength, this has a significant effect on measurable tablet property performance. The aspartame compacts were approximately 5 times stronger than the sucrose compacts, 7 times stronger than the acesulfame compacts, and 2.5 times stronger than the saccharin compacts. Therefore, one would generally select aspartame (top 50%) as a superior material to improve tablet crushing strength. In contrast, acesulfame and sucrose (lower 15%) could be detrimental to robust tablet formulation in significant quantities. This phenomenon was most likely due to their relatively large particle size and perhaps their low interparticulate bonding strength. A smaller particle size of these materials would increase particle-to-particle interactions and improve their tensile strength. Saccharin ranked in the lower 30% of the excipient population suggesting its interparticulate bonds may not markedly increase or decrease overall tablet tensile strength.

The measurement of the compromised tensile strength is also of interest because it demonstrates a compact's ability to accommodate imperfections, i.e. cracks. The ranking of compromised tensile strength followed the same trend as the regular tensile strength measurements, aspartame $>$ saccharin $>$ sucrose $>$ acesulfame. However, it is the relationship between these measurements that can provide valuable information on the brittleness of the material. This will be discussed in the following section.

3.4. Indices of tableting performance

Hiestand (2002) suggested that the tensile strength, ductility, and elasticity of the formulation components each contribute to tablet manufacturing performance. Ratios of some of these mechanical properties, more commonly known as the tableting indices, were used in this work to characterize each material's tableting potential by describing the multi-mechanistic nature of tablet formation (Hiestand and Smith, 1984). It has been the authors' experience that the brittle fracture index (BFI), the best-case bonding index (BI_b), the worst-case bonding index (BI_w), and the viscoelastic index (VI) are rather helpful in differentiating among the tableting potentials of various pharmaceutical solid dosage materials. The indices for the compacted sweetener powders are summarized in Table 6 and will be referred to throughout this section.

The BFI describes a compact's ability to relieve shear stresses by localized shear flow and has been related to capping and lamination tendencies (Eq. (1)).

$$\mathrm{BFI} = \frac{1}{2}\left(\frac{\mathrm{TS}}{\mathrm{TS}_0} - 1\right) \tag{1}$$

It was determined by measuring the tensile strength of a "perfect" compact (TS) and a compact with a controlled defect or hole (TS_0). This concept is based on Griffith crack theory, which suggests that a completely brittle compact will have a BFI equal to unity (i.e. $TS_0 = TS/3$) and will be extremely sensitive to flaws. Typically good tableting materials, such as microcrystalline cellulose or spray dried lactose, demonstrate a BFI under 0.30 and thus are desirable for robust formulation ingredient selection (Hiestand et al., 1977).

The data in Table 6 suggests that levels of saccharin and aspartame should be kept low in tablet formulations because they are brittle materials (BFI $\gg$ 0.30). This should be possible for these high-intensity sweeteners because they are typically used at low levels. Aspartame actually had a BFI greater than unity, which could be attributed to the precision of the tensile strength measurements that are used in the BFI calculation or due to slight flaws in the regular tensile strength compacts. This is not uncommon with extremely brittle materials. In contrast, the low brittleness of acesulfame and sucrose should decrease the likelihood of capping and lamination in a formulation that contains other highly brittle materials, e.g. most active pharmaceutical ingredients.

The indentation hardness and tensile strength values can be used to describe the interparticulate bonding in a compact by way of two "bonding indices" (BI) as shown in Eqs. (2) and (3) (Hiestand and Smith, 1991). The bonding ability of a material is considered to improve as tensile strength (TS) increases and the indentation hardness (H) decreases. The subscript on

Table 6
Tableting indices for sweetener compacts (at a compact porosity of 15%)

Material	Brittle fracture index	Bonding index (worst case) $\times 10^2$	Bonding index (best case) $\times 10^2$	Viscoelastic index
Sucrose XFG	0.12	0.3	2.3	6.7
Acesulfame potassium	0.08	0.7	1.8	2.6
Aspartame	1.05	0.8	5.3	6.8
Saccharin sodium	0.56	0.8	4.2	5.4
Typical range[a]	0.05–0.68	0.3–3.2	1.4–14.6	3–11
Mean[a]	0.27	1.8	7.8	6

[a] Unpublished data generated in the authors' laboratory. The 10th to 90th percentile and mean of over 100 excipients evaluated. Low brittle fracture index and viscoelastic index are desired. High bonding indices are desired.

the indentation hardness represents the approximate dwell time (minutes) of the indenter.

$$BI_w = \frac{TS}{H_0} \quad (2)$$

$$BI_b = \frac{TS}{H_{10}} \quad (3)$$

The BI_w is considered to be more predictive of high-speed tableting performance than the BI_b. This assumption is based upon using an indentation rate in the bonding equation, which is indicative of real tablet compression speeds (H_0: 1558 mm/s versus H_{10}: 0.008 mm/s). Perhaps the BI_b is more intuitively related to compact formation during slow speed compressions such as roller compaction. Although the bonding ability of each sweetener was below average, the bonding in sucrose was considerably worse than the other materials (BI_w: aspartame $\cong$ sodium saccharin $\cong$ acesulfame $>$ sucrose). In general, these materials lie in the lower 50% of excipient bonding ability and would not profoundly contribute to improved tablet strength and robustness at high loadings.

It has been suggested that the relationship between the dynamic indention hardness and the quasi-static indentation hardness can be used to characterize the viscoelasticity of a material, commonly known as the VI as in Eq. (4) (Hiestand and Smith, 1984):

$$VI = \frac{H_0}{H_{10}} \quad (4)$$

The degree of viscoelasticity in a compact indicates a powder's ability to undergo stress relaxation during compression (Hiestand, 1997). In theory, extremely high viscoelasticity is undesirable because it indicates that tablet performance would be very sensitive to the speed of the tablet press. Extremely low viscoelasticity is also undesirable because it indicates that tablet strength is not enhanced by viscoelastic properties. As of yet, no one has correlated this index directly to tableting speed sensitivity. One plausible explanation for this is that varying tablet production rates only change punch tip velocity by approximately one order of magnitude, rather than six. These materials showed viscoelasticity within the 20th to 80th percentiles suggesting that they demonstrated no unusual viscoelastic properties.

3.5. General techniques for sweetener selection

The selection of an appropriate sweetener for a new tablet formulation is clearly dependent on tablet size, component loading, desired sweetening intensity, processing pathway, as well as the powder flow and compact mechanical properties, but general recommendations can be developed based on the reported data.

- The *sucrose* sample was relatively large in particle size, demonstrated good powder flowability and its compacts exhibited low brittleness despite their low compact strength. The large particle size of this sucrose grade may exacerbate a potential for content uniformity problems if blended with smaller particle size drug substances. Hypothetically, this low intensity sweetener could be useful in situations where a highly brittle drug substance required moderate quantities of a sweetening diluent to reduce the likelihood of capping and lamination during tablet production.
- The *acesulfame* particles were about half the size of the sucrose particles and its compacts were much

more ductile, however, in general, the two materials demonstrated similar flow and mechanical properties. This sweetener could be used to replace sucrose in a tablet formulation in much smaller quantities and still achieve the same degree of sweetening intensity and desirable manufacturing properties.

- The particles of the *aspartame* sample were small and needle-shaped, which contributed to poor powder flowability and high cohesivity. Its high compact strength is considered a mechanical property attribute, while its high brittleness is a deficiency. One would choose this particular material in situations where a high-intensity sweetener was required to promote good compact strength even in low proportions. This sweetener would not be useful in high quantities because it may adversely affect blend or tablet homogeneity and contribute to lamination during roll and tablet pressing.
- The *saccharin* sample can be considered a marginally performing high-intensity sweetener. Overall, its poor powder flowability and high compact brittleness dominate over its moderate compact ductility and strength. As a high-intensity sweetener, the saccharin may be valuable in small quantities to not significantly impact the mechanical or flow property performance of a solid dosage tablet formulation.

4. Conclusion

The physical, flow, and mechanical property evaluation of the four sweetener samples suggest that each material exhibits characteristic attributes and deficiencies that will affect their selection in solid dosage formulation development. The varied physical properties of each of material had a significant effect on their respective mechanical and flow properties. In general, the acesulfame and sucrose may be attractive sweeteners to use to enhance flowability of a blend and reduce the lamination tendency of a tablet. However, their relatively low compact strengths will most likely have a negative effect on tablet robustness, e.g. tablet crushing strength. The saccharin may not improve tablet strength, and will be detrimental to powder flow and tablet brittleness. The aspartame may help to improve tablet strength, but its extremely poor flowability and high brittleness make it undesirable in high proportions. Consideration of the properties of each ingredient in the formulation and the available processing methods will be key factors in selecting the appropriate sweetener from these materials.

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