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Dependence of tablet brittleness on tensile strength and porosity

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ABSTRACT

An analysis of data collected from 25 sets of diverse pharmaceutical powders has identified that an exponential growth function satisfactorily describes the relationship between tablet brittleness and tablet porosity while a power law function well describes the relationship between tablet brittleness and tensile strength. These equations have the potential to facilitate better characterization of tablet mechanical properties and to guide the design and optimization of pharmaceutical tablet products.

1. Introduction

Brittleness is an important material property that should be considered in order to design high quality tablet products. Tablets with high brittleness are usually preferred for chewable tablets. However, brittle tablets also tend to be more friable and easily chipped. Since highly friable tablets cannot survive common handling, such as coating and shipping, they usually require protective packages, e.g., blister packages, for marketing. In either case, maintaining a balance between brittleness and other mechanical properties suitable for the intended performance is of significance in the development of tablet products. Owing to its importance in tablet formulation design and manufacture, several brittle indices have been proposed to quantify brittleness of pharmaceutical solids. These include brittle fracture index (BFI) (Hiestand et al., 1977; Hiestand and Smith, 1984), brittle/ductile index (BDI) (Sönnergaard, 2013), and tablet brittleness index (TBI) (Gong and Sun, 2015). BFI and BDI were proposed to quantify material brittleness. However, using TBI, have shown that tablet brittleness is a tablet property that is affected by not only material property but also tablet structure, such as porosity (Gong and Sun, 2015). TBI is calculated using Eq. (1) using data routinely available during tablet diametral breaking tests. Therefore, TBI is a more reliable and convenient way for quantifying tablet brittleness, where a higher TBI value corresponds to a more brittle tablet.

$$\mathrm{TBI} = \frac{1}{\text{Elastic strain at fracture}} = \frac{\text{Tablet diameter}}{\text{Maximum elastic deformation length}} \quad (1)$$

Without the prior knowledge of the brittleness of excipients and the active pharmaceutical ingredient, the design of a formulation exhibiting a balanced brittleness and ductility cannot be efficiently done. As a general guide, threshold value of 150 for TBI was recommended for meeting the <1% friability criterion for commercial tablets (Gong and Sun, 2015).

Because of the dependence of tablet brittleness on porosity, TBI at a single porosity value does not provide a complete assessment on the brittleness. Instead, a function between TBI and porosity should be sought for comprehensive characterization of a given material. The TBI extrapolated to zero porosity can likely be used to quantify brittleness of the material in absence of pores. For the extrapolation approach to work, a reliable mathematical function that describes the relationship between TBI and tablet porosity valid for a variety of pharmaceutical powders is necessary.

In addition, it has been commonly observed that a stronger tablet tends to be less brittle for the same powder. A quantitative understanding on the relationship between tablet tensile strength and brittleness is, therefore, useful to the development of tablet products with appropriately balanced mechanical properties. In

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particular, a mathematical function that reasonably describes such a relationship will be valuable. A general understanding of the relationships of TBI—tablet porosity and TBI—tensile strength is expected to play an important role in guiding efficient design of high quality tablet formulations. However, such equations are not yet available. The objective of this work was to fill this knowledge gap by identifying equations that can be used to describe the dependence of TBI on tablet tensile strength and porosity.

2. Materials and methods

2.1. Materials

In order to gain confidence on the general applicability of equations that may be identified, we have compiled literature data of as many powders as we can. Additional powders were studied to expand the diversity of powders. Microcrystalline cellulose (MCC, Avicel PH101, Lot: P108819435) was received from FMC Biopolymer (Philadelphia, PA). Anhydrous theophylline (Lot: 45,701AX10) was received from BASF Chemical Co. (Geismar, Germany). Amlodipine, glyburide, and sildenafil citrate were gifts from Pfizer Inc. Magnesium stearate (MgSt) was received from Mallinckrodt (St Louis, Missouri).

2.2. Methods

Tablet diametral testing data were collected either in our previous studies or in this work. Experimental details of literature data can be found in corresponding references given in Table 1.

For data collected in this work, cylindrical tablets were compressed under different pressures on either a universal material testing machine (Model 1485, Zwick, Germany) using flat-faced 8 mm round tooling or a compaction simulator (Presster, Metropolitan Computing Company, East Hanover, NJ) using flat-faced 9.5 mm round tooling. A total of 12–24 tablets for each powder were prepared and relaxed overnight before further characterization.

For the determination of tensile strength and TBI, tablets were fractured diametrically using a Texture Analyzer (TA-XT2i, Texture Technologies Corp., NY, USA). Maximum breaking force, tablet diameter, and tablet thickness were used to calculate tensile strength, σ (MPa), according to Eq. (2).

Table 1
Fitting results using Eqs. (3) and (5).

No.	Materials	True density (g/cm^3) Mean(SE)	Eq. (3)			Eq. (5)			# of data points
			A_0 Mean(SE)	A_1 Mean(SE)	R^2	C_0 Mean(SE)	C_1 Mean(SE)	R^2	
1	Ibuprofen formulation	1.12[a]	30.15(1.36)	8.57(0.29)	0.977	40.82(1.63)	−0.62(0.02)	0.971	20
2	Ibuprofen formulation with 0.1% silica	1.14[a]	18.41(0.94)	9.40(0.23)	0.991	38.99(0.79)	−0.67(0.01)	0.997	19
3	Ibuprofen formulation with 0.5% silica	1.14[a]	18.86(0.95)	7.67(0.27)	0.970	37.71(0.70)	−0.65(0.01)	0.989	22
4	Avicel PH102 with 0.1% silica	1.46[b]	8.01(0.11)	4.04(0.04)	0.997	33.06(0.41)	−0.54(0.01)	0.989	27
5	Avicel PH102 with 0.5% silica	1.46[b]	7.85(0.17)	4.20(0.07)	0.990	34.34(0.52)	−0.57(0.01)	0.984	27
6	Avicel PH102 with 1% silica	1.46[b]	7.75(0.24)	5.60(0.08)	0.996	41.65(0.58)	−0.62(0.01)	0.992	27
7	Avicel PH102 with 2% silica	1.46[b]	7.92(0.28)	6.47(0.09)	0.993	43.34(0.72)	−0.63(0.01)	0.990	30
8	97% MCC + 2.5% PVP + 0.5% MgSt (granulated with 35% water)	1.44[c]	87.87(1.91)	1.83(0.09)	0.919	121.05(1.57)	−0.20(0.01)	0.911	31
9	97% MCC + 2.5% PVP + 0.5% MgSt	1.44[c]	26.88(0.47)	1.97(0.09)	0.909	58.02(1.45)	−0.33(0.01)	0.915	39
10	19% MCC + 78% LM + 2.5% PVP + 0.5%MgSt	1.49 (0.01)[d]	85.11(2.42)	3.20(0.13)	0.948	150.71(2.02)	−0.24(0.01)	0.948	29
11	Danshen root extract (59.9%), Notoginseng (37.9%) + Borneol (2.2%)	1.47 (0.05)[e]	84.13(3.93)	1.85(0.21)	0.918	112.01(3.21)	−0.15(0.02)	0.891	8
12	Danshen root extract (59.9%), Notoginseng (37.9%), Borneol (2.2%), and 1% silica	1.44 (0.02)[e]	68.91(3.03)	2.23(0.21)	0.944	99.57(2.30)	−0.19(0.02)	0.945	8
13	Panax notoginseng (66.7%) + MCC (33.3%)	1.33 (0.01)[e]	75.77(1.06)	1.75(0.14)	0.960	89.59(0.72)	−0.14(0.01)	0.988	8
14	Powder #13 + 1% silica	1.35 (0.02)[e]	62.58(0.77)	1.92(0.13)	0.969	82.47(0.95)	−0.16(0.01)	0.979	8
15	Danshen (66.7%) + MCC (33.3%) + 1% silica	1.45 (0.02)[e]	40.02(2.28)	2.92(0.24)	0.958	75.46(2.49)	−0.26(0.02)	0.947	8
16	MCC + 0.5% MgSt	1.45[f]	37.14(2.08)	1.92(0.19)	0.929	73.31(1.01)	−0.22(0.02)	0.963	8
17	LM + 0.5% MgSt	1.55[f]	92.49(9.59)	6.05(0.69)	0.939	180.02(3.72)	−0.31(0.02)	0.972	7
18	(75% MCC + 25% LM) + 0.5% MgSt	1.47[f]	43.43(2.37)	2.14(0.16)	0.969	81.29(0.61)	−0.21(0.01)	0.985	8
19	FCOXA21 formulation	1.72[g]	122.56(4.51)	2.59(0.23)	0.954	171.35(1.89)	−0.14(0.01)	0.967	8
20	Anhydrate theophylline	1.42[h]	78.18(1.46)	2.65(0.21)	0.950	123.21(2.93)	−0.23(0.02)	0.930	8
21	Avicel PH101	1.40 (0.03)[i]	31.31(0.50)	2.46(0.05)	0.997	79.46(1.23)	−0.35(0.01)	0.993	8
22	10% amlodipine + 90% MCC	1.43 (0.01)[i]	46.01(1.80)	2.01(0.15)	0.936	82.04(1.78)	−0.26(0.02)	0.934	16
23	10% glyburide + 90% MCC	1.45 (0.02)[i]	48.45(1.54)	1.81(0.11)	0.950	83.37(1.73)	−0.23(0.02)	0.930	15
24	Avicel PH102	1.45 (0.01)[i]	41.96(1.19)	1.44(0.09)	0.957	72.64(1.16)	−0.22(0.01)	0.965	12
25	10% sildenafil citrate + 90% MCC	1.42 (0.01)[i]	44.68(1.89)	1.98(0.14)	0.954	82.12(1.78)	−0.25(0.02)	0.949	12

[a] Ref. (Zhou et al., 2013).
[b] Ref. (Zhou et al., 2012).
[c] Ref. (Osei-Yeboah et al., 2014a).
[d] Ref. (Osei-Yeboah et al., 2014b).
[e] Ref. (Yuan et al., 2013).
[f] Ref. (Gong and Sun, 2015).
[g] Ref. (Perumalla and Sun, 2014).
[h] Ref. (Sun, 2004).
[i] This work.