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A Powder Tabletability Equation

Gerrit Vreeman, and Changquan Calvin Sun*

Department of Pharmaceutics, University of Minnesota

CONTACT INFORMATION: vreem012@umn.edu, sunx0053@umn.edu*

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PURPOSE

- Tabletability is the relationship between tablet tensile strength (σ) and compaction pressure (P).
- σ is a function of interparticulate bonding area (BA) and bonding strength (BS), which are deconvoluted via compressibility (porosity (ε) vs P) and compactibility (σ vs ε).
- The existence of the relationship between σ vs ε and ε vs P indicates a relationship between σ and P.
- Such a relationship would describe both the BA and BS of a powder in a single plot.

OBJECTIVES

Derive a function describing σ versus P from the well-known $\sigma-\varepsilon$ and $\varepsilon-P$ relationships.

Evaluate the effectiveness of such a equation in describing the tabletability of a range of materials

METHODS

Materials

Microcrystalline cellulose PH102 (MCC), dicalcium phosphate dihydrate (DCPD), dicalcium phosphate anhydrous (DCPA), mannitol 200SD (Mann), lactose monohydrate (LM), urea, and ferulic acid (FA) were used as received.

Methods

Tablets were prepared using a compaction simulator (Styl'One Evolution, MedelPharm, Beynost, France) using round, flat faced tooling with a diameter of 11.28 mm on a single compression cycle. Mixtures of MCC with DCPA and MCC with magnesium stearate (MgSt) were also evaluated. MgSt spray (Styl'One MIST) was used to externally lubricate the die wall and punch tips before each compression for all powders and mixtures except for MCC and the MCC 1% MgSt mixture.

Tablet tensile strength was determined by measuring tablet dimensions and breaking force with a texture analyzer. Porosity was determined from the material true density, as measured by helium pycnometry, and tablet density. The in-die Heckel analysis was performed to obtain a plasticity parameter, mean yield pressure (P_y).

RESULTS

Derivation

- The Kuentz-Leuenberger (KL) equation describes P as a function of ε.
  - $P = \frac{1}{C}\left[\varepsilon - \varepsilon_c - \varepsilon_c \ln\left(\frac{\varepsilon}{\varepsilon_c}\right)\right]$
  - $\frac{1}{C}$ is a powder plasticity parameter and ε_c is a critical porosity at which a powder begins to gain mechanical rigidity.
- The KL equation may be solved for ε versus P
  - $\varepsilon = -\varepsilon_c W\left(-e^{-\frac{PC}{\varepsilon_c}-1}\right)$
  - W is the Lambert W function
- The Ryshkewitch equation describes σ as a function of ε.
  - $\sigma = \sigma_0 e^{-b\varepsilon}$
  - σ_0 is the tensile strength at zero porosity and b is a decay constant.
- A combination of the KL and Ryshkewitch equation results in a function relating σ and P.
  - $\sigma = \sigma_{max} e^{\alpha W\left(-e^{-\frac{P}{\beta}-1}\right)}$
  - $\sigma_{max} = \sigma_0, \alpha = b\varepsilon_0, \beta = \frac{\varepsilon_c}{C}$
- This tabletability equation describes an asymmetric sigmoidal function (Figure 1).

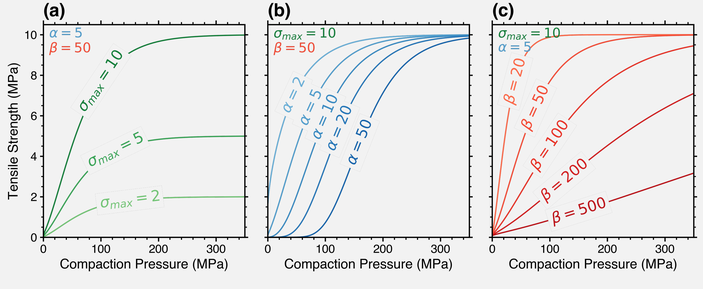

Figure 1: *The impact of (a) σ_{max}, (b) α, and (c) β on theoretical tabletability profiles.*

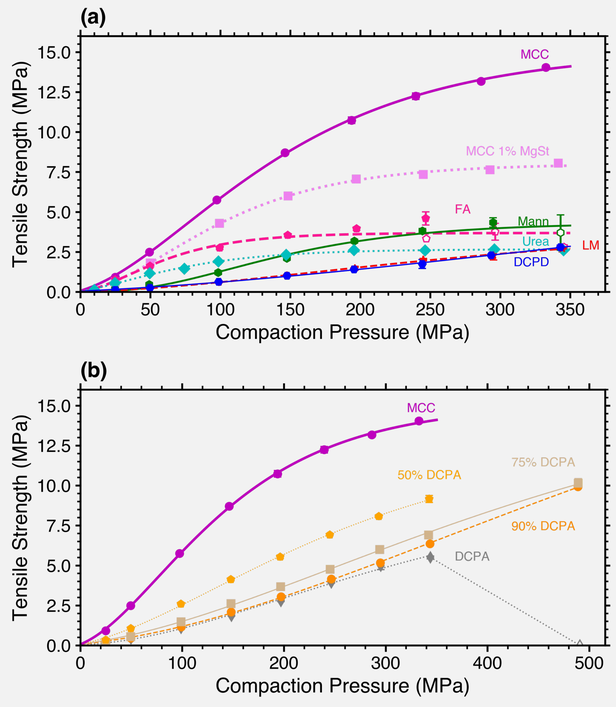

Figure 2. *σ versus P fitted with the tabletability equation for (a) various excipients and APIs and (b) physical mixtures of MCC with DCPA. Markers plotted with open symbols indicate overcompressed tablets, where tensile strength decreases as compaction pressure increases and are not included in the fitting.*

Evaluation

- The tabletability equation well-describes the relationship between σ and P for a wide variety of materials (Figure 2).
- The fitted parameter σ_{max} describes the BS of the material.
- The fitted parameter β describes the high pressure curvature, and correlates strongly correlates with in-die mean yield pressure (P_y) (Figure 3), indicating that β describes plasticity and thus BA.
- The tabletability equation allows for an assessment of BA and BS interplay without considering ε, which is often problematic to accurately determine.

CONCLUSIONS

- The derived tabletability equation adequately describes the tabletability of a wide range of pharmaceutical powders.
- Two parameters obtained from fitting tabletability data with this novel equation can be used to asses BA (β) and BS (σ_{max}).

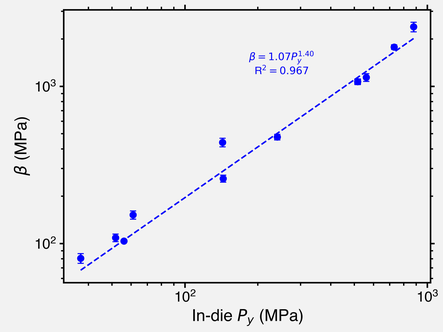

Figure 3. *β versus P_y for a wide variety of materials.*

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