Tabletability, compactibility and compressibility: a complex relationship easily displayed with JMP.

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Summary

• Tablets and powder compression
• Compaction studies
• Data modelling
• Data visualization
• Real case studies
Tablets are the most popular drug delivery dosage form
Compression

Applied Force (kN)

Powder
- Density
- Particle Size
- Particle Shape
- Flowability

Tablets
- Shape → area
- Thickness
- Volume
- Weight
- Hardness
Compaction Pressure

\[ \text{Pressure} = \frac{\text{Applied Force}}{\text{Area}} \]

Tensile Strength

\[ Ts = \frac{2 \cdot F}{\pi DT} \]

True Density

The powder density once all voids are removed.

Solid Fraction

\[ \text{Solid Fraction} = \frac{\text{Tablet Density}}{\text{True Density}} \]

Porosity = 1 – Solid Fraction
Compaction Studies

**Compressibility profile**
Solid fraction by Compaction pressure

**Compactibility profile**
Tensile strength by Solid fraction

**Tabletability profile**
Tensile strength by Compaction pressure
Flat-face punch ∅ 11.89 mm – Area 1 cm²
True Density Estimation


\[ P = \frac{1}{C} \left[ (1 - \varepsilon_c) - \frac{\rho_{\text{tablet}}}{\rho_{\text{true}}} - \varepsilon_c \ln \left( \frac{1 - \rho_{\text{tablet}}}{\varepsilon_c} \right) \right] \]

Heckel equation

Analyze>Specialized Modeling>Nonlinear

Non linear model library

where:  \( C, b \) and \( d \) are parameters
\( \rho_{\text{tablet}} \) is the variable \( X \)
\( \rho_{\text{true}} \) is the parameter \( d \)
**True Density Estimation**


\[ P = \frac{1}{C} \left[ (1 - \varepsilon_c) - \frac{\rho_{\text{tablet}}}{\rho_{\text{true}}} - \varepsilon_c \ln \left( \frac{1 - \frac{\rho_{\text{tablet}}}{\rho_{\text{true}}}}{\varepsilon_c} \right) \right] \]

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Compressibility

Kawakita, Tsutsumi, A Comparison of Equations for Powder Compression, (1966)
Physical Properties and Compact Analysis of Commonly Used Yeli Zhang, Yuet Law, and Sibu Chakrabarti, Direct Compression Binders, 2003

\[
P \frac{C}{a} + \frac{1}{ab} = \frac{V_0 - V}{V_0} \quad \text{or} \quad C = \frac{SF_0 - SF}{SF_0}
\]

\begin{align*}
&V_0 \text{ starting vol.} \\
&V \text{ vol. at applied pressure} \\
&SF_0 \text{ starting solid fraction} \\
&SF \text{ solid fraction at applied pressure}
\end{align*}

**Kawakita equation**

**Analyze>Specialized Modeling>Nonlinear**

**Non linear model library**

where: \( a \) and \( b \) are parameters
\( P \) is the variable \( X \)
\( SF \) is the variable \( Y \)
Compressibility

Kawakita, Tsutsumi, A Comparison of Equations for Powder Compression, (1966)
Physical Properties and Compact Analysis of Commonly Used Yeli Zhang, Yuet Law, and Sibu Chakrabarti, Direct Compression Binders, 2003

\[
\frac{P}{C} = \frac{P}{a} + \frac{1}{ab}
\]

\[
C = \frac{V_0 - V}{V_0}
\]

or

\[
C = \frac{SF_0 - SF}{SF_0}
\]

Kawakita equation

Analyze>Specialized Modeling>Nonlinear

Non linear model library

Nonlinear Fit
Response: Solid Fraction, Predictor: Kawakita_Equation

Plot

Nonlinear fit

Solution

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>ApproxStdErr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da</td>
<td>0,0605603482</td>
<td>0,1112878</td>
</tr>
<tr>
<td>a</td>
<td>-16,19845696</td>
<td>31,5351507</td>
</tr>
<tr>
<td>b</td>
<td>0,0538835229</td>
<td>0,00980698</td>
</tr>
</tbody>
</table>

Solved By: Analytic Gauss-Newton
Compressibility

The ability of a material to reduce in volume as a result of an applied pressure.
Compactibility


\[ TensileStrength = \sigma_0 e^{-b(1 - SolidFraction)} \]

Ryshkewitch equation

Fit Y by X platform

Simply doing a “Fit special” with Y transformed as logarithm

\[ \text{Log(Tensile Strength (MPa))} = -4.144067 + 6.8751709 \times \text{Solid Fraction} \]

Summary of Fit

- R^2: 0.997629
- R^2 Adj: 0.997498
- Root Mean Square Error: 0.032703
- Mean of Response: 2.217537
- Observations (or Sum Wgts): 20
Compactibility

The ability to produce tablets with sufficient strength, under the effect of densification
Tabletability

The capacity of a powder to be transformed into a tablet of specified strength under the effect of compaction pressure
3D Scatterplot
Compaction studies on cellulose, lactose and placebo formulations
Cellulose

Lactose
Compaction studies on real tablets formulation, using manufacturing punches (EU standard tooling)
Single punch press Vs Rotary press

**Natoli NP-RD10A**
Single punch
Alternative

**Korsch PH103**
Rotary press
Dwell time is defined as the amount of time that the compression force applied when forming the tablet is above 90% of its peak value.

Thank you

References:
• Kawakita, Tsutsumi, A Comparison of Equations for Powder Compression, Bulletin of Chemical Society of Japan, (1966)
• C. Sun, Decoding Powder Tabletability: Roles of Particle Adhesion and Plasticity, Journal of Adhesion Science and Technology, (2011)