An evaluation of various direct compression excipients using the Gamlen Tablet Press GTP-1

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Motivation: Tablet Formulation

• The modern tablet needs to satisfy numerous properties that make it ‘Fit for Purpose’
  • Physicochemical
  • Stability
  • Manufacturing

Drug Substance
Excipients
Lubricant

Tablet
Tablet Formulation Experimentation

- API availability
- Equipment

Our approach
- Milligram quantities of material
- Objective method
- Practical
The Gamlen Tablet Press GTP-1

- Ideal instrument for formulation development
- Bench top computer controlled
- Milligram quantities of material
- Dual mode-tablet press and strength tester
Computer control

- Can be linked to any laptop or PC.
- Real time data recording.
- Force displacement curves.
- Ejection force.
- Fracture load of compact.
Tablet tensile strength

- Most important tablet physical parameter
- Objective as it takes into account not only tablet hardness but tablet thickness too
- Scaleable to different size and shapes of tablets
Making valid comparisons

Tensile fracture stress for 3mm and 6mm diameter Avicel PH-102 tablets

- 6mm tablets
- 3mm tablets

Compaction pressure (MPa) vs Tensile Fracture Stress (MPa)
Evaluating compressibility

- Tensile strength measured over a range of forces
- Enables ranking of formulations
- Example of DC v wet granulated blend
Compressibility assessment

Tensile fracture stress comparison of various Direct Compression and Wet Granulated formulations

- Extra Avicel
- Agglomerated lactose 80
- Spray dried lactose
- Wet granulated
- Sieved lactose
- Lactose powder 200
- Partially regelatinised starch

Compression pressure (MPa)

Tensile fracture stress (MPa)
Development of a DC paracetamol tablet

**Preliminary experiments**

- 10% paracetamol
- 0.5% MgSt
- 8 x mannitol
- 2-x isomaltulose

**Main experiments**

Selection of 3 most compressible formulations
Methods

- 100g blends were made using a Turbula mixer
- 75mg round, flat faced 5mm tablets made at 5 different compression forces
- Tablets subjected to fracture, friability and disintegration testing
- Powder flow properties also tested
Ejection stress calculation

\[ ES = \frac{F}{\pi dt} \]

- \( ES \) = ejection stress (MPa)
- \( F \) = ejection force (N)
- \( d \) = diameter of tablet (mm)
- \( t \) = thickness of tablet (mm)
Galen IQ grades ejection stress

- GalenIQ720
- Galen IQ721

Ejection stress (MPa) vs. Compression pressure (MPa)
Preliminary experiments: Friability
<table>
<thead>
<tr>
<th>Parteck M200</th>
<th>MERCK</th>
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<tbody>
<tr>
<td>Perlitol 200SD</td>
<td>ROQUETTE</td>
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<tr>
<td>Galen IQ721</td>
<td>beneo</td>
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<tr>
<td>L-HPC21</td>
<td>ShinEtsu</td>
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Ejection stress of Galen and paracetamol

- Galen 0.1%
- Galen 1%
- Galen 10%

Compression pressure (MPa)

Ejection stress (MPa)
Main expts: Friability

![Bar chart showing friability percentages for different formulations.](chart.png)
Decision matrix based on compressibility and flow

- **Galen LHPC21 0.1%**
- **Galen LHPC21 1%**
- **Galen LHPC21 10%**

**Compression gradient**
- GOOD COMPRESSIBILITY
- GOOD FLOW

**Minimum orifice size**
- POOR COMPRESSIBILITY
- POOR FLOW

- **Parteck**
- **Perlitol**
- **Galen**
- **Starch/lactose LHPC**
- **Parteck LHPC**
- **Perlitol LHPC**
- **Galen LHPC**
Summary

• Compressibility is a useful approach to screen formulations
• GTP generates useful comparative data to help evaluate different grades of excipient and drug content
• A ‘Decision matrix’ is a useful way of visualizing the data
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