

INTRODUCTION

- The experimental methods of bulk powder characterisation are briefly described together with the practical application of compaction simulation to formulation design and process scale-up.
- The processing properties of excipients for tablet formulation can be assessed using measurements of mechanical properties such as compressibility and tensile strength.
- It is then possible to assemble a database of excipient properties to support decisions in the development of a new product.



TABLET FORMULATION

Excipient Selection

■ Filler

- mcc, lactose, dcp, mannitol, starch,

■ Disintegrant

- AcDiSol, starch glycollate....

■ Lubricant

- Stearate

Drug Product

■ Stability

- Excipient Compatibility

■ Drug Release

- Dissolution

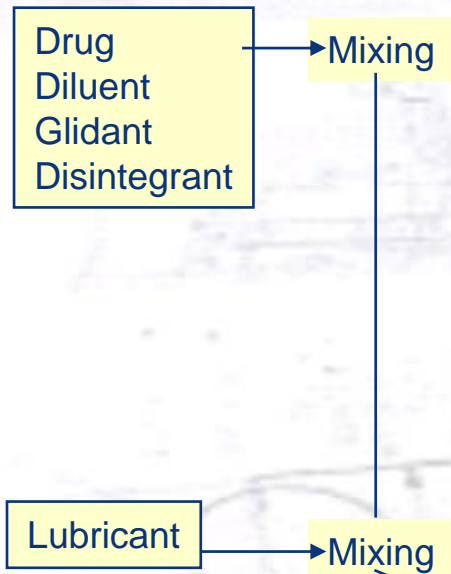
■ Manufacturable

- Mechanical Properties

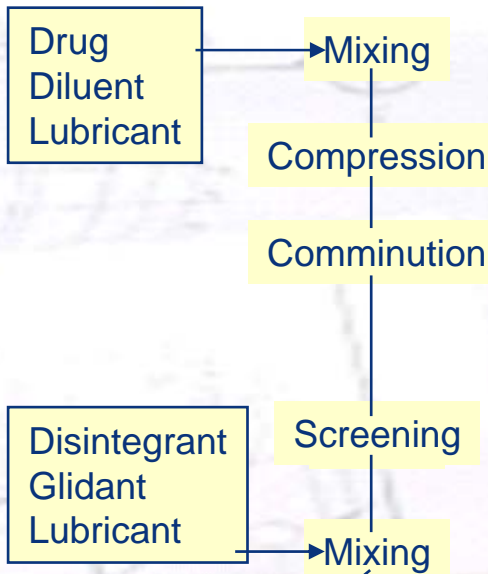


Process Route for Tablet Manufacture

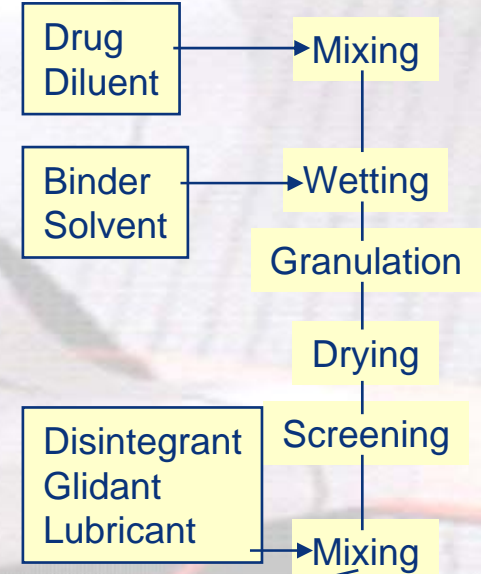
Direct Compression



Dry Granulation



Wet Granulation



Compression Mix

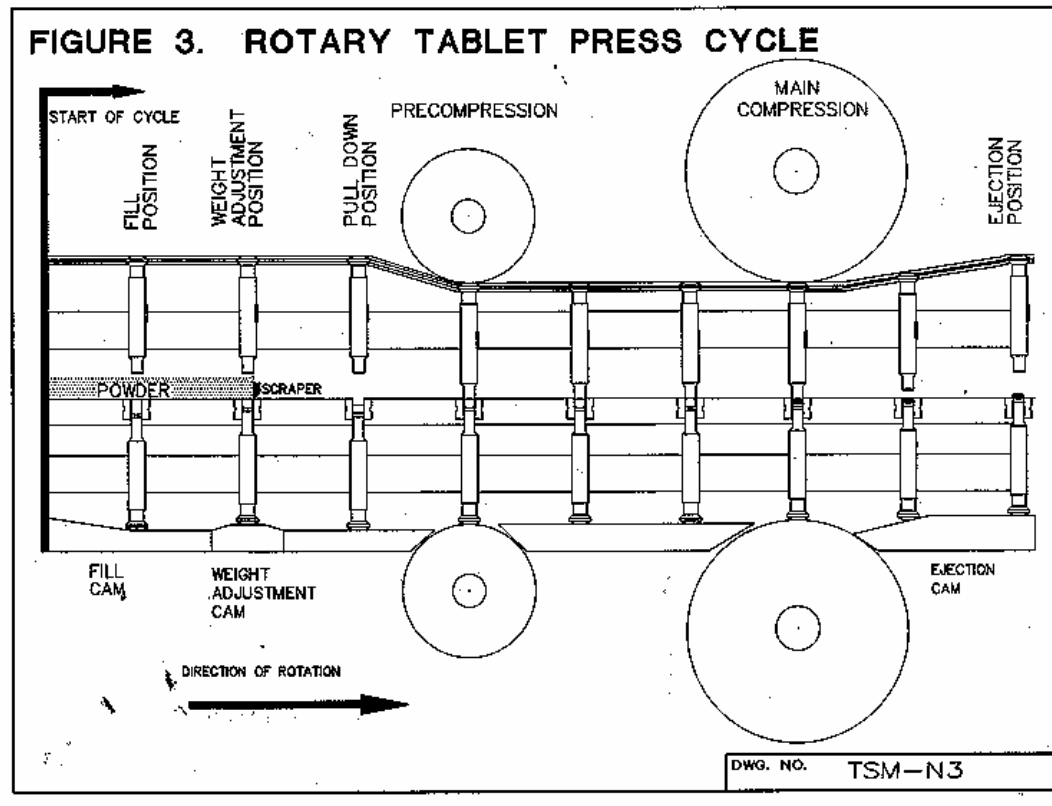
Fill Die, Compress Tablet, Eject Tablet

Metal check, Dedusting, Coating, Packaging etc..

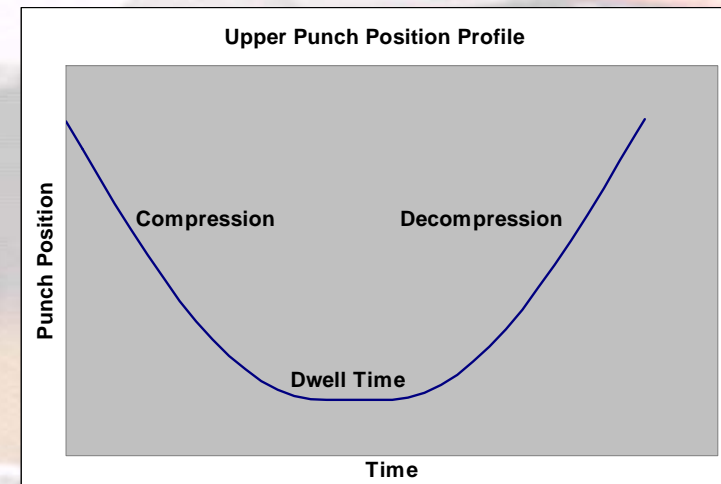


Compression Cycle

Rotary Tablet Press



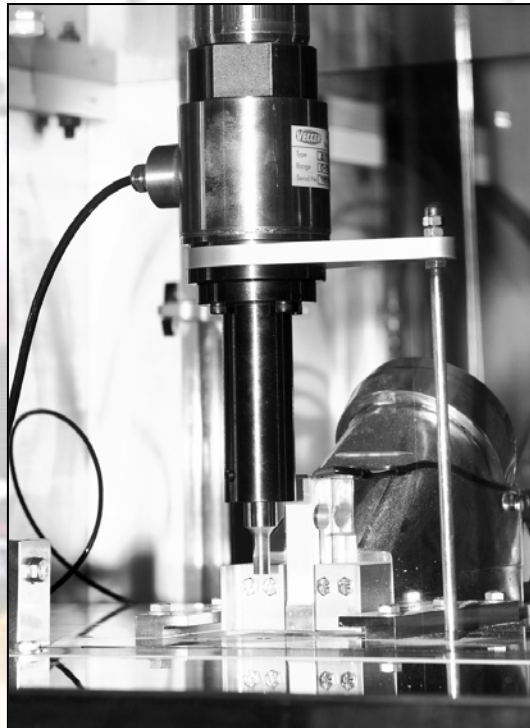
The shape of this profile may change *significantly* depending on the tablet press and tablet production rate.



Compaction Simulator

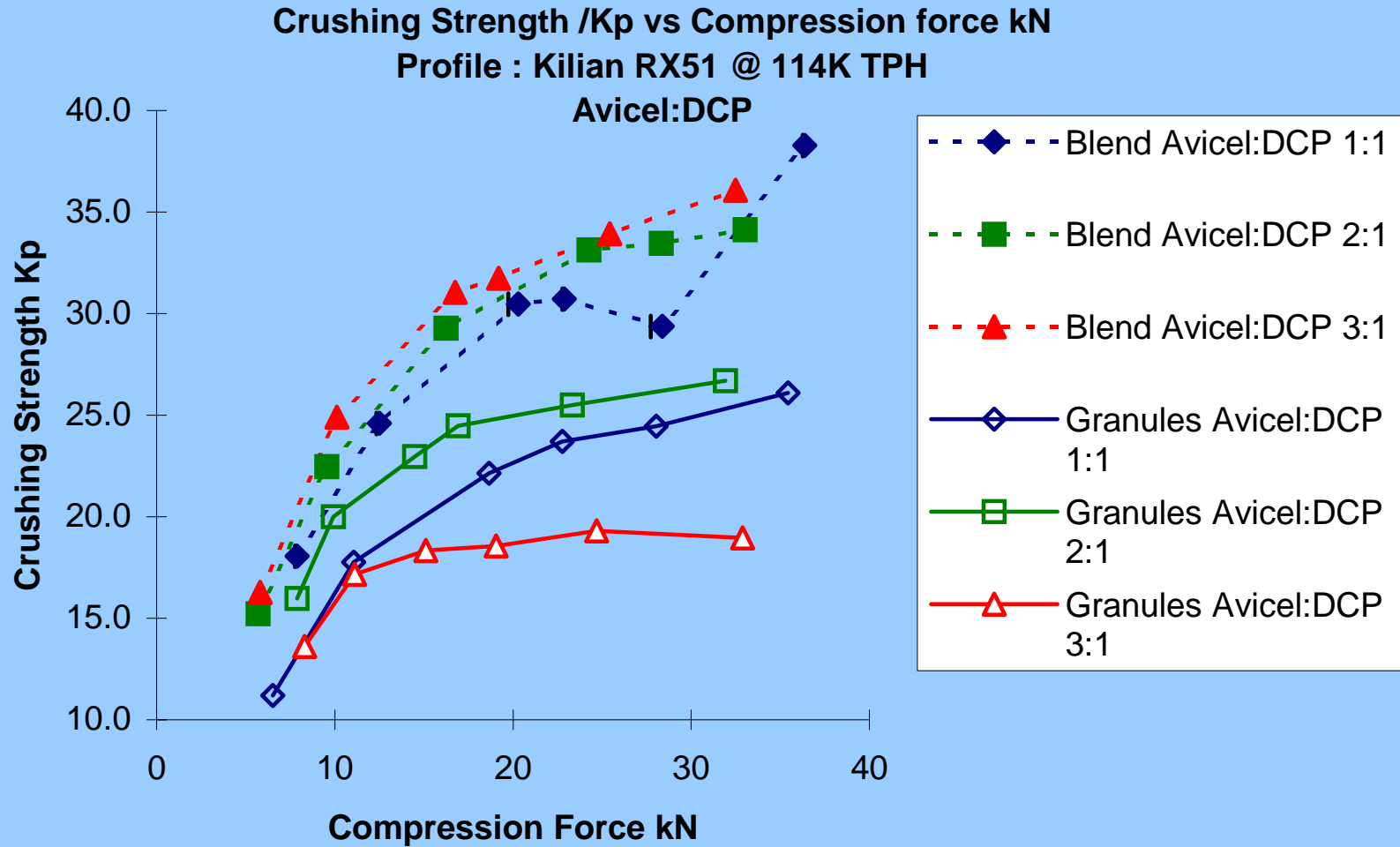
Hydraulic Compression, *ESH*

- Computer-controlled tablet press, Force, Displacement
- Hydraulically driven, capable of punch velocities up to 1 m s^{-1}
- Programme the compaction profile of commercial tablet presses



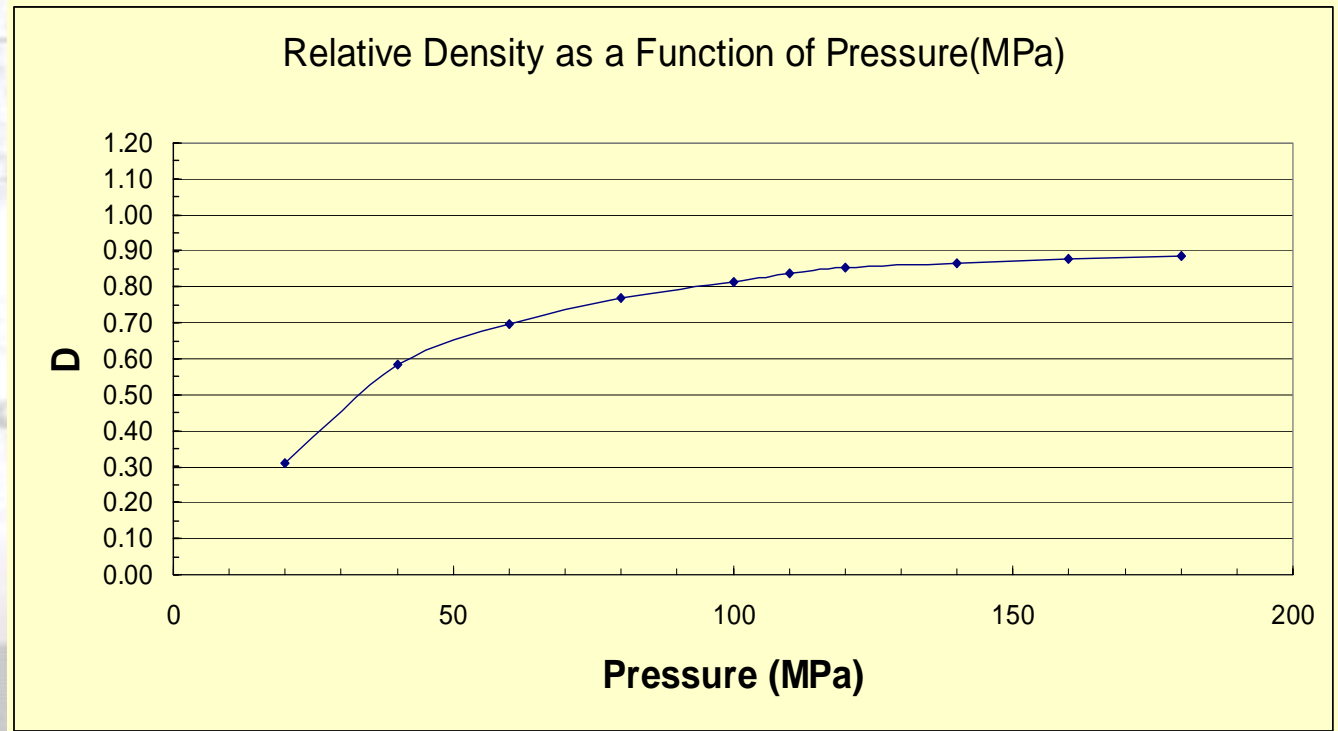
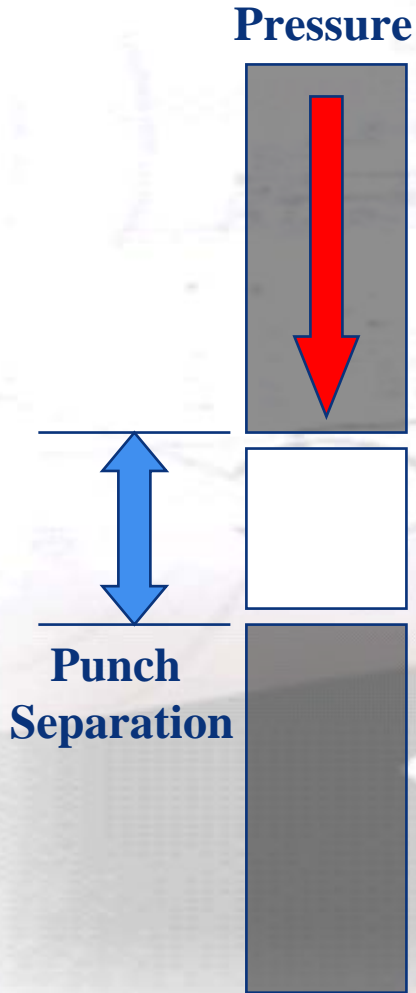
Formulation Development

Force - Hardness: Blends and Granulations



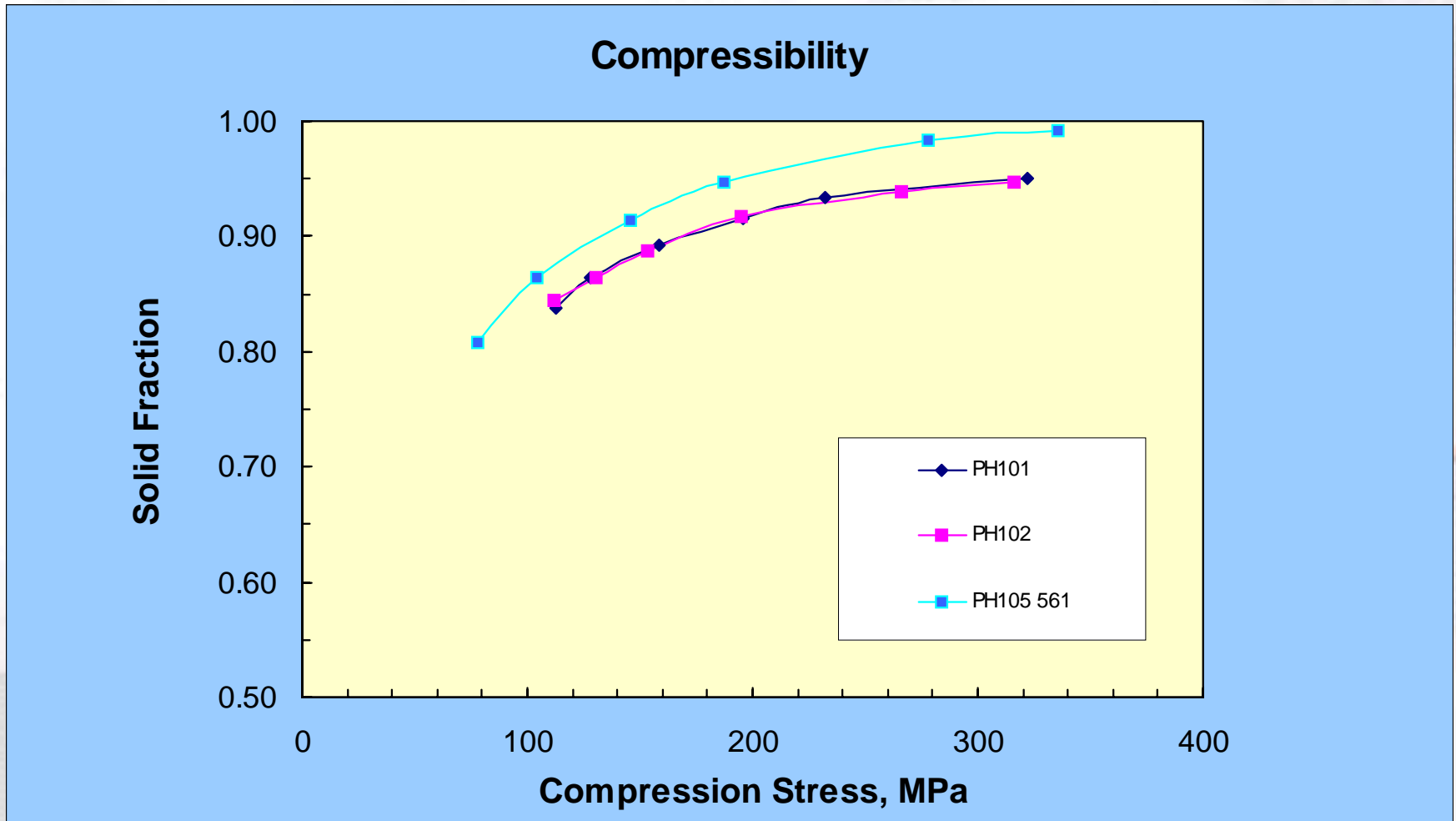
Material Assessment

Powder Compressibility



Material Assessment

Compression Data, mcc, RX51, 8mm src

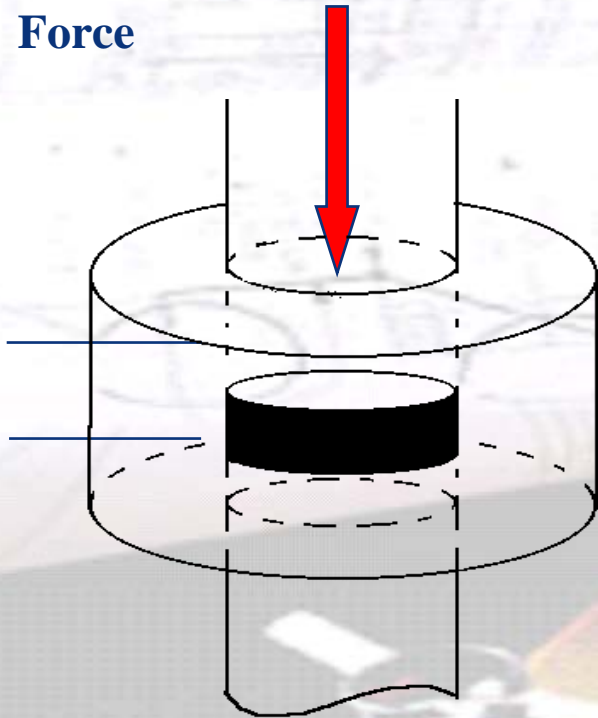


Material Assessment

Radial Tensile Strength

1. Compression

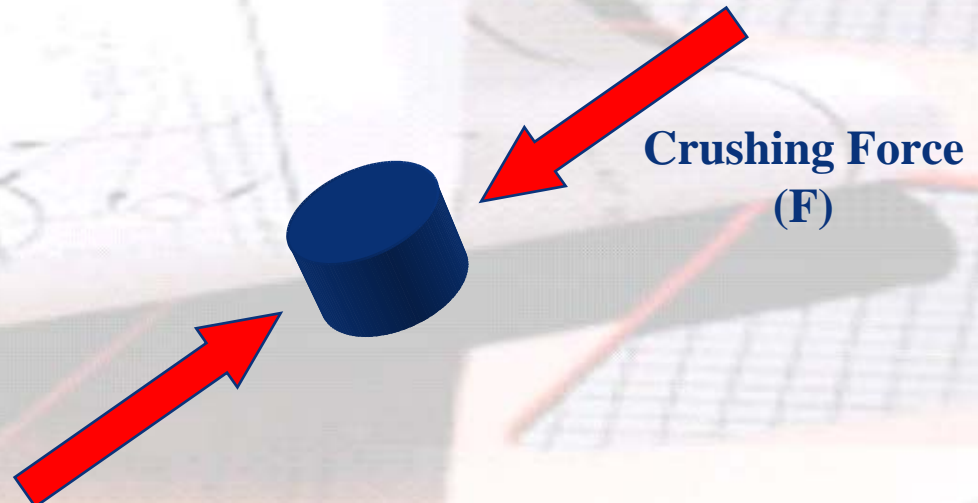
**Compression
Force**



2. Hardness Tester

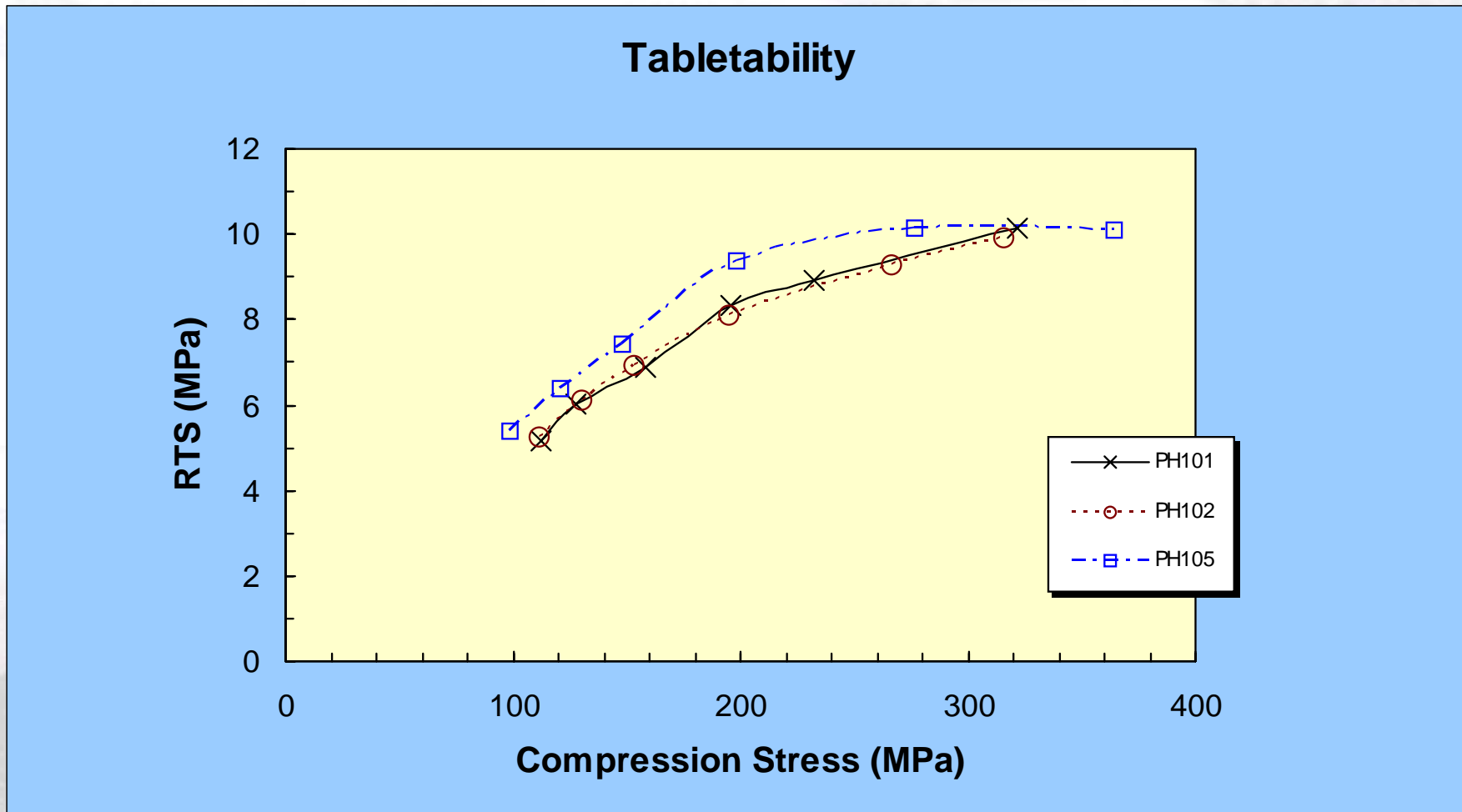
Radial Tensile Strength

$$RTS = 2F/\pi dt$$



Material Assessment

Compaction Data, mcc, RX51, 8mm, src



MATERIAL PROPERTIES

Powder Physical Properties

Particle Properties

- Particle Size, SA, Shape,
- Solid ('True') Density
- Hardness, Young's modulus

Bulk Properties

- Relative Density (D)
 - Bulk Density, Tap Density
- Compressibility (D vs Applied Force)
- Compact-ability (Tensile Strength vs D)



Solid Density

Helium Pycnometer

- *True (Absolute) Density* measured by fluid (He) displacement
- Relative Density, D , (solid fraction) of material can be determined
- API 1-2 g/cm³
- MCC 1.55 g/cm³
- Lactose 1.50 g/cm³
- DCP 2.80 g/cm³



Material Properties

Bulk Density, Relative Density, D

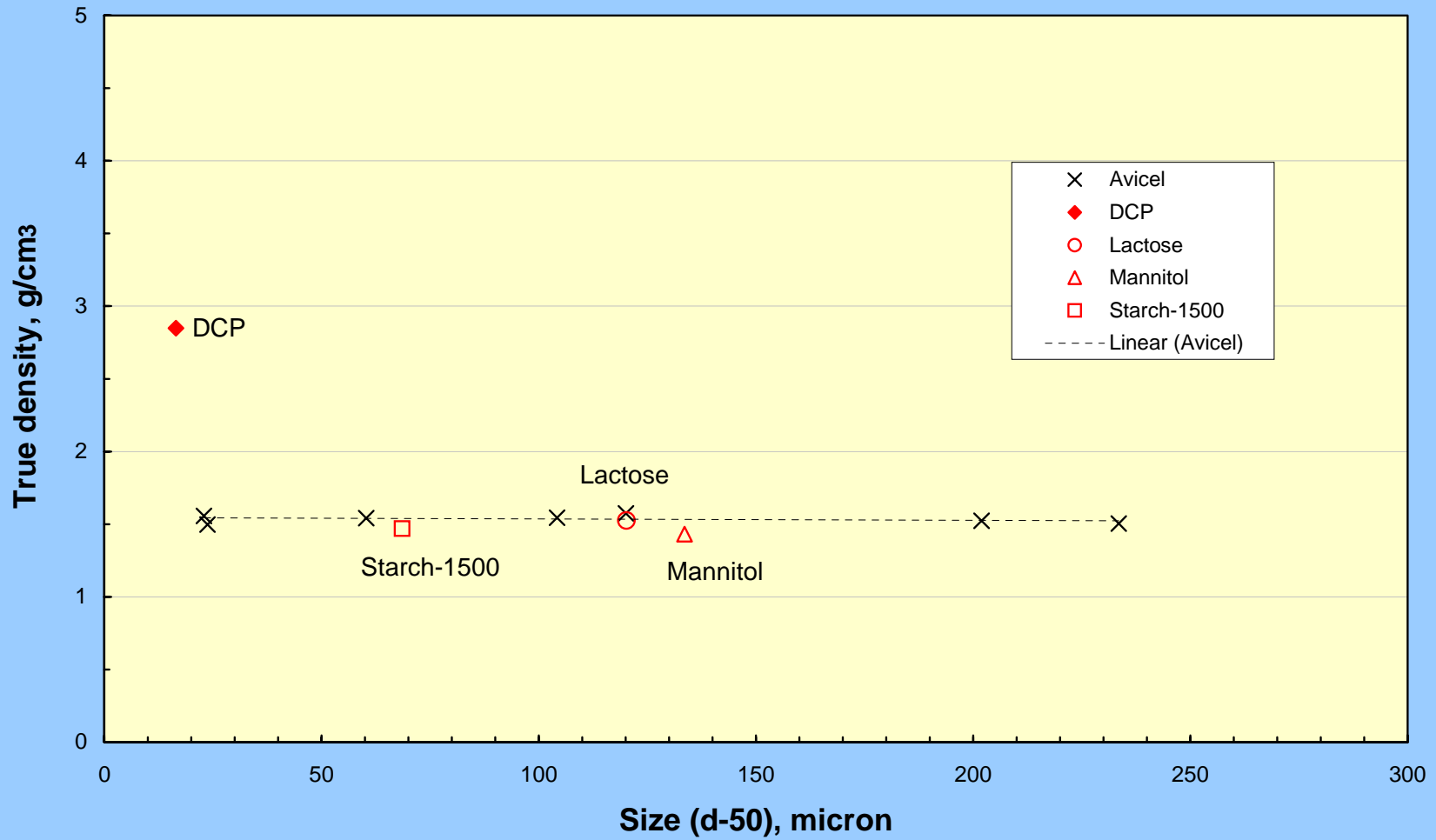
	Excipient Blend	Ribbon	Granulation	Tablet	
'True' density	1.5	1.5	1.5	1.5	g/cm ³
Apparent density	0.1-0.7	0.1-0.7	0.9-1.2	0.3-0.9	g/cm ³
Solid Fraction (%)	10-50	10-50	60-80	20-60	80-90

Hancock et al (2003), 'The Relative Densities of Pharmaceutical Powders,.....'
 Pharm. Technol. April 2003 pp 64-80
'..density ... equipment-independent scaling parameter ... for manufacturing operations.'



True Density

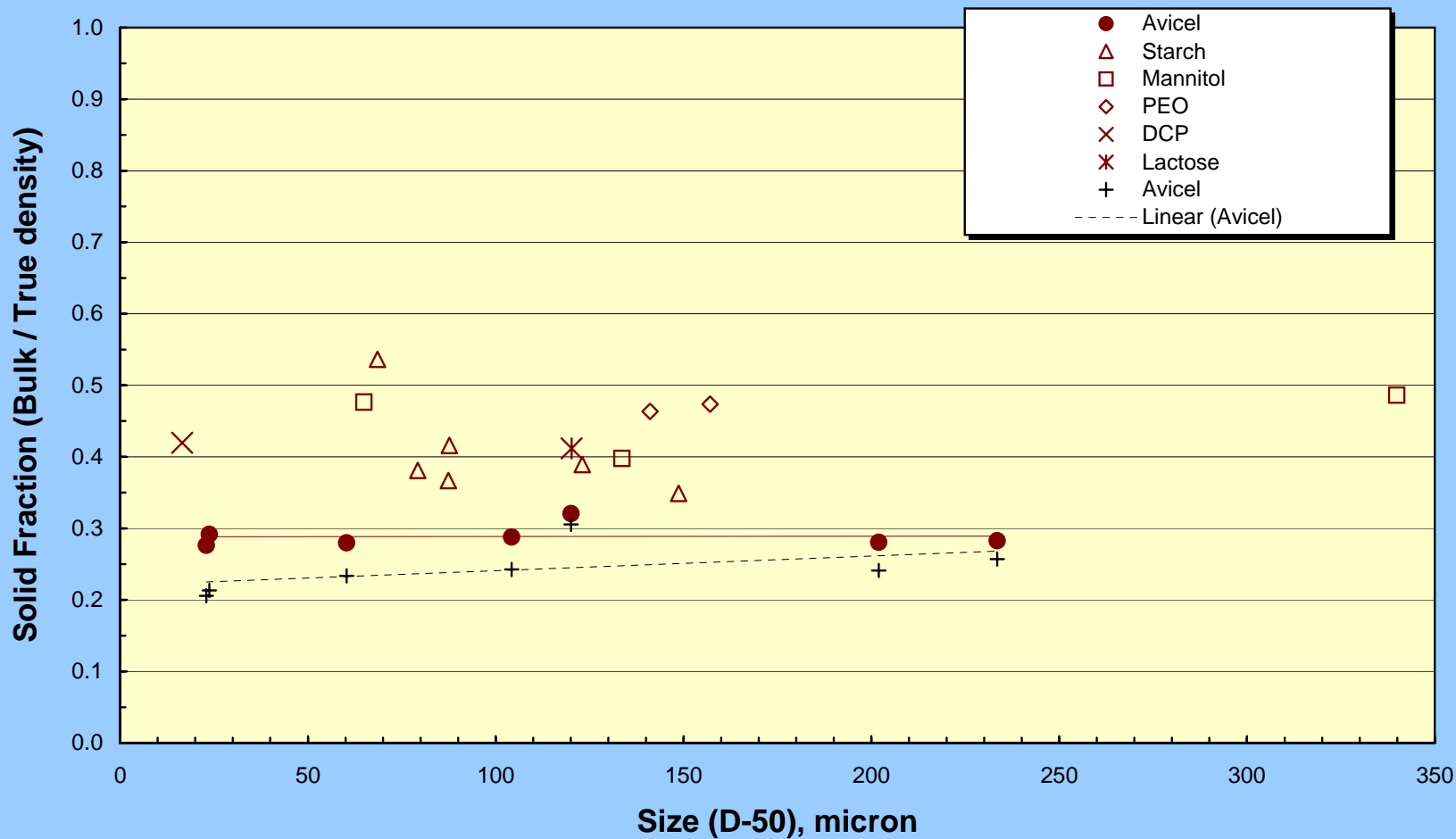
Excipient Data



Excipient

Powder *Solid Fraction*

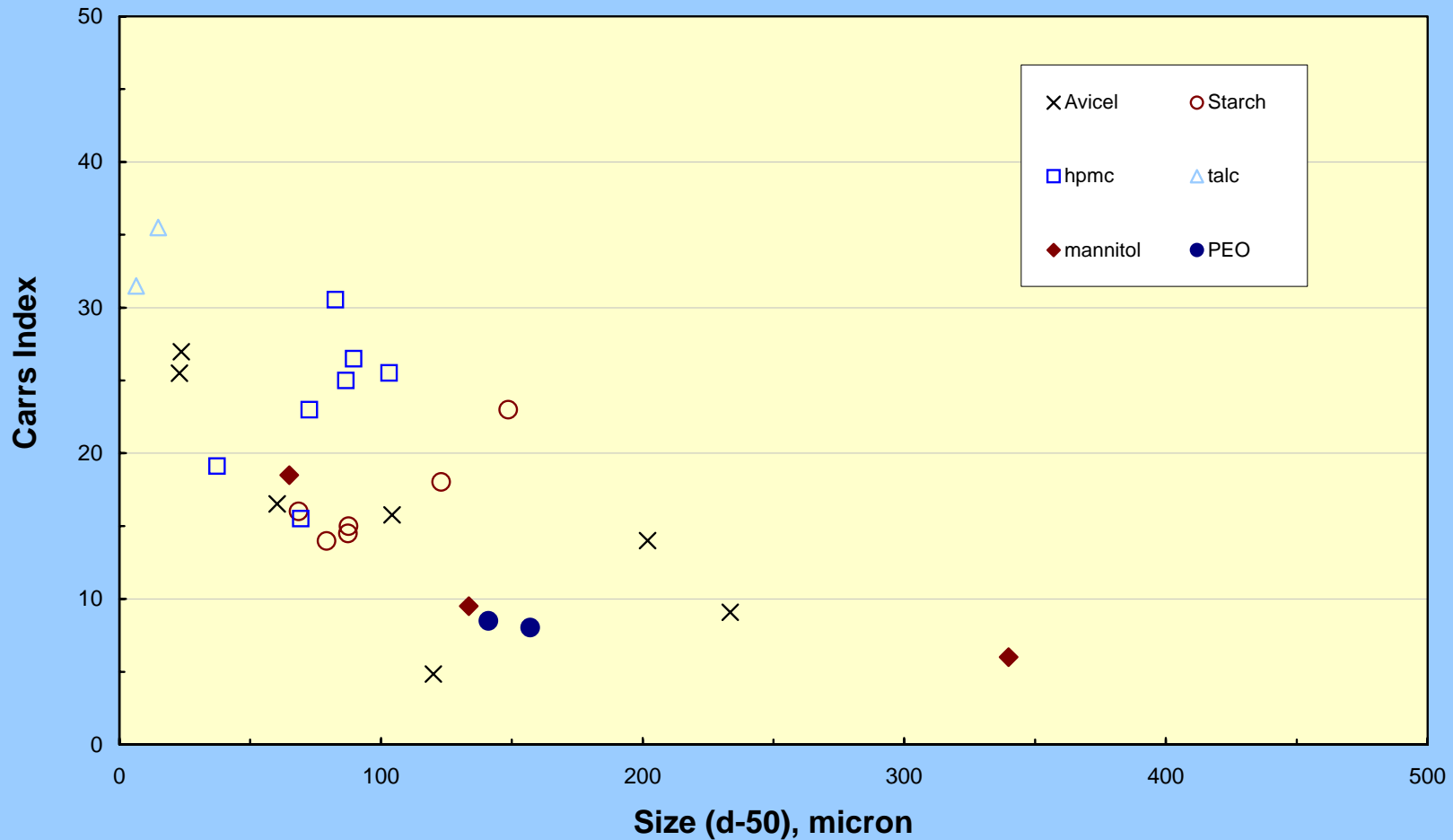
Excipient Powders -
Tapped Density Solid Fractions



Material Characterisation

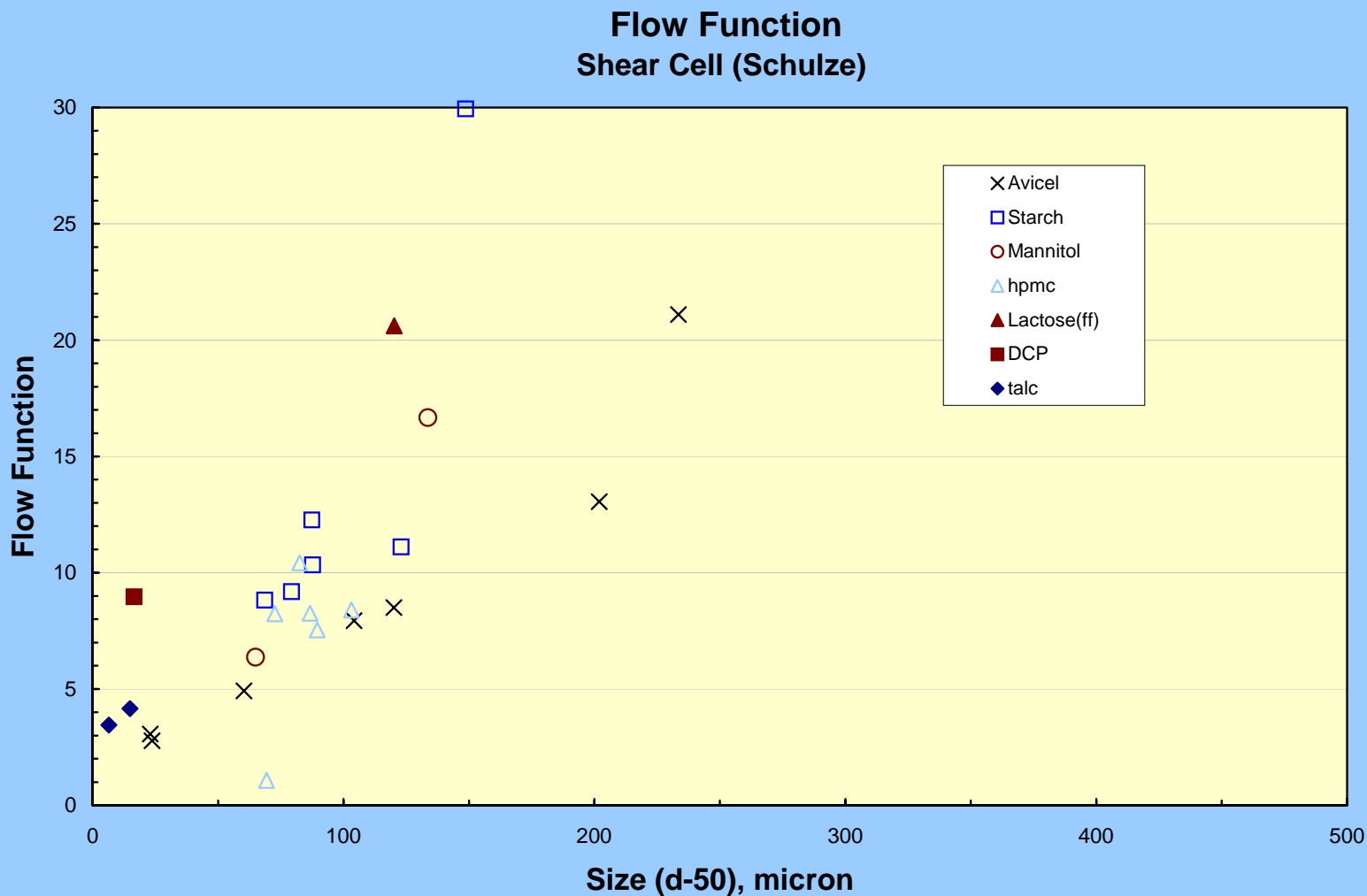
Bulk Density / Tap Density

Carrs Index



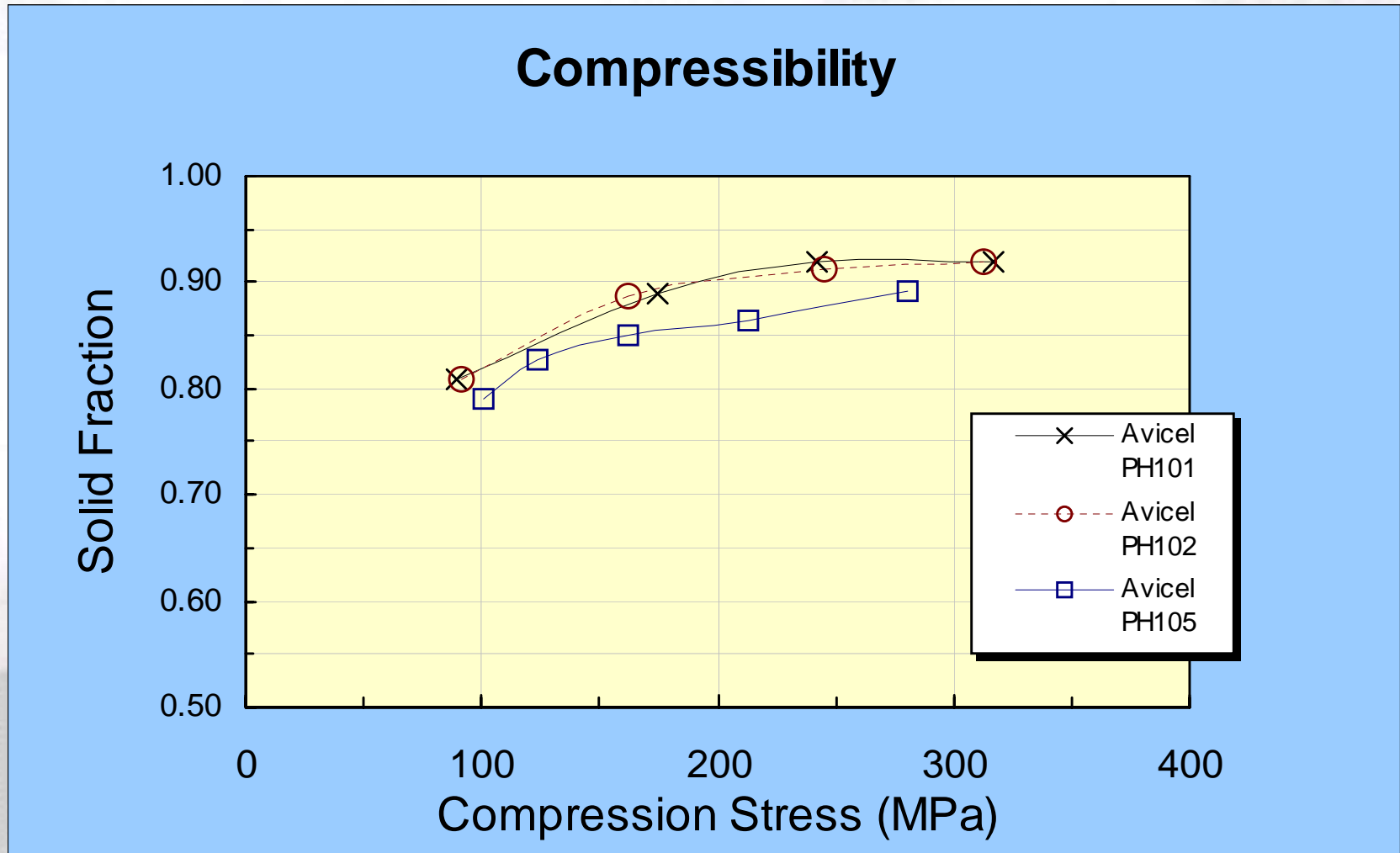
Material Characterisation

Flow Function, Shear Cell



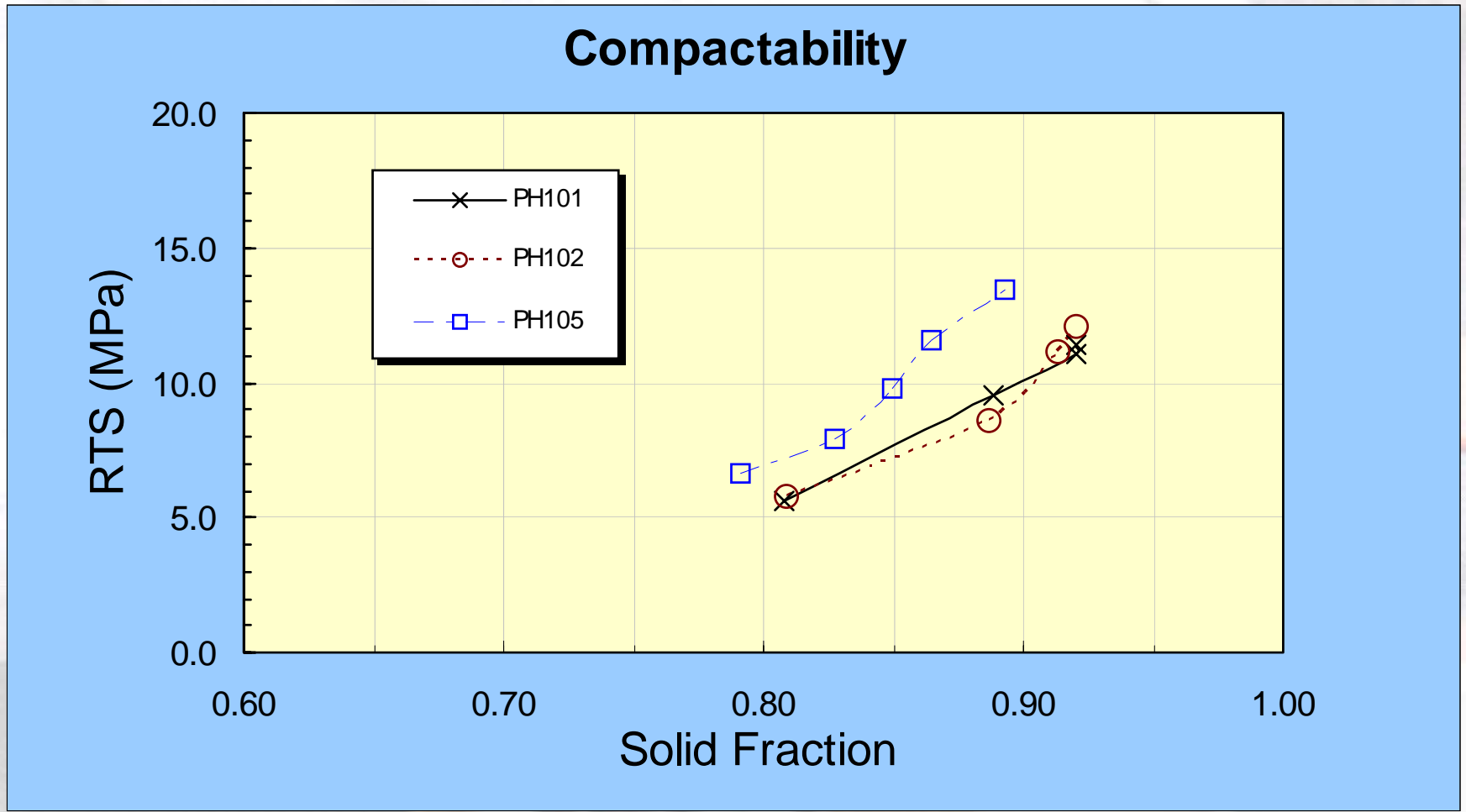
Material Characterisation

Compressibility, 0.3 mm/s, 8mm ff.



Material Characterisation

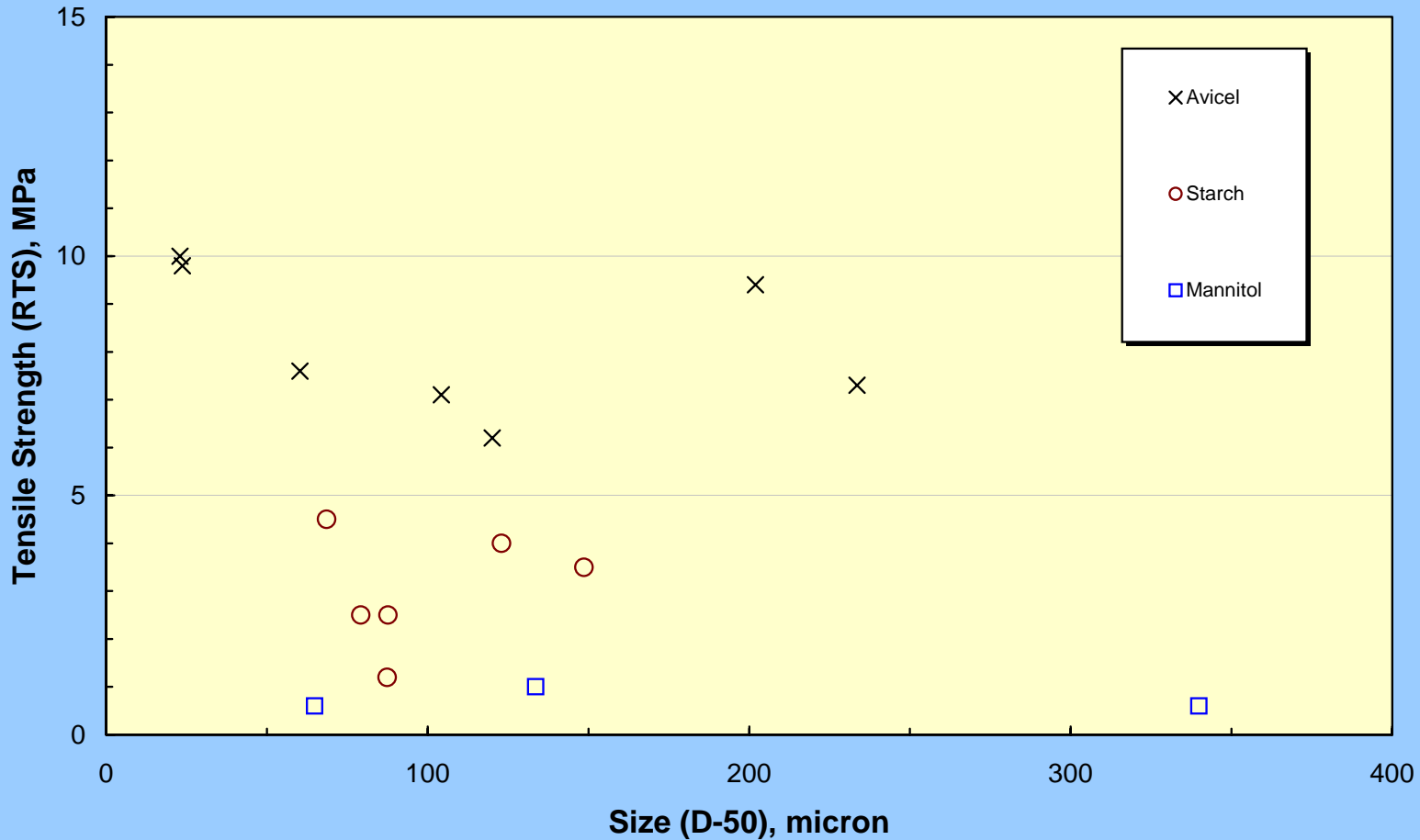
Compaction, 0.3 mm/s, 8mm ff



Material Characterisation

Compaction, 0.3 mm/s, 8mm ff

Excipient Compaction
Compression 0.3 mm/s, SF=0.85, 8mm ff.



CONCLUSIONS

- Excipient Physical properties can be related to product formulation (e.g. IR Tablet)
- Mechanical Properties defined as
 - Density
 - Flow
 - Compression
 - Compaction
- Properties have been illustrated with a range of excipient grades for microcrystalline cellulose, starch, mannitol, lacose and di-calcium phosphate



Acknowledgements

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