INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Material Properties of Solid Dosage Forms

Course BSc (Pharm) or BSc (ATT)

Year 2024-2025 II

Module Medicines: Pharmaceutics 2 (MP2)

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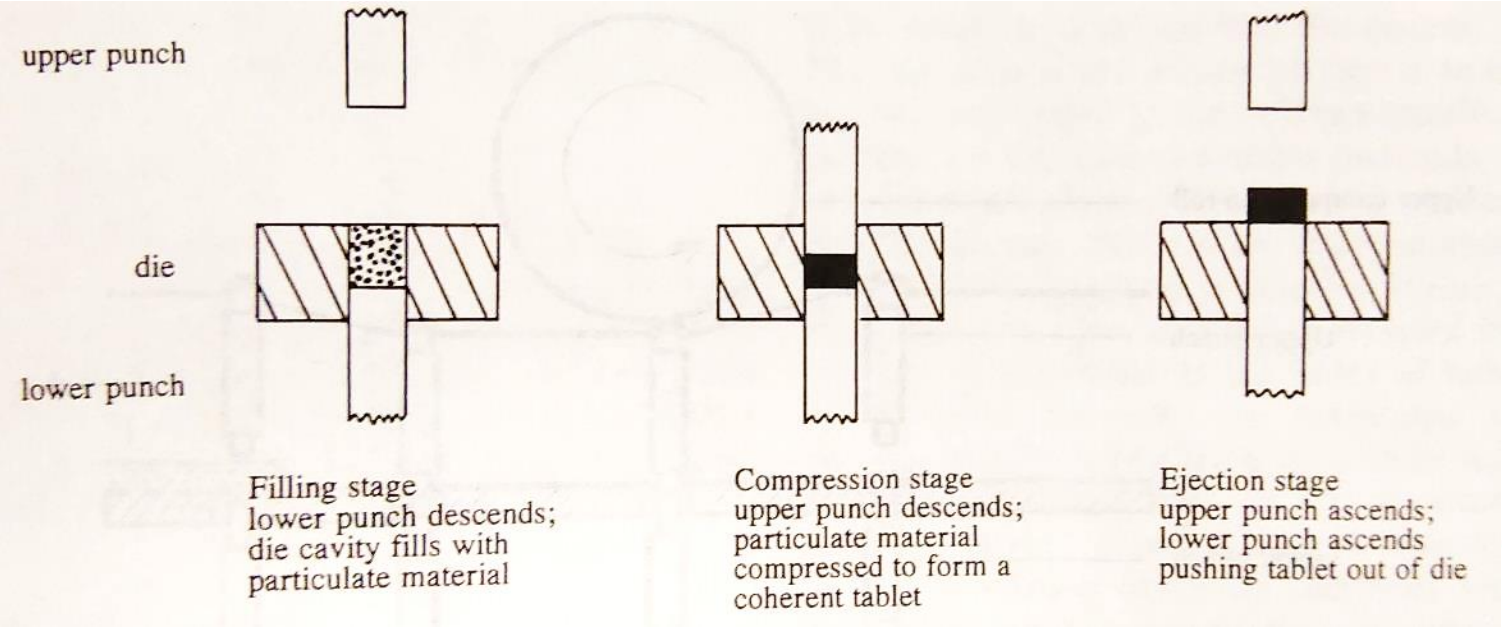
Learning Outcomes

1. Describe the essential concepts relating to material properties, including mechanical stress, strain, material deformation and fracture

2. Distinguish between the terms compression and compaction

3. Explain the evaluation of tablet strength through analysis of mechanical properties of materials

4. Illustrate the relationship between material properties and tablets through case studies



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Material Properties of Importance for Solid Dosage Forms

- Plasticity
- Elasticity
- Viscoelasticity

Deformation

- Brittleness
- Ductility

Fracture

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Material Properties: Essential Concepts of Stress and Strain

- Stress (σ)
  - Stress is an applied force per unit area
  - For tablet processes, this is generally in the form of the application of pressure

- Strain (γ)
  - Strain is the deformation that occurs as a result of the applied mechanical stress
  - It is a form of displacement
  - For tablet processes, this is often the compression of a powder into a smaller volume

- Fracture
  - Fracture is the separation of a solid body into two or more parts
  - Can occur in certain materials once a certain stress has been reached

- Stress-strain curves are plotted to determine the relationship between stress and strain for a solid form and to determine its material properties

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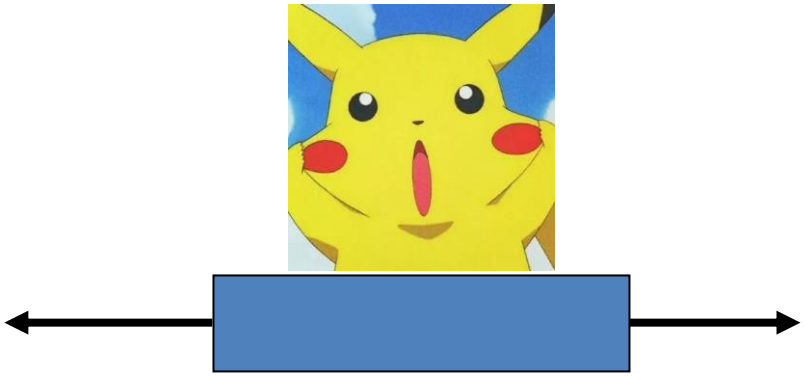
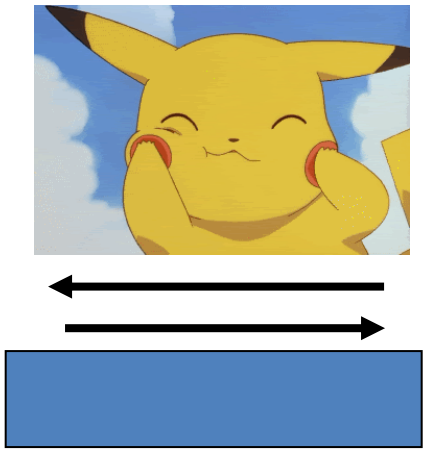
Material Properties: Types of Stress

Compressive



Tensile



Shear
(Attrition)

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Material Properties: Relevance to Stress-Strain & Fracture

- Plastic deformation
  - Plastic deformation is the permanent change in shape due to the applied stress
  - Deformation occurs by sliding of the molecules along slip planes where intermolecular reactions are weaker
  - For tabletting, this is most favourable for tabletting as the compressed material is maintained in the desired size and shape

- Elastic deformation
  - Elastic deformation is a change in shape that is reversible following the removal of the applied stress
  - Deformation occurs by a reduction in the intermolecular spacing
  - For tabletting, this is generally undesirable

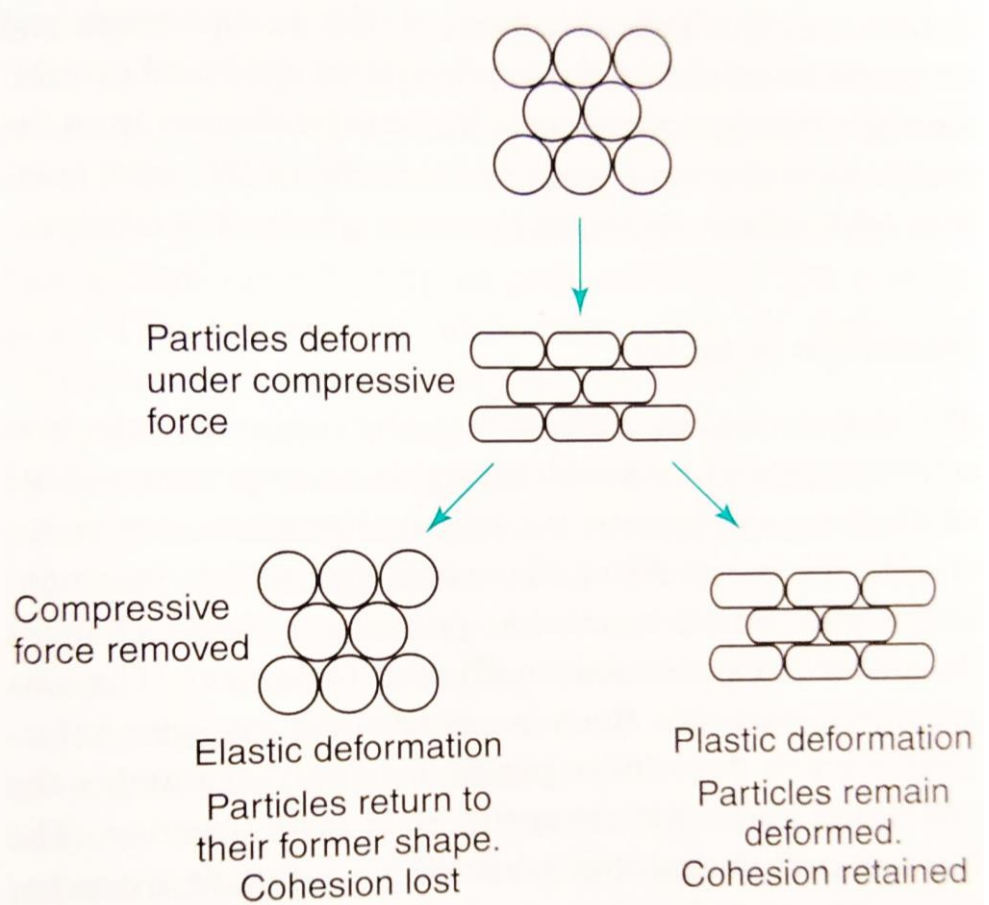

Fig. 31.24 Schematic illustration of particle deformation, elastic and plastic, during compression. (From Armstrong 1982.)

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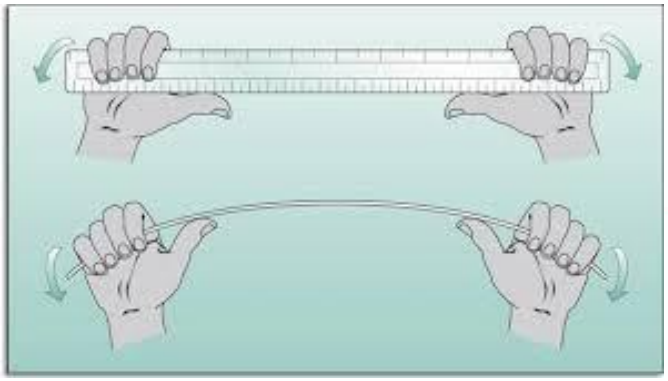
Fracture: Brittle & Ductile Materials

- Brittle fracture
  - Little to no apparent plastic deformation takes place before fracture
  - Fracture occurs by the rapid propagation of a crack
  - Common for most tablets to be brittle

- Ductile fracture
  - Extensive plastic deformation takes place before fracture
  - Rather than cracking, the materials are “pulled apart”
  - Uncommon for tablets



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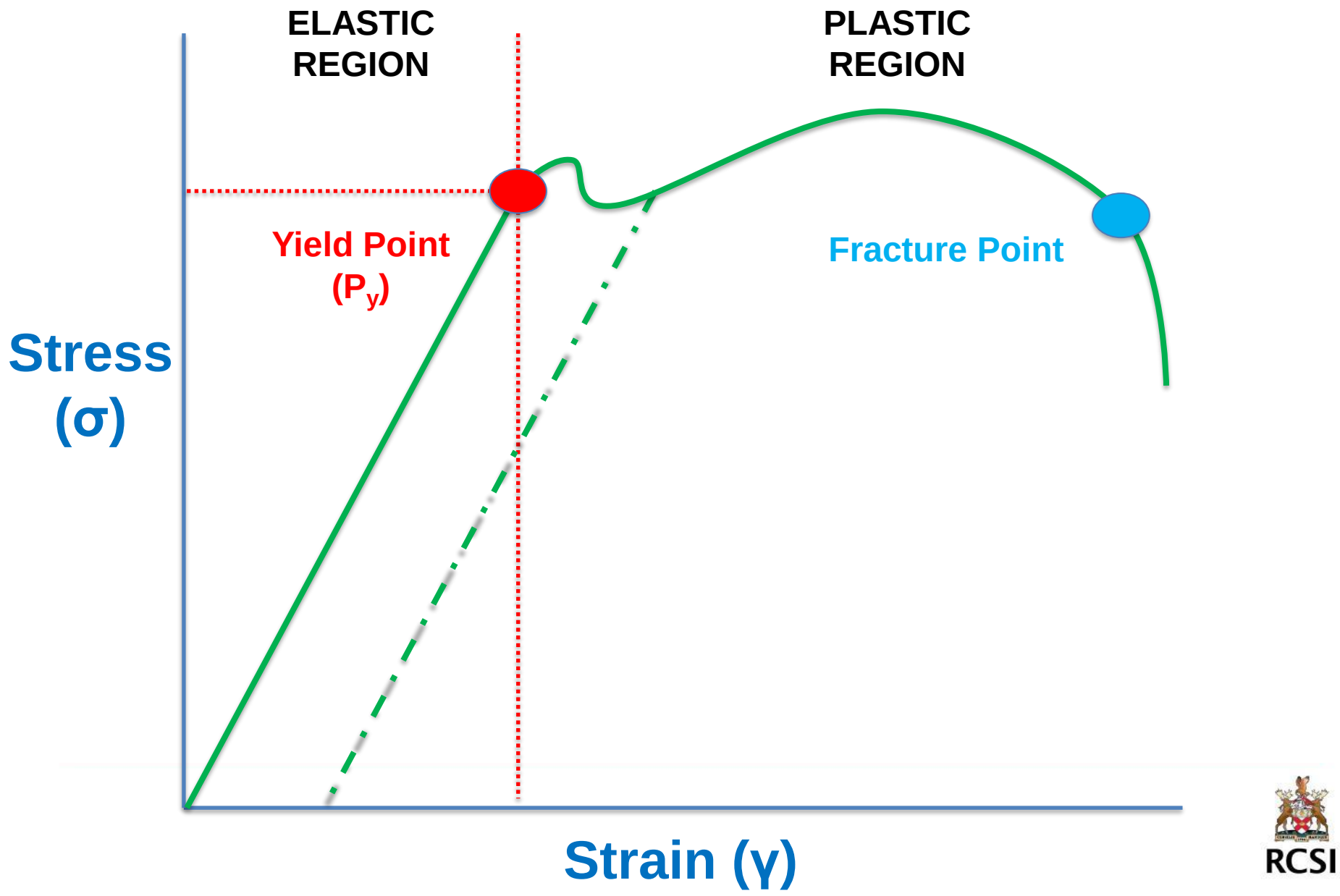
Plastic and Elastic Deformation: The Stress-Strain Curve



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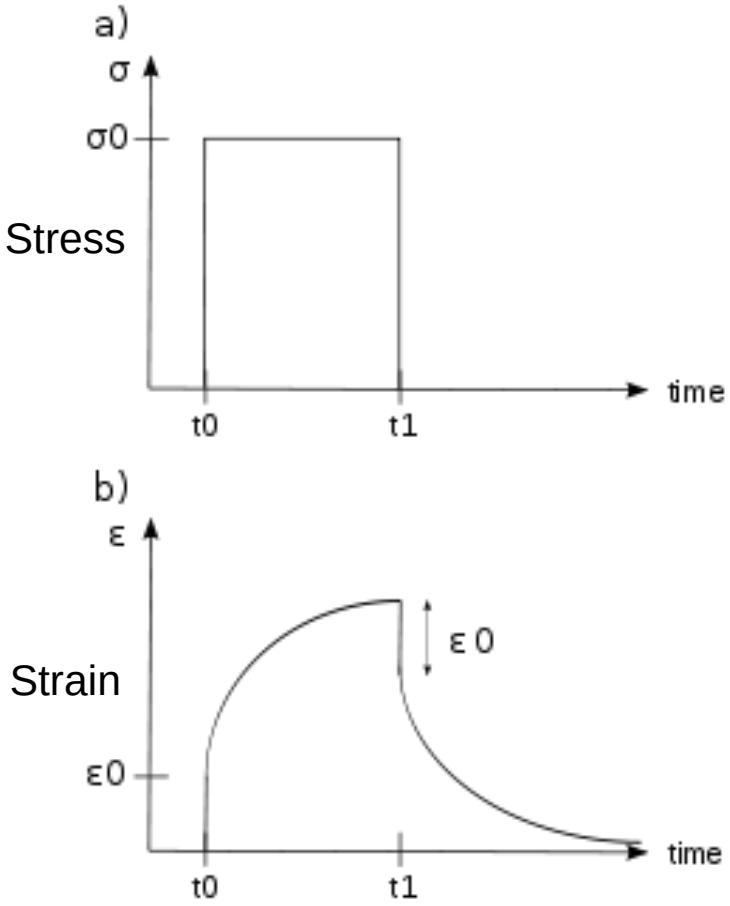
Viscoelastic Behaviour of Materials

- Viscoelastic materials
  - Many pharmaceutical materials exhibit viscoelastic properties under deformation
  - These materials exhibit time-dependent deformation
  - The deformation can be reversible or partly reversible

- Relevance to Tabletting
  - Many pharmaceutical materials exhibit viscoelastic properties to varying degrees
  - The degree to which they are influenced depends on the core material(s)



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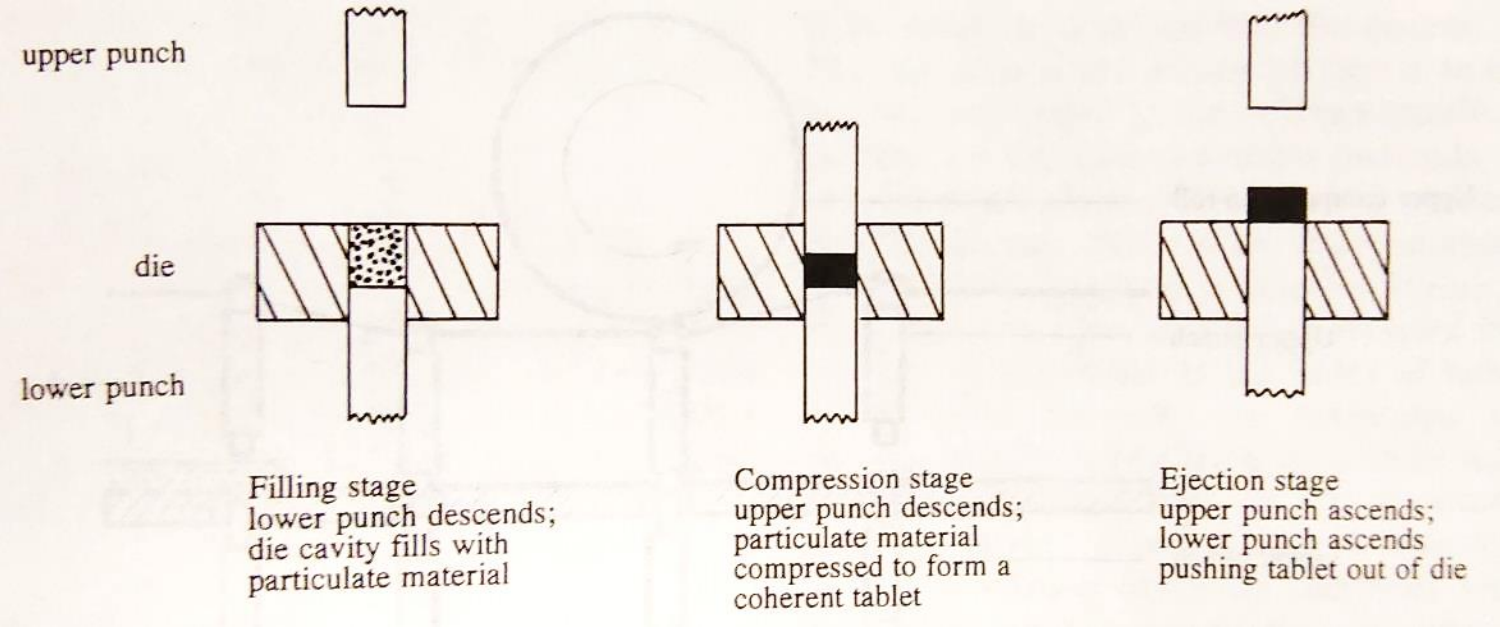
Powder Compression & Compaction



- Compression
  - The reduction in volume when loaded in a confined space

Table 31.2 Dominating compression mechanisms for dense particles and granules (porous particles)

Dense particles	Granules
Repositioning of particles	Repositioning of granules
Particle deformation	Granule deformation
elastic	(permanent)
plastic	Granule densification
viscous/viscoelastic	Granule fragmentation/attrition
Particle fragmentation	Deformation of primary particles

- Compaction
  - The propensity of a powder to form a coherent tablet (“compact”)
  - Fundamentally a bonding process between particles
  - High compactability means the resultant tablet will have high resistance towards fracture
  - Plastic deformation and brittle fracture produce strong compacts

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Evaluation of Materials: Mechanical Property Characterisation

- Tensile strength
  - Compactability reflects a material's ability to exhibit tablet strength as a function of the solid fraction within the compact
  - This strength refers to the tensile strength of the tablet
  - Tablet strength, however, is most often determined by compressive hardness testing
  - Tablet hardness can be converted to tensile strength which is independent of tablet shape and dimension-> Useful for comparison

Compressive

Tensile

- Young's Modulus
  - Young's modulus defines the stiffness and toughness of a material
  - High Young's modulus means greater stiffness (e.g. hard rigid materials)
  - Low Young's modulus means lower stiffness (e.g. soft elastic materials)

$$E = \frac{\sigma}{\varepsilon}$$

E	=	Young's elastic modulus
σ	=	Deformation stress
ε	=	Deformation strain

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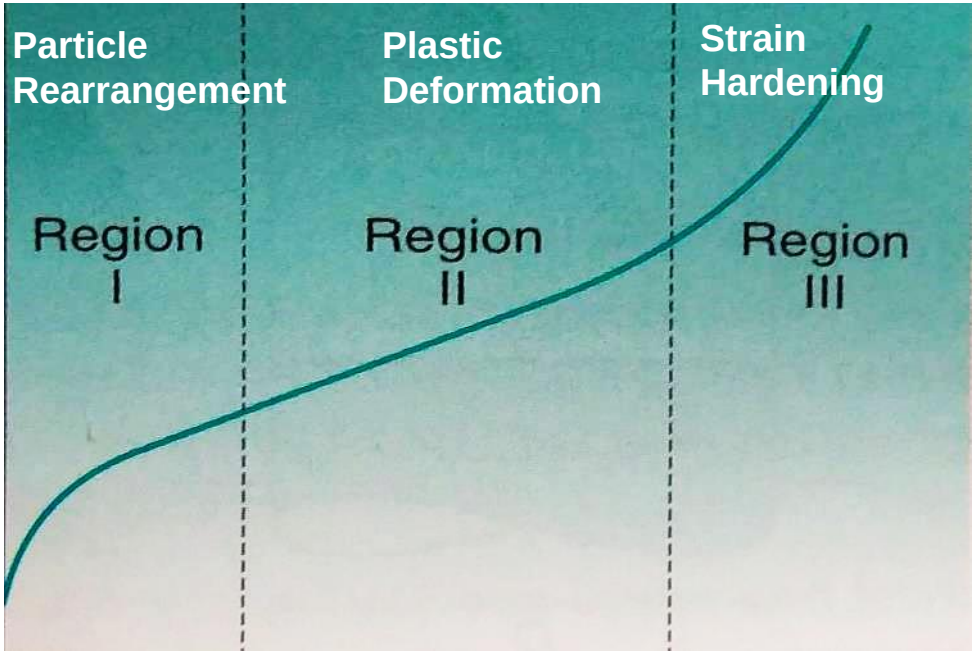
Evaluation of Materials: Mechanical Property Characterisation

$$\text{Ln}\,(1/(1-D)) = kP + A$$

$$y = mx + c$$

D = Relative Density
k = Heckel Constant
P = Applied Pressure
A = Particle Rearrangement & Bonding before compression



- Heckel plots
  - Heckel plot and Heckel equation describes powder compressibility
  - Heckel's equation examines the relationship between porosity and applied compression pressure
  - The equation describes powder compression as a first order reaction where density is a reactant and solid densification is the product
  - The Heckel constant provides information on the yield value of the material and also its plasticity
  - Reciprocal of slope (1/k) gives the yield value (P_y); the magnitude of P_y provides information on when plastic deformation will occur

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Evaluation of Materials: Mechanical Property Characterisation

- Tabletting Indices
  - "Index" (Pl. "Indices")-> Reference
  - Developed by Everett Hiestand-> Made indices using a triaxial press that allows control of horizontal and vertical pressures within a die cavity
  - Two indices of importance-> Bonding index (BI) and Brittle fracture index (BFI)
  - Indices used to evaluate compactability, select lead drug candidates, detect batch variations in manufacture and examine excipient compatibility

$$BI = \frac{T}{H}$$

$$BFI = 0.5 \times \left(\frac{T}{T_0} - 1\right)$$

T	=	Tensile strength of compact
T_0	=	Tensile strength of compact with a hole in it
H	=	Tablet Hardness

BI: Ability of particles to form a high tensile strength tablet

BFI: Ability of a tablet to resist fracture during handling

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Example: Tabletting Indices and Excipient Selection

TABLE 18.1 Examples of values observed for tableting indices (modified from Table 3 in reference 39)

Material ($\rho_r = 0.9$)	$BI_W \times 10^2$	$BI_b \times 10^2$	BFI
Avicel[a]	3.4	13.5	0.03
Sorbitol	0.46	13.7	0.03
Lactose, spray dried	0.36	1.1	0.12
Sucrose	0.40	2.3	0.68
Ibuprofen[b]	0.76	4.1	0.06
Aspirin	2.1	5.1	0.19
Caffeine	1.4	4.5	0.47
Phenacetin	0.88[c]	1.4	0.43
$CaSO_4 \cdot 2H_2O$	0.79	1.3	0.08

[a]PH-101, microcrystalline cellulose
[b]Lot-to-lot variation regularly observed
[c]Compression pressure slightly $> H_0$

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Application of Material Properties to Tablet Formulation

- The relationships between compaction pressure, tensile strength and solid fraction are critical to characterise the compaction process for a given powder mixture during tabletting

- This relationship is described by three parameters:
  1. Compactability-> Relationship b/w tensile strength and solid fraction
  2. Tabletability-> Relationship b/w tensile strength and compression pressure
  3. Compressibility-> Relationship between compaction pressure and solid fraction

- Evaluation of these factors provides valuable information on a tablet formulation
  1. Insight into the compaction process and mechanical properties of a material
  2. Assessment of deformation mechanism, yield pressure and porosity

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Let's revisit some of the data from some of the last lecture's examples…

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Application of Material Properties to Tablet Formulation: Case Studies

- 1998: Nichols et al., J. Pharm Sci.
  - Investigation of properties of two polymorphs of paracetamol
  - One form was less stable at room temperature but could be directly compressed without any binders

Table 4—Results from the Compaction Simulator Experiments Conducted on Paracetamol Forms I and II with Punch Velocities of 2 and 220 mm s^{-1}

sample	1st run (MPa)	2nd run (MPa)	3rd run (MPa)	mean (MPa)	standard deviation	strain rate sensitivity (%)
2 mm s^{-1}						
form I	70.06	72.30	72.92	71.76	1.23	
form II	48.42	43.67	42.52	44.87	2.55	
220 mm s^{-1}						
form I	76.59	79.28	79.88	78.58	1.43	9.5
form II	53.87	56.53	56.87	55.76	1.34	24.3

Form II of paracetamol is compacted at a lower stress than Form I

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Application of Material Properties to Tablet Formulation: Case Studies

- 2001: Sun et al., Pharm. Res.
  - Investigation of properties of two polymorphs of sulphamerazine

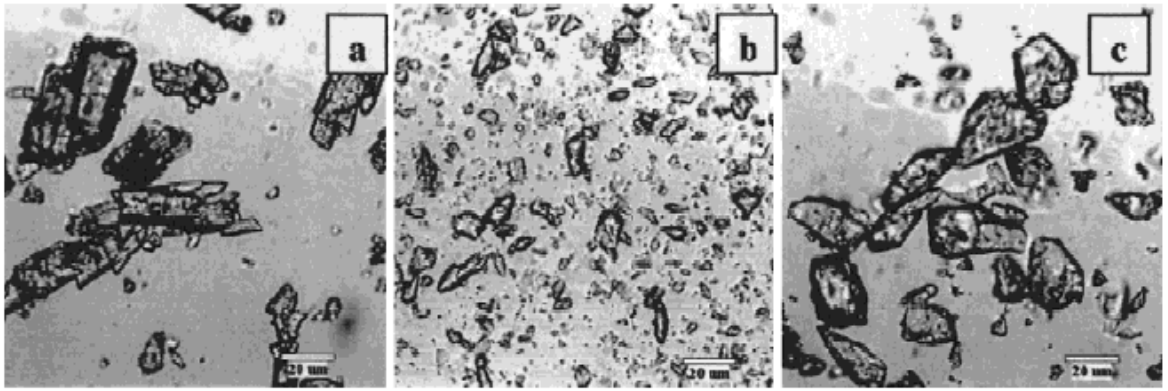

Fig. 1. Photomicrographs of three sulfamerazine powders: (a) **I**; (b) **II(A)**; (c) **II(B)**.

Table I. Densities and Mechanical Properties of Three Sulfamerazine Powders (Standard Deviations in Parentheses)

Powder form	Particle size (μm)	True density[a] (g/cm^3) (n = 3)	Tapped density (g/cm^3) (n = 3)	σ_0 (MPa)[b] (n = 3)	P_y (MPa)[c] (n = 3)
I	10–40	1.335 (0.004)	0.633 (0.004)	5.10	68.4 (1.5)
II(A)	1–15	1.415 (0.005)	0.683 (0.008)	5.77	77.5 (4.5)
II(B)	10–40	1.414 (0.003)	0.751 (0.003)	3.93	86.2 (5.6)

[a] True density is measured using helium pycnometry.

[b] σ_0 is tensile strength extrapolated to zero porosity in Eq. (3).

[c] P_y is the mean yield pressure, which is derived from Heckel analysis, Eq. (2).

Application of Material Properties to Tablet Formulation: Case Studies

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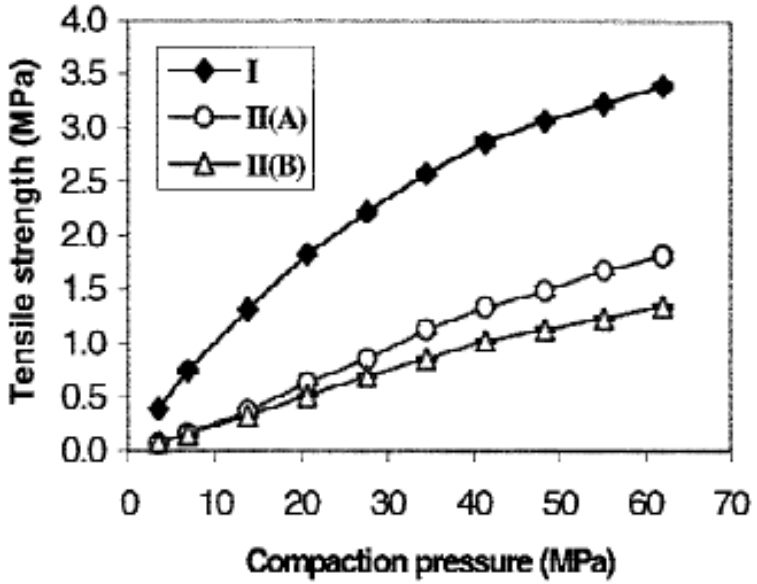

Fig. 3. Plots of tensile strength against compaction pressure, showing the tabletability of three powders of sulfamerazine, **I**, **II(A)**, and **II(B)**. The tabletability follows the order: **I** >> **II(A)** > **II(B)**.

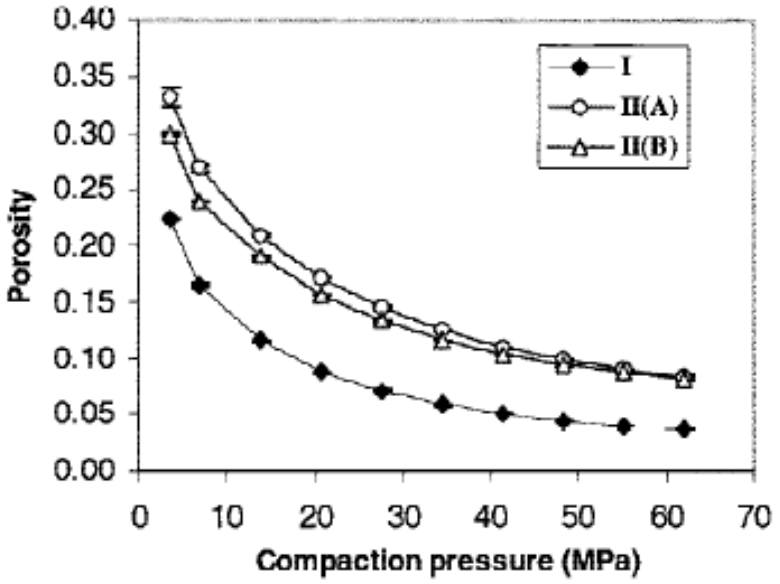

Fig. 4. Plots of tablet porosity against compaction pressure, showing the compressibility of three powders of sulfamerazine, **I**, **II(A)**, and **II(B)**. The compressibility follows the order: **I** >> **II(B)** > **II(A)**.

Form I of sulphamerazine exhibits:
Lowest yield value
Greatest tensile strength
Greatest compressibility

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Learning Outcomes

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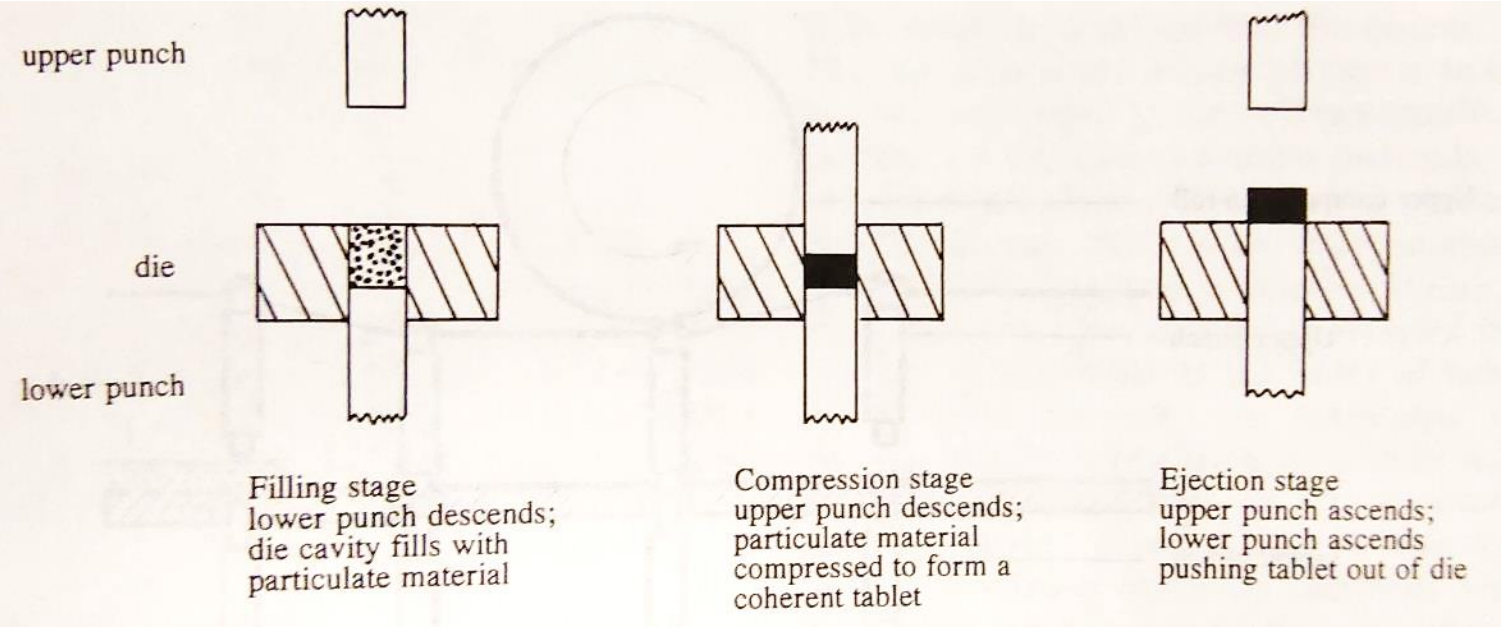

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