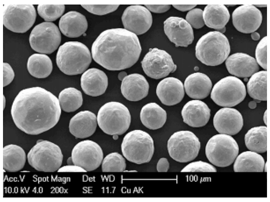
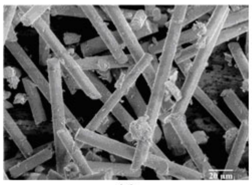
Microscopic examination

- It gives an indication of:
  - particle shape (crystallography)
  - size range
  - Crystal structure
- Importance:
- Problems in formulation processing can be attributable to particle shape and size.
  - Free flowability is dependant on particle size and shape.





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Microscopic examination

- Problem with crystallography (Can be detected by phtomicrograph):
  - Change in crystal habit may occur during manufacturing and/or storage.
  - Reason is conditions of crystal growth
  - Crystals are characterized by repetition of atoms or molecules in a regular three-dimensional structure.
  - Crystal growth should be controlled

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Heat of Vaporization

- Vapor pressure is important in the operation of:
  - Implantable pumps delivering medications
  - Aerosol dosage forms.
  - Nasal inhalants
  - Some volatile drugs can even migrate within a tablet dosage form so the distribution may not be uniform any longer.

Heat of Vaporization

- Exposure of personnel to hazardous drugs due to handling, spilling, or aerosolizing of drugs that may vaporize (**oncology agents**) is another application as the increase in mobility of the hazardous drug molecules may be related to temperature of the environment.

	MEASURED VAPOR PRESSURE (PA)	
COMPOUND	20°C	40°C
Carmustine	0.019	0.530
Cisplatin	0.0018	0.0031
Cyclophosphamide	0.0033	0.0090
Etoposide	0.0026	0.0038
Fluorouracil	0.0014	0.0039

Melting point depression

- Melting point: Temperature at which the pure liquid and solid exist in equilibrium.

Importance:

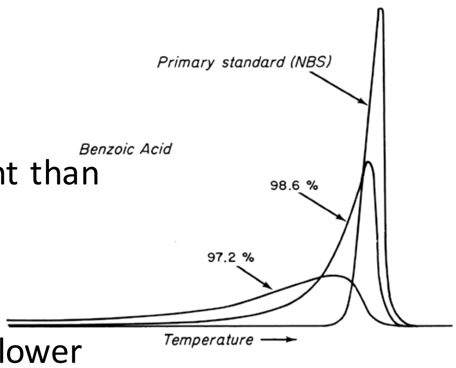
1. A measure of purity.
   - Change in melting point if substance impure
2. Melting during processing
   - For low melting point substances, Drugs may soften during a processing step in which heat is generated, such as particle size reduction, compression

Melting point depression

A measure of purity.

- Change in melting point if substance impure

Pure substance has a sharp peak at a certain temp



Role: Pure substances have higher melting point than impure ones

The addition of a second component to a pure compound will result in a melting point that is lower than that of the pure compound

Melting point depression

$$\Delta T = \frac{2.303\ RTT_0}{\Delta H_f} \log N_A$$

ΔT: Heat absorbed
ΔH_f: Molar heat of fusion.
T: Equilibrium temp.
T_0: Melting point of the pure sub.
N_A: Mole fraction of the second added sub.
R: Gas constant

The molar heat of fusion (ΔH_f) is the quantity of heat absorbed when 1 mole of a solid melts.

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Melting point depression

$$\Delta T = \frac{2.303\ RTT_0}{\Delta H_f} \log N_A$$

- Melting point has an inverse relationship with mole fraction of the second added sub
- When a second ingredient is added to a compound with a low molar heat of fusion, a large lowering of the melting point is observed

Melting point depression

$$\Delta T = \frac{2.303\, RTT_0}{\Delta H_f} \log N_A$$

- Substances with a high molar heat of fusion will show little change in melting point with the addition of a second component.
- Compounds with low melting points are affected to a greater extent than compounds with high melting points upon the addition of a second component

Phase Diagrams

- Diagrams that show visual picture of presence of **solids** and **liquids** phases in **binary**, **tertiary** and other systems.