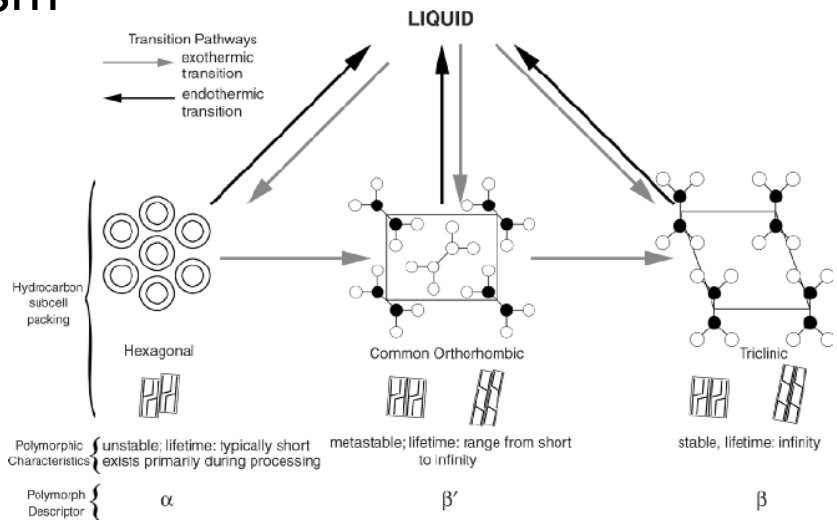
Polymorphism



63

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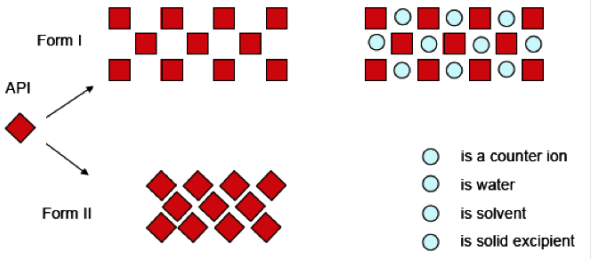
Hydrates and solvates



- If water is present in crystal lattice material is a hydrate
- If a solvent molecule is present in crystal lattice material is a solvate

64

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Amorphous material

- Molecules can also occur in non-crystalline or amorphous structure.
- The amorphous form of a compound is always more soluble than a corresponding crystal form.
  - The energy required for a molecule of drug to escape from a crystal is much greater than is required to escape from an amorphous powder.

65

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Insulin – Zinc Mixture

- In the presence of acetate buffer, zinc combines with insulin to form an extremely insoluble complex.
- This complex is either **amorphous** precipitate or **crystalline** product depending on environmental pH.
- The amorphous form, containing particles of no uniform shape and smaller than 2 μm, is absorbed following intramuscular or subcutaneous injection and has a short duration of action.
- The crystalline product, consisting of 10–40 μm sized rhombohedral crystals, is more slowly absorbed and has a longer duration of action.

66

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Techniques for studies of crystals

- Microscopy
- Hot stage microscopy
- Thermal analysis
- X-ray diffraction

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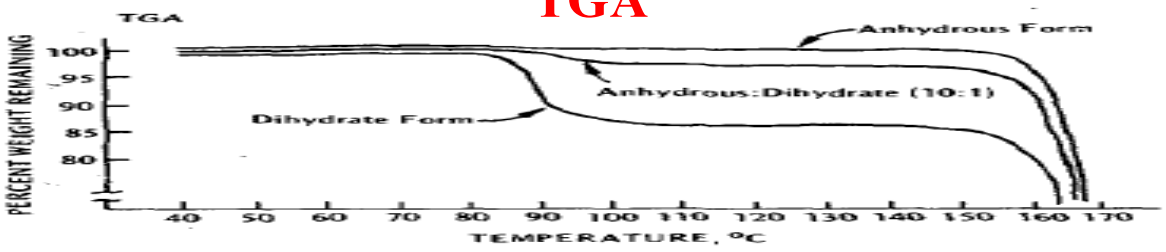
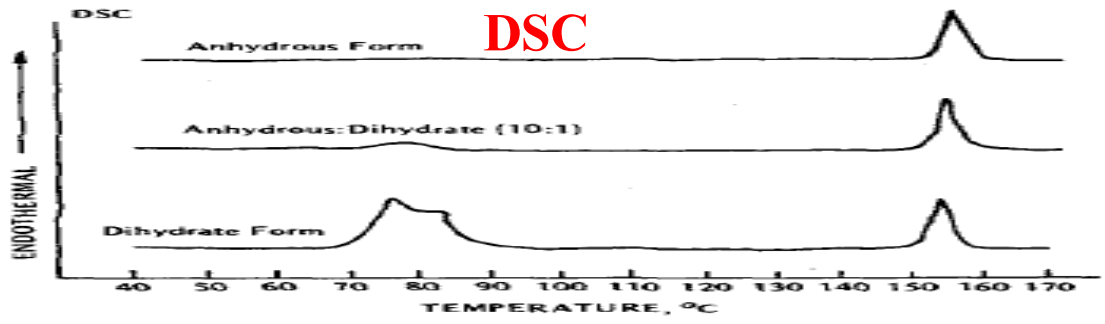
TGA



DSC



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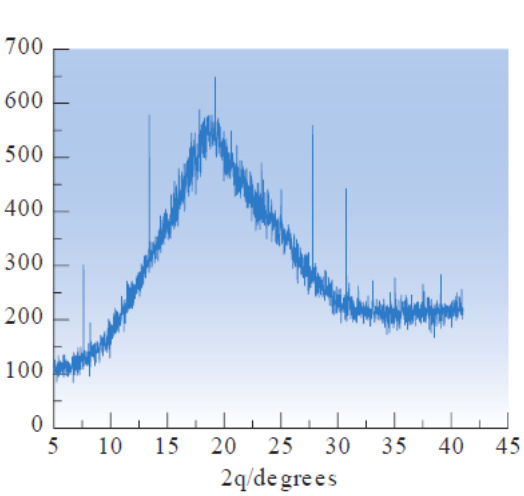

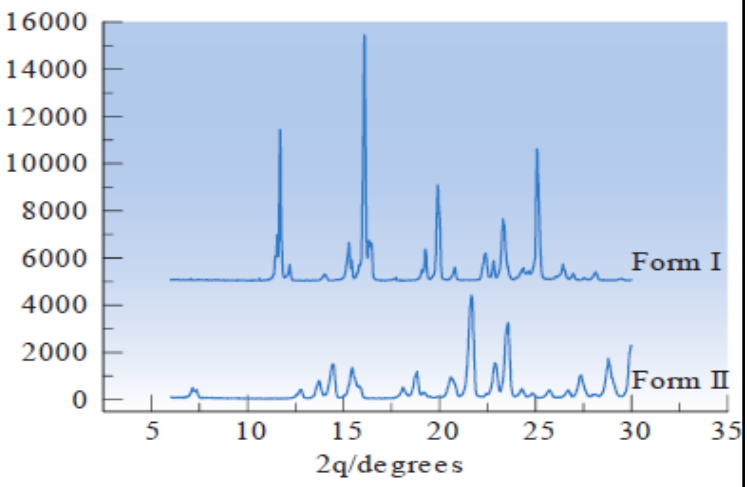

Fig. 23.13 • XRPD diffractograms for two polymorphs of sulfapyridine.

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Solubility

- The concentration of solute in saturated solution, at a certain temp.
- High solubility is usually preferred as it is accompanied by high dissolution rate.
- Usually determined by the equilibrium solubility method.
  - By which an excess of the drug is placed in a solvent and shaken at a constant temperature over a long period until equilibrium is obtained.
  - Concentration is then determined by analysis.
  - Usually carried out at 37ºC, or at 4ºC (why?)
- Kaplan (1972) suggested that unless a compound has an aqueous solubility in excess of 1% (10 mg/mL) over the pH range 1-7 at 37°C, potential bio-absorption problems may occur.

70

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Solubility

- Oral ingestion is the most convenient and commonly employed route of drug delivery
- The major challenge with the design of oral dosage forms lies within their poor bioavailability. The cause of low oral bioavailability is the poor solubility and low permeability.
- Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption.
- More than 40% of newly synthesized molecules developed in the pharmaceutical industry are insoluble in water

71

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General Method of Increasing the Solubility