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T or F with explanation:

- **If solubility is <1mg/ml indicates need for salt formation to improve solubility.**
- **If solubility is <1mg/ml in pH= 1 to 7, preformulation study should be initiated.**

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Dissolution Rate

- The process of dissolving a solid substance into a solvent to make a solution
- Time needed for the drug to dissolute (converts from solid to liquid).
- A rate limiting step for oral and intramuscular administration.
- It can influence bioavailability, onset of action, duration, intensity of effect

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Dissolution Rate depend on:

$$\frac{dm}{dt} = \frac{k_l A(C_S - C)}{h}$$

- *A* = surface area of undissolved solid
- Cs = solubility of solid in dissolution medium.
- *C* = concentration of solute in solution at time *t*
- *K* = dissolution rate constant

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Dissolution Rate

- It can be increased by:
  - Decreasing the drug's particle size.
  - Increasing drug's solubility (e.g. salt formation)
- Soluble salt of a weak acid will precipitate as free acid in the bulk phase of gastric fluid (How this will improve bioavailability?)
- Dissolution rate may be needed to be decreased in some instances (When?)

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- Dissolution rate of a chemical compound can be determined by:

1. Constant-surface method.

2. Particulate dissolution method.

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Constant-surface method

- Provides the intrinsic dissolution rate of the agent.
- Uses a compressed disc of known area.
- Eliminates surface area and surface electrical charges as dissolution variables.
- The dissolution rate here is characteristic of each solid compound and a given solvent in the fixed experimental conditions.
- The value is expressed as milligrams dissolved per minute per centimetres squared ($mg/min/cm^2$)
- Useful in predicting **probable absorption problems** due to dissolution rate.

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Particulate dissolution

- Weighed amount of powdered sample is added to the dissolution medium in a constant agitation system.
- This method is frequently used to study the influence of particle size, surface area, and excipients.
- The surface properties of the drug produce an inverse relationship of particle size to dissolution.
- Surface charge and/or agglomeration results in the reduced particle size form of the drug presenting a lower effective surface area to the solvent due to incomplete wetting or agglomeration.

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Membrane Permeability

- Early assessment of passage of drug molecules across biologic membranes.
- Biological membranes are fat barriers.
  - Lipophilic drugs pass by passive diffusion.
  - Lipophobic drugs are more difficult to pass.
- Affected by:
  - pKa
  - pH of absorption site.
  - Lipid solubility.
  - Dissolution rate.

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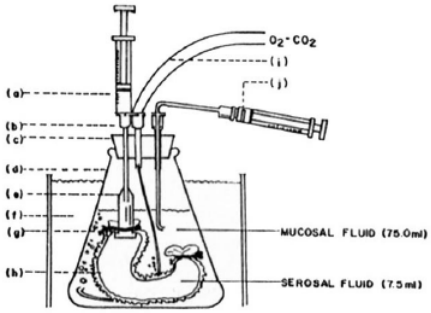
Everted intestinal sac

- Used to evaluate absorption characteristics of drug substances.
- A piece of intestine is removed from an intact animal and filled with a solution of the drug substance.
- Degree and rate of passage of the drug through the membrane sac are determined.
- This method allows evaluation of both passive and active transport.



CANNULATED EVERTED INTESTINE
(IN VITRO)

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Partition Coefficient

- Best measure of lipophilicity.
- Calculated from the distribution of solute (unionised form) between 2 immiscible liquids at a constant temperature.

$$K = Co/Cw$$

- Extraction of crude drugs and determination of solubility
- Extraction of drugs from biologic fluids for therapeutic drug monitoring.
- Predict the pharmacokinetics of the drug.
- Absorption of drugs from dosage forms (ointments, suppositories, transdermal patches)
- Study of the distribution of flavoring oil between oil and water phases.
- Recovery of antibiotics from fermentation broth.

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