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It's Important to Know!

BP302T — Physical Pharmaceutics I

B.Pharm Semester 3 · Unit 4 — Complexation and protein binding

Unit IV: Complexation and protein binding

Complexation

Complexation is reversible association between a central species and one or more ligands. Complexes may be coordination complexes, chelates, molecular complexes, inclusion complexes or ion-pair systems. The classification depends on the interacting species and the type of bonding or enclosure.

The stability constant describes the equilibrium preference for complex formation. A larger conditional stability constant indicates stronger association under the stated conditions. Temperature, pH, ionic strength and competing ligands change the observed value.

Analysis and applications

Complexes may be studied by phase-solubility analysis, spectroscopic methods, distribution measurements, potentiometry or other validated approaches. Complexation can increase apparent solubility, protect a labile group, reduce irritation, alter taste, change membrane transport or modify release. It can also reduce free drug concentration and cause incompatibility.

Protein binding

Protein binding is usually reversible and may involve hydrophobic, ionic, hydrogen-bonding or van der Waals interactions. The free fraction can cross membranes and interact with targets, while bound drug acts as a reservoir. Binding is influenced by protein concentration, affinity, pH, competing substances and disease-related changes. A bound fraction is not automatically inactive.

Unit IV: Frequently asked questions

Q: What is a stability constant?

A: It is an equilibrium constant that describes the extent of association between a complexing species and its ligand under stated conditions.

Q: Why can complexation change drug solubility?

A: The complex may have different water affinity and may reduce the activity of free drug, changing the measured total concentration.

Q: Why is free drug important in protein binding?

A: The free fraction is generally the fraction available for diffusion, distribution and direct interaction, although the relationship is dynamic.

Unit IV: Key takeaways

- Complexes form reversibly through several possible interaction types.
- Stability constants are conditional on experimental conditions.
- Complexation can help or harm formulation performance.
- Protein binding changes the distribution between free and associated drug.
- Complexation must be evaluated with the final formulation components.

Unit IV: Practical correlation

Practical correlation: incompatibility screening. A formulation should be checked for complex formation between drug, excipient and container-related substances. The acceptable interaction level for a named product is set out in its approved specification.