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BP302T — Physical Pharmaceutics I

B.Pharm Semester 3
3 hrs/week · 4 credits · 45 hours · 100 marks (25 internal + 75 end-semester, 3 hr paper)

Complete notes — all 5 units in one PDF

- Unit 1 — Solubility and distribution phenomena
- Unit 2 — States of matter and physicochemical properties
- Unit 3 — Surface and interfacial phenomena
- Unit 4 — Complexation and protein binding
- Unit 5 — pH, buffers and isotonic solutions

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BP302T — Physical Pharmaceutics I

B.Pharm Semester 3 · Unit 1 — Solubility and distribution phenomena

Unit I: Solubility and distribution phenomena

Solubility and expressions

Solubility is the amount of solute that dissolves in a specified amount of solvent at a specified temperature and pressure. It may be expressed as mass per volume, molarity, molality, mole fraction or percentage. Intrinsic solubility describes the neutral form, while total solubility can include ionised forms.

Solute-solvent interaction, crystal lattice energy, temperature, pH, particle size, salt form, polymorphism and cosolvents can affect dissolution. A solution is ideal when intermolecular interactions are sufficiently similar for activity to approximate concentration. Real solutions show activity coefficients that differ from one.

Gas and liquid solubility

Gas solubility in a liquid commonly changes with pressure and temperature. Henry-type relationships describe dilute gas systems, but the constant and concentration convention must be specified. Miscible liquids form a single phase over the composition range. Partially miscible liquids have limited mutual solubility and may show a critical solution temperature.

Raoult's law relates the partial vapour pressure of a component in an ideal solution to its mole fraction and pure-component vapour pressure. Deviations occur when unlike and like molecular interactions differ. Exact treatment of a named system should be checked against the prescribed text.

Distribution law and diffusion

At equilibrium, a solute distributes between two immiscible solvents in a constant ratio when it remains in the same molecular state and the system is dilute. Ionisation, association, complexation and concentration can invalidate the simple form. Distribution behaviour supports extraction and can influence membrane transport.

Diffusion is net movement caused by a concentration gradient. Fick's laws describe steady and unsteady diffusion. In biological systems, membrane area, path length, partitioning, viscosity and the concentration gradient affect flux.

Unit I: Frequently asked questions

Q: What is intrinsic solubility?

A: It is the equilibrium solubility of the neutral form of a compound, without the contribution from ionised species.

Q: Why can pH change drug solubility?

A: Ionisation changes the balance between neutral and charged species, and charged species often have different aqueous solubility.

Q: What is the main condition for a simple distribution law?

A: The solute should remain in the same molecular form in both phases and the system should be sufficiently dilute and at equilibrium.

Unit I: Key takeaways

- Solubility depends on both solute-solvent interactions and solid-state energy.
- pH and ionisation can change apparent solubility.
- Ideal and real solutions differ in activity behaviour.
- Distribution law supports extraction but has important limitations.
- Diffusion depends on gradient, area, path length and resistance.

Unit I: Practical correlation

Practical correlation: formulation screening. A preformulation study should record temperature, pH, solid form, equilibration time and analytical method when measuring solubility. The acceptance range for a named product is set out in its approved specification.

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BP302T — Physical Pharmaceutics I

B.Pharm Semester 3 · Unit 2 — States of matter and physicochemical properties

Unit II: States of matter and physicochemical properties

States and transitions

Solids have defined shape and volume, liquids have defined volume but flow, and gases expand to fill their container. Melting, freezing, vaporisation, condensation, sublimation and deposition are phase changes. Latent heat is absorbed or released during a phase change without a temperature change at equilibrium.

Vapour pressure is the pressure of vapour in equilibrium with its condensed phase. It rises with temperature. The critical point is the end of the liquid-gas coexistence curve. Eutectic mixtures can melt at a temperature lower than either pure component. These concepts matter in drying, storage and processing.

Pharmaceutical solid states

Crystalline solids have long-range order. Amorphous solids lack that long-range order and often have higher apparent energy and faster dissolution, but may be less physically stable. Polymorphs have the same chemical composition but different crystal arrangements. A glassy state is a non-equilibrium amorphous state with a glass-transition temperature.

Relative humidity expresses the amount of water vapour present compared with the saturation amount at that temperature. Moisture can change powder flow, chemical stability and solid form. Aerosols and inhalers require control of particle size, propellant or gas behaviour and delivered dose. Device-specific details should be checked against the manufacturer's instructions.

Physicochemical properties

Refractive index relates the speed of light in a medium to that in a reference medium. Optical rotation describes rotation of plane-polarised light by an optically active substance. Dielectric constant reflects a medium's ability to reduce electrostatic interaction. Dipole moment describes charge separation. Dissociation constant and pKa describe ionisation equilibrium. Each property requires a defined temperature, solvent and method.

Unit II: Frequently asked questions

Q: Why can an amorphous solid dissolve faster than a crystal?

A: Its molecules are not held in a regular crystal lattice and may have higher free energy, although physical instability can follow.

Q: What is a eutectic mixture?

A: It is a mixture with a composition that melts at the lowest temperature in that binary system.

Q: What does pKa describe?

A: It is the negative logarithm of the acid dissociation constant and indicates the tendency of an acid to ionise in a specified medium.

Unit II: Key takeaways

- Phase changes involve latent heat at equilibrium.
- Crystal form, amorphous form, polymorphism and glass transition affect performance.
- Humidity can alter both physical and chemical stability.
- Refractive index, optical rotation, dielectric constant and dipole moment are measured properties with defined conditions.
- Ionisation data are medium-dependent.

Unit II: Practical correlation

Practical correlation: solid-form control. A formulation team should compare polymorph, amorphous content, moisture and thermal behaviour before selecting a manufacturing process. The required solid form for a named drug is set out in its approved specification.

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BP302T — Physical Pharmaceutics I

B.Pharm Semester 3 · Unit 3 — Surface and interfacial phenomena

Unit III: Surface and interfacial phenomena

Surface tension and interfacial tension

Surface tension is the force or free-energy effect associated with a liquid surface. Interfacial tension occurs at the boundary between immiscible phases. Both arise from unbalanced molecular forces at an interface. Methods include capillary rise, drop weight, drop volume, ring and plate methods. Method selection and correction factors are set out in the prescribed text.

The spreading coefficient helps predict whether one liquid spreads over another surface. Lowering interfacial tension can improve wetting, dispersion and emulsification, but does not alone guarantee physical stability.

Surface-active agents and HLB

Surfactants contain a portion compatible with the continuous phase and a portion attracted to another phase or interface. They adsorb at interfaces and can lower surface or interfacial tension. The hydrophile-lipophile balance system provides a practical way to compare surfactant tendencies. Exact HLB ranges for a specific application should be checked against the prescribed text.

Surfactants support wetting, detergency, solubilisation, emulsification and micelle formation. Concentration above the critical micelle concentration can produce aggregates. The effect depends on temperature, electrolyte, pH, surfactant structure and drug interactions.

Adsorption at solid interfaces

Adsorption is accumulation at an interface, unlike absorption into the bulk. Physical adsorption is usually weaker and more reversible than chemisorption. Isotherms relate the amount adsorbed to equilibrium concentration or pressure. Adsorbents can remove impurities, alter drug availability or stabilise a dispersion.

Unit III: Frequently asked questions

Q: What is the difference between surface and interfacial tension?

A: Surface tension describes a liquid-gas boundary, while interfacial tension describes a boundary between two immiscible phases.

Q: What is the critical micelle concentration?

A: It is the approximate concentration above which added surfactant increasingly forms micelles rather than only increasing monomer concentration.

Q: How is adsorption different from absorption?

A: Adsorption occurs mainly at a surface, while absorption involves entry into the bulk of a material.

Unit III: Key takeaways

- Interfacial energy affects wetting, dispersion and emulsification.
- Surfactants can lower tension and form micelles.
- HLB is a practical guide, not a complete formulation rule.
- Adsorption can be physical or chemical and changes with surface and solute properties.
- Measurement method and conditions must be reported.

Unit III: Practical correlation

Practical correlation: suspension wetting. A poorly wetted powder may float or form lumps; a suitable wetting agent and mixing sequence can improve dispersion. The surfactant concentration and compatibility for a specific formula are set out in its approved specification.

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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.

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BP302T — Physical Pharmaceutics I

B.Pharm Semester 3 · Unit 5 — pH, buffers and isotonic solutions

Unit V: pH, buffers and isotonic solutions

pH and measurement

pH is a logarithmic expression related to hydrogen-ion activity. A pH meter uses an indicator electrode and a reference system, with calibration against appropriate standard buffers. Temperature, junction potential, electrode condition and sample composition affect the result. Colour indicators provide approximate rather than universal values.

Buffers

A buffer resists a change in pH after addition of a small amount of acid or base. It usually contains a weak acid and its conjugate base, or a weak base and its conjugate acid. The Henderson-Hasselbalch equation links pH with pKa and the ratio of conjugate base to acid, within its assumptions. Buffer capacity depends on total concentration, ratio and proximity of pH to pKa.

Buffers support stability, solubility, preservative action, comfort and biological compatibility. A buffer can also accelerate degradation or reduce solubility if selected poorly.

Isotonic solutions

An isotonic solution has an effective osmotic pressure compatible with the intended biological site. Tonicity differs from simple molar concentration because solute dissociation and membrane permeability matter. Sodium chloride equivalent, freezing-point depression and other validated methods can be used to adjust tonicity. The method and target depend on route and are set out in the applicable pharmacopoeia.

Unit V: Frequently asked questions

Q: What is buffer capacity?

A: It is the amount of strong acid or base needed to change the pH of a specified buffer system by a defined amount.

Q: Why should pH be measured after calibration?

A: Calibration relates the electrode response to known standards and helps identify slope or offset errors.

Q: Why is isotonicity important for parenteral or ophthalmic products?

A: A large osmotic difference can cause discomfort, tissue irritation or cell-volume changes at sensitive biological sites.

Unit V: Key takeaways

- pH is related to hydrogen-ion activity and must be measured under controlled conditions.
- Buffers resist pH change but have finite capacity.
- Buffer selection must balance pH, stability, solubility and compatibility.
- Tonicity depends on effective osmotic behaviour, not only concentration.
- Adjustment calculations require the intended route and validated method.

Unit V: Practical correlation

Practical correlation: ophthalmic formulation. pH and tonicity should be adjusted within a range compatible with the eye while preserving drug stability and antimicrobial control. The acceptable product range is set out in the approved specification.