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M.Pharm Practical Notes

Industrial Pharmacy Practicals II

Semester 2

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Dissolution Improvement by Solid Dispersion

Practical 1 - Bench formulation practical

Aim

To prepare a drug-carrier dispersion and compare dissolution with the untreated drug and a physical mixture.

Principle

A solid dispersion distributes drug within a solid carrier. Dissolution may change through wetting, size reduction, altered crystallinity or other drug-carrier interactions. Improved release does not automatically establish an amorphous product.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved slightly soluble model drug and carrier
- Selected fusion or solvent-removal arrangement
- Assay, dissolution and suitable solid-state characterisation methods
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Define the drug-to-carrier ratio and prepare untreated-drug and physical-mixture controls.
4. Use the approved fusion or solvent-removal method, recording temperatures or solvent-removal conditions relevant to material stability.
5. Recover, condition and size the preparation by the specified method, documenting yield and content uniformity.
6. Compare dissolution under identical conditions and use appropriate solid-state evidence when discussing the mechanism.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Preparation	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Drug and carrier ratio	Record the adopted method	Record	Evaluate
Measured content	Record the adopted method	Record	Evaluate
Dissolution / solid-state evidence	Record the adopted method	Record	Evaluate

Calculations

- Theoretical loading (%) = input drug mass / total input solids x 100
- Drug recovery (%) = measured recovered drug / input drug x 100

Worked Example

Illustrative input: 1.00 g drug and 4.00 g carrier give 20.0% theoretical loading.
If the recovered material contains 0.95 g drug, drug recovery is 95.0%.
Compare the dispersion with the physical mixture as well as the untreated drug to distinguish process effects from simple carrier addition.

Result and Interpretation

- Report recovery, content, dissolution and the evidence supporting the proposed physical state.
- State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

- Choose a process within the drug and carrier stability limits.
- Evaluate residual solvent when relevant.
- Avoid equating a missing thermal peak alone with proven amorphisation.
- Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

Why include a physical mixture?

It separates the effects of carrier addition from the preparation process.

Must every dispersion be amorphous?

No; dispersions can contain different material states.

Does faster dissolution prove better clinical exposure?

That requires additional evidence.

Comparison of Dissolution Profiles Between Brands

Practical 2 - Bench practical

Aim

To compare two product release profiles using matched conditions and an appropriate comparison method.

Principle

A dissolution test measures transfer of drug into a defined medium under controlled hydrodynamic conditions. A profile provides information across time and may reveal lag, burst release or incomplete release.

Temperature, apparatus, medium, speed, sampling and analytical method are selected for the product and study purpose. An in-vitro profile alone does not establish a clinical duration of action.

Materials and Requirements

- Qualified dissolution apparatus and the specified vessels
- Product-specific medium and calibrated temperature measurement
- Validated sampling and assay arrangement
- Reference standard and dosage units

Procedure

1. Record product, batch, dose, apparatus, medium composition and volume, agitation, temperature and sampling schedule.
2. Verify apparatus readiness and the method-required medium preparation and deaeration conditions.
3. Introduce units using the prescribed technique and collect individual-vessel samples at the planned times.
4. Use the validated sampling location and filtration procedure. Replace withdrawn volume where specified and document the exact scheme.
5. Measure concentrations within the established assay range using appropriate standards and blanks.
6. Correct for removed drug and dilution. Plot individual and mean cumulative release, retain variability and compare with the applicable criteria.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Time	Measured concentration	Corrected released mass	Release percentage
Initial	Record baseline	Calculate	Calculate
Time point 1	Record	Calculate	Calculate
Time point 2	Record	Calculate	Calculate
Final planned point	Record	Calculate	Calculate

Calculations

- For equal-volume replacement: Mn = V x Cn + v x sum(Ci for earlier samples)
- Release (%) = Mn / initial drug amount x 100

Worked Example

Illustrative V = 900 mL and replacement sample volume v = 10 mL. Concentrations at three times are 0.010, 0.020 and 0.030 mg/mL.

Corrected mass at the third point = 900 x 0.030 + 10 x (0.010 + 0.020) = 27.3 mg.

For a 50.0 mg initial amount, release is 54.6%. This calculation assumes the stated replacement scheme and a stable dissolved analyte.

Profile comparison

- Use the same sampling schedule and method, and retain individual-vessel data for both products.
- For a valid conventional f2 comparison, apply the relevant guidance on unit numbers, variability and late time points. Product-specific conditions take priority.
- f2 = 50 log10(100 / sqrt(1 + mean((R - T)^2))). A value within the conventional similarity range is interpreted only when the prerequisites for that comparison are met.

Result and Interpretation

- Report the entire profile, individual-unit variability and the actual conditions.
- Compare controlled-release products using an appropriate product-specific design and acceptance approach.
- Distinguish incomplete release from analytical loss or an unsuitable test condition.

Precautions

- Maintain method-specified temperature and hydrodynamics.
- Control sampling time, filter recovery and volume replacement.
- Avoid treating pooled samples as evidence of individual-unit uniformity.
- Investigate apparatus or assay failures before interpreting the profile.

Viva Questions and Answers

Why correct for sampling?

Withdrawn fluid removes drug that contributes to cumulative release.

Why examine individual units?

A similar mean can conceal large unit-to-unit variation.

Does faster dissolution always mean a better controlled-release product?

No; performance must match the intended release target.

Comparison of Protein Binding Between Two Drugs

Practical 3 - Practical study

Aim

To compare unbound fractions of two model drugs using an approved equilibrium-dialysis or ultrafiltration dataset.

Principle

Only unbound concentration is used in the binding-fraction calculation. Membrane adsorption, volume shifts, equilibration and nonspecific losses can bias a separation; measured recovery must therefore accompany the binding estimate.

Materials and Requirements

- Supplied total and unbound concentration data or an approved nonclinical model
- Qualified separation system, protein matrix and protein-free controls
- Suitable assay and recovery controls
- Approved method or teaching-data pack and a dated record sheet

Procedure

1. Define the preparation or dataset, study question and method version. Record identities, units and the criteria to be used before examining the outcome.
2. Record protein concentration, buffer, pH, temperature, incubation condition and separation method for both drugs.
3. Measure total concentration and the separated unbound fraction, correcting for dilution and volume changes according to the method.
4. Evaluate membrane adsorption and mass balance with appropriate protein-free and recovery controls.
5. Calculate unbound and bound fractions for independent preparations at matched total concentrations.
6. Retain the original observations and calculations. State deviations, missing information and the limits of the conclusion; do not replace measured values with expected results.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Drug / control	Total concentration	Unbound concentration	Unbound / bound fraction
Drug A	Enter mg/L	Enter mg/L	Calculate
Drug B	Enter mg/L	Enter mg/L	Calculate
Protein-free recovery	Input amount	Recovered amount	Calculate

Calculations

- Unbound fraction fu = Cu / Ctotal
- Bound fraction = 1 - fu; bound (%) = 100 x (1 - fu)

Worked Example

Illustrative A: total 10 mg/L, unbound 1 mg/L gives fu = 0.10 and 90% bound. B: total 10 mg/L, unbound 3 mg/L gives fu = 0.30 and 70% bound.

These comparisons apply to the measured conditions. Concentration-dependent binding and different clinical matrices can change the result.

Result and Interpretation

- Report replicate variability, recovery and the conditions of the comparison.
- Do not convert a binding result directly into a clinical dose recommendation.

Precautions

- Check for protein leakage and membrane adsorption.
- Avoid interpreting poor recovery as binding.
- Keep protein and separation conditions matched.

Viva Questions and Answers

What is fu?

The unbound concentration divided by the total concentration.

Why use a protein-free control?

It helps detect nonspecific losses to the device.

Is binding always concentration independent?

Saturable binding can make the fraction change with concentration.

Paracetamol Bioavailability Data Analysis

Practical 4 - Dataset-based practical

Aim

To calculate dose-normalised paracetamol bioavailability from a supplied animal-study teaching dataset.

Principle

Noncompartmental analysis estimates exposure from the concentration-time profile without first assuming a fixed compartmental structure. Terminal extrapolation requires a defensible terminal phase. IVIVC additionally needs an appropriate relationship between in-vitro release and in-vivo input or response; two similar-looking curves do not establish it.

Keep the supplied data, transformations, software version, analysis settings and complete output together. Record units explicitly and distinguish assumptions from observations.

Materials and Requirements

- Supplied concentration-time data, dose, route and subject identifiers
- Dissolution profiles where an IVIVC investigation is intended
- Spreadsheet or institution-approved analysis software
- Raw-data dictionary and analysis worksheet

Procedure

1. Define the analysis question and the variables, units, identifiers and missing-data conventions in the dataset.
2. Import a working copy and check values against the original file. Inspect ranges, duplicates, timing and unit consistency.
3. Map concentration, time, dose and subject columns and select the intended route and exposure calculation.
4. Inspect the profile and choose the integration method, terminal observations and treatment of below-quantitation values through the stated analysis plan.
5. Calculate Cmax, Tmax, AUC, terminal rate where justified, half-life and extrapolated fraction. Review terminal-fit diagnostics.
6. In WinNonlin or the selected implementation, preserve the model and settings report. For IVIVC, identify the development and validation datasets and the appropriate input-estimation method.
7. Retain diagnostics, intermediate calculations and the selected analysis settings. Explain exclusions and sensitivity checks.
8. Write a conclusion that addresses the stated question and the limitations of the design rather than relying on one fitted statistic.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Parameter	Input or method	Calculated value	Diagnostic / units
Cmax and Tmax	Observed profile	Record	State units
AUC	Selected integration	Record	Check sampling
Terminal slope	Justified points	Record	Review fit

Parameter	Input or method	Calculated value	Diagnostic / units
IVIVC	Development and validation design	Record	State evidence

Calculations

- Linear trapezoid area = (C1 + C2)/2 x (t2 - t1)
- AUC_infinity = AUC_last + C_last/lambda_z, where terminal extrapolation is justified
- Half-life = ln(2)/lambda_z
- After extravascular dosing, dose/AUC estimates CL/F rather than true clearance unless F is known.

Worked Example

Illustrative oral profile: times 0, 1, 2, 4, 6 and 8 h; concentrations 0, 8, 4, 2, 1 and 0.5 mg/L.

Linear trapezoidal AUC to 8 h is 20.5 mg.h/L. The illustrated terminal decline from 2 to 8 h halves every 2 h, giving lambda_z = 0.3466 h^-1.

Tail area = 0.5/0.3466 = 1.443 mg.h/L; AUC_infinity is about 21.943 mg.h/L and half-life is 2.00 h.

A formal analysis uses adequate observations, prespecified methods and appropriate terminal-fit assessment.

Bioavailability record

- Use institution-supplied or explicitly simulated concentration-time data; the record does not require student animal dosing.
- Record study approvals, species, preparation, dose units, sampling plan and validated analytical method when reviewing a real authorised study.
- Illustrative dose-normalised AUC values are 0.18 and 0.24 exposure units per dose unit for oral and intravenous routes. Absolute bioavailability = 0.18/0.24 x 100 = 75.0%.

Result and Interpretation

- Report the exposure parameters and their data basis. Evaluate extrapolated exposure and the adequacy of terminal sampling.
- State separately whether an IVIVC was developed, tested or only proposed.

Precautions

- Do not mix concentration or time units.
- Distinguish observed from model-derived values.
- A regression between dissolution and plasma concentration is not automatically a validated Level A IVIVC.
- Preserve the original dataset and a reproducible record of the analysis.

Viva Questions and Answers

Why select the terminal phase carefully?

The selected slope affects half-life and extrapolated exposure.

What is CL/F?

Apparent clearance after an extravascular dose when absolute bioavailability is not established.

Why use separate IVIVC validation evidence?

The fitted relationship must predict data beyond the observations used to develop it.

Pharmacokinetic and IVIVC Analysis in WinNonlin

Practical 5 - Software and data-analysis practical

Aim

To perform noncompartmental pharmacokinetic calculations and evaluate the evidence needed for an IVIVC analysis.

Principle

Noncompartmental analysis estimates exposure from the concentration-time profile without first assuming a fixed compartmental structure. Terminal extrapolation requires a defensible terminal phase. IVIVC additionally needs an appropriate relationship between in-vitro release and in-vivo input or response; two similar-looking curves do not establish it.

Keep the supplied data, transformations, software version, analysis settings and complete output together. Record units explicitly and distinguish assumptions from observations.

Materials and Requirements

- Supplied concentration-time data, dose, route and subject identifiers
- Dissolution profiles where an IVIVC investigation is intended
- Spreadsheet or institution-approved analysis software
- Raw-data dictionary and analysis worksheet

Procedure

1. Define the analysis question and the variables, units, identifiers and missing-data conventions in the dataset.
2. Import a working copy and check values against the original file. Inspect ranges, duplicates, timing and unit consistency.
3. Map concentration, time, dose and subject columns and select the intended route and exposure calculation.
4. Inspect the profile and choose the integration method, terminal observations and treatment of below-quantitation values through the stated analysis plan.
5. Calculate Cmax, Tmax, AUC, terminal rate where justified, half-life and extrapolated fraction. Review terminal-fit diagnostics.
6. In WinNonlin or the selected implementation, preserve the model and settings report. For IVIVC, identify the development and validation datasets and the appropriate input-estimation method.
7. Retain diagnostics, intermediate calculations and the selected analysis settings. Explain exclusions and sensitivity checks.
8. Write a conclusion that addresses the stated question and the limitations of the design rather than relying on one fitted statistic.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Parameter	Input or method	Calculated value	Diagnostic / units
Cmax and Tmax	Observed profile	Record	State units
AUC	Selected integration	Record	Check sampling

Parameter	Input or method	Calculated value	Diagnostic / units
Terminal slope	Justified points	Record	Review fit
IVIVC	Development and validation design	Record	State evidence

Calculations

- Linear trapezoid area = (C1 + C2)/2 x (t2 - t1)
- AUC_infinity = AUC_last + C_last/lambda_z, where terminal extrapolation is justified
- Half-life = ln(2)/lambda_z
- After extravascular dosing, dose/AUC estimates CL/F rather than true clearance unless F is known.

Worked Example

Illustrative oral profile: times 0, 1, 2, 4, 6 and 8 h; concentrations 0, 8, 4, 2, 1 and 0.5 mg/L.

Linear trapezoidal AUC to 8 h is 20.5 mg.h/L. The illustrated terminal decline from 2 to 8 h halves every 2 h, giving lambda_z = 0.3466 h^-1.

Tail area = 0.5/0.3466 = 1.443 mg.h/L; AUC_infinity is about 21.943 mg.h/L and half-life is 2.00 h.

A formal analysis uses adequate observations, prespecified methods and appropriate terminal-fit assessment.

Result and Interpretation

- Report the exposure parameters and their data basis. Evaluate extrapolated exposure and the adequacy of terminal sampling.
- State separately whether an IVIVC was developed, tested or only proposed.

Precautions

- Do not mix concentration or time units.
- Distinguish observed from model-derived values.
- A regression between dissolution and plasma concentration is not automatically a validated Level A IVIVC.
- Preserve the original dataset and a reproducible record of the analysis.

Viva Questions and Answers

Why select the terminal phase carefully?

The selected slope affects half-life and extrapolated exposure.

What is CL/F?

Apparent clearance after an extravascular dose when absolute bioavailability is not established.

Why use separate IVIVC validation evidence?

The fitted relationship must predict data beyond the observations used to develop it.

Cell Permeability and Metabolism Data Interpretation

Practical 6 - Software and data-analysis practical

Aim

To calculate apparent permeability and interpret cell-based metabolism observations from a supplied approved dataset.

Principle

A permeability experiment measures transport across a defined barrier under controlled donor and receiver conditions. Apparent permeability reflects the chosen system and requires area, concentration, time, recovery and barrier-integrity information. Disappearance of parent compound alone does not establish metabolism. Keep the supplied data, transformations, software version, analysis settings and complete output together. Record units explicitly and distinguish assumptions from observations.

Materials and Requirements

- Institution-supplied permeability or metabolism dataset
- Membrane or authorised cell-system description, area and donor concentration
- Integrity controls and analytical recovery information
- Spreadsheet or institution-approved analysis software
- Raw-data dictionary and analysis worksheet

Procedure

1. Define the analysis question and the variables, units, identifiers and missing-data conventions in the dataset.
2. Import a working copy and check values against the original file. Inspect ranges, duplicates, timing and unit consistency.
3. Record the barrier system, direction, area, concentrations and sampling and replacement scheme.
4. Verify that the dataset includes appropriate blanks, integrity evidence, donor and receiver measurements and recovery checks.
5. Identify a justified approximately linear transport interval and calculate the transported amount per unit time.
6. Calculate apparent permeability with the correct area and concentration units. Compare reverse-direction or control data only when the design supports it.
7. For metabolism observations, examine parent and metabolite evidence, binding and recovery before attributing loss to enzymatic conversion.
8. Retain diagnostics, intermediate calculations and the selected analysis settings. Explain exclusions and sensitivity checks.
9. Write a conclusion that addresses the stated question and the limitations of the design rather than relying on one fitted statistic.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Interval / preparation	Transported amount	Integrity / recovery	Calculated response
Control	Record	Record	Assess
Test interval 1	Record	Record	Calculate
Test interval 2	Record	Record	Calculate
Reverse direction if supplied	Record	Record	Compare

Calculations

- Papp = (dQ/dt) / (A x Cdonor)
- For consistent units, nmol/s divided by cm^2 x nmol/cm^3 gives cm/s.

Worked Example

Illustrative dQ/dt = 0.020 nmol/s, area = 1.00 cm^2 and maintained donor concentration = 100 nmol/cm^3.
Papp = 0.020/(1.00 x 100) = 2.0 x 10^-4 cm/s.
Interpret with barrier integrity, recovery and the interval assumptions. This value does not directly specify human absorption.

Result and Interpretation

- State system-specific limitations and distinguish transport, binding, degradation and metabolism evidence.

Precautions

- Use supplied or institution-approved data and systems.
- Correct sampling and concentration units.
- Avoid biological interpretation when barrier integrity or recovery is inadequate.
- Preserve the original dataset and a reproducible record of the analysis.

Viva Questions and Answers

Why assess barrier integrity?

A damaged barrier can produce misleadingly high transport.

Why measure recovery?

Material can bind, degrade or be lost during handling.

Does parent loss prove metabolism?

No; other processes can also reduce parent concentration.

Formulation and Evaluation of Tablets

Practical 7 - Bench formulation practical

Aim

To prepare a tablet batch by the selected process and evaluate relevant in-process and finished attributes.

Principle

Tablet quality depends on material attributes, blend uniformity, flow, granulation where used, lubrication and compaction. Different manufacturing processes need different controls; direct compression and wet granulation are not interchangeable instructions.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved teaching formula and identified raw materials
- Selected blending or granulation process
- Guarded tablet press operated by trained staff and qualified evaluation equipment
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Issue the batch sheet for the selected route and calculate material quantities on the stated potency and moisture basis.
4. Prepare the blend or granules using the approved sequence and record intermediate weights, conditioning and blend or granule observations.
5. Have the trained operator compress at the planned settings, checking unit mass and relevant in-process attributes.
6. Evaluate appearance, dimensions, mechanical properties, content and release attributes required by the intended tablet.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Blend / granule record	Record the adopted method	Record	Evaluate
In-process unit measurements	Record the adopted method	Record	Evaluate
Content and physical tests	Record the adopted method	Record	Evaluate
Release result	Record the adopted method	Record	Evaluate

Calculations

• Average unit mass = total mass of units / number of units
• Friability loss (%) = (initial dedusted mass - final dedusted mass) / initial dedusted mass x 100

Worked Example

Illustrative initial and final dedusted masses in the adopted friability test are 6.000 and 5.970 g.
Mass loss = 0.030 g; friability loss = 0.50%. Apply the actual product and test requirements.
If 20 units weigh 8.000 g together, average unit mass is 400.0 mg.

Result and Interpretation

• Report each applicable quality attribute separately and investigate discordant results.
• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Use equipment guards and trained operators.
• Maintain material and batch identity throughout processing.
• Apply the adopted compendial or product method rather than a universal pass rule.
• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

Is unit mass the same as content uniformity?

No; drug distribution can vary even when unit mass is consistent.

Why remove loose dust for friability?

The method defines a consistent mass-loss basis.

Why retain in-process data?

They connect process behaviour to final quality.

Formulation and Evaluation of Capsules

Practical 8 - Bench formulation practical

Aim

To prepare a capsule teaching batch and evaluate fill and relevant quality attributes.

Principle

Capsule quality depends on the shell, fill material and filling process. Powder flow, packing and compatibility can influence filling consistency and subsequent product performance.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved fill formula and capsule shell specification
- Suitable capsule-filling arrangement
- Balance and required physical, assay and release tests
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Calculate target fill composition and choose the shell size through the selected bulk-volume and compatibility assessment.
4. Prepare the blend and assess relevant flow and packing properties before filling.
5. Fill using the specified process and record shell identity, fill mass and process observations.
6. Evaluate mass variation, appearance, content and the disintegration or dissolution characteristics required for the product.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Shell and fill identity	Record the adopted method	Record	Evaluate
Fill mass	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Content / physical tests	Record the adopted method	Record	Evaluate
Release evaluation	Record the adopted method	Record	Evaluate

Calculations

• Net fill mass = filled capsule mass - corresponding empty shell mass
• Relative fill deviation (%) = (individual fill - mean fill) / mean fill x 100

Worked Example

Illustrative filled and empty shell masses are 420 and 90 mg: net fill is 330 mg.
For a mean fill of 325 mg, this unit differs by (330-325)/325 x 100 = 1.54%.
Use the relevant method and sample-size requirements when drawing a formal conclusion.

Result and Interpretation

• Distinguish shell variation from fill variation and state the complete quality evidence.
• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Use suitable shell conditioning and approved materials.
• Control segregation and fill handling.
• Avoid inferring drug-content uniformity from fill mass alone.
• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

Why consider shell compatibility?

Moisture and chemical interactions can affect product stability and function.

What does bulk volume help estimate?

The space required for the selected fill mass.

Does a consistent fill guarantee dissolution?

Release performance requires its own test.

Injection Formulation and Sterile-Production Records

Practical 9 - Placebo and documentation practical

Aim

To prepare a parenteral-formulation development record and assess an approved placebo or supplied-product dataset.

Principle

Preformulation connects material properties to manufacturing and performance risks. Relevant attributes include identity, solid state, solubility, ionisation, particle characteristics, stability and compatibility.

The investigation is driven by the intended route and dosage form. Oral solid development may emphasise flow and compactability, whereas a parenteral concept also requires consideration of aqueous behaviour, route-compatible excipients and sterile-product development.

Materials and Requirements

- Identified drug and candidate excipients
- Suitable solubility, thermal, spectroscopic and particle-characterisation methods
- Calibrated balances and controlled-condition containers
- Material and experimental-design records

Procedure

1. Define the intended dosage form, target product attributes and the questions the study must answer.
2. Review identity and available material information, then select tests that address actual development risks.
3. Determine equilibrium solubility under defined conditions and examine pH dependence when scientifically appropriate.
4. Assess particle size, morphology, flow or compaction behaviour for solid-dose development. Record the measurement method and limitations.
5. Compare the drug, individual excipients and selected mixtures by suitable methods such as FTIR and DSC, supported by relevant storage studies.
6. Prepare a risk matrix linking each result to a formulation or process decision. Identify experiments needed to resolve uncertainty.
7. Write the preformulation report with raw data, material grades, conditions and the rationale for the selected development approach.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute	Method and conditions	Result	Development implication
Identity / solid state	Record	Record	Assess
Solubility / pH	Record	Record	Assess
Particle / flow attributes	Record	Record	Assess

Attribute	Method and conditions	Result	Development implication
Compatibility / stability	Record	Record	Assess

Calculations

• Solubility = dissolved analyte mass / equilibrated liquid volume
• Recovery (%) = recovered measured amount / expected amount x 100

Worked Example

Illustrative equilibrium determination: 12.0 mg analyte is measured in 10.0 mL equilibrated supernatant after correcting the assay dilution.
Solubility = 1.20 mg/mL under the recorded pH and temperature.
A second condition giving 3.60 mg/mL shows a three-fold analytical difference. Stability and material-state changes must be checked before assigning the change solely to improved solubilisation.

Parenteral development record

• Use an institution-approved placebo or provided product records for the exercise. Specify solvent, excipient compatibility, pH, osmolality, particles, container interaction and analytical controls.
• Map the proposed sterile-manufacturing strategy and required evidence to the development report. A laboratory physical-test result does not authorise a product for injection.
• Record aseptic-process or terminal-sterilisation requirements through the approved facility procedures and qualified staff.

Result and Interpretation

• Summarise the development risks and the evidence for the chosen formulation strategy.
• Spectral or thermal changes are investigated in context; a single shifted peak is not sufficient proof of incompatibility.
• Identify the conditions for which the results apply.

Precautions

• Avoid confusing kinetic dissolution with equilibrium solubility.
• Control temperature, equilibration and separation conditions.
• Assess analyte loss to filters or containers.
• Evaluate material and excipient grades relevant to the intended product.

Viva Questions and Answers

Why study preformulation?

It identifies material-related risks before committing to a formulation or process.

Does an FTIR change always prove a chemical reaction?

No; physical interactions and measurement conditions can also alter spectra.

Why specify dosage form?

Different routes and manufacturing processes require different material attributes.

Formulation and Evaluation of an Emulsion

Practical 10 - Bench formulation practical

Aim

To prepare and evaluate an emulsion using a defined phase composition and emulsification method.

Principle

An emulsion disperses one immiscible liquid in another with an appropriate emulsifier system. Droplet size, phase ratio and continuous-phase properties affect physical behaviour. Creaming can be reversible, while coalescence can indicate loss of droplet integrity.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved oil, water and emulsifier system
- Controlled mixing equipment
- Methods for droplet observation, emulsion type, viscosity and phase behaviour
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Prepare the phases and emulsifier system through the adopted method and record phase quantities and process temperature.
4. Combine phases in the specified sequence with controlled shear and duration.
5. Evaluate emulsion type, droplet observations, viscosity and the defined physical-stability measures.
6. Record creaming and any irreversible separation separately, and compare independent preparations.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Phase composition	Record the adopted method	Record	Evaluate
Emulsion type / droplets	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Viscosity	Record the adopted method	Record	Evaluate
Creaming or separation	Record the adopted method	Record	Evaluate

Calculations

• Creaming index (%) = defined cream-layer height / total preparation height x 100, with the convention stated
• State whether a reported layer is a cream layer or a separated phase.

Worked Example

Illustrative cream-layer height 1.5 cm in a 10.0 cm total column gives a creaming index of 15.0%.

Interpret with redispersibility and other evidence; the same numerical index may have different implications for different products.

Result and Interpretation

• State the method and observation period when describing physical stability.
• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Control the phase ratio and mixing conditions.
• Check the meaning of each height measurement.
• Use approved teaching materials and preservation procedures.
• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

What distinguishes creaming from coalescence?

Creaming redistributes droplets; coalescence merges droplets.

Why identify emulsion type?

The continuous phase affects dilution and product behaviour.

Why state observation time?

Physical changes evolve during storage.

Formulation and Evaluation of a Suspension

Practical 11 - Bench formulation practical

Aim

To prepare and evaluate a suspension with controlled dispersion and redispersibility.

Principle

A suspension contains dispersed solid particles in a liquid medium. Wetting, particle characteristics, flocculation and vehicle rheology influence settling and redispersion. Slow sedimentation alone is not sufficient evidence of a satisfactory product.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved insoluble model material and vehicle
- Selected wetting and suspending agents
- Sedimentation, redispersion and relevant content-test equipment
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Wet and disperse the selected solid using the adopted order and levigation or mixing procedure.
4. Incorporate the structured vehicle while maintaining the intended composition and avoiding uncontrolled aeration.
5. Record sedimentation over the defined period and assess redispersibility through the specified procedure.
6. Evaluate uniformity of the redispersed preparation, relevant particle properties, pH and flow behaviour.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Preparation and time	Record the adopted method	Record	Evaluate
Sediment volume	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Redispersion response	Record the adopted method	Record	Evaluate
Uniformity / flow	Record the adopted method	Record	Evaluate

Calculations

• Sedimentation-volume ratio F = ultimate sediment volume / original suspension volume, using the stated measurement convention

Worked Example

Illustrative original volume 100 mL and defined sediment volume 60 mL give F = 0.60.

A second preparation may have a smaller sediment but better redispersibility; compare the full set of intended quality attributes.

Result and Interpretation

• Discuss settling, caking, redispersion and dose uniformity as distinct observations.

• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Use representative sampling after the defined redispersion method.

• Avoid comparing different container geometries without justification.

• Keep wetting and mixing conditions controlled.

• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

Why can caking be undesirable?

It can prevent reliable redispersion and uniform dosing.

Does the largest sedimentation volume always identify the best product?

The complete performance target and redispersibility must be considered.

Why assess the redispersed preparation?

That is the state from which a dose would be withdrawn.

Enteric-Coated Tablets

Practical 12 - Bench formulation practical

Aim

To evaluate an enteric-coated model through defined acid and buffer-stage tests.

Principle

An enteric system is designed to resist release under one set of conditions and permit release under another. Polymer chemistry, coating continuity, coat mass and curing influence the response.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved coated cores or supervised coating process
- Coating-record and physical-inspection methods
- Qualified two-stage release or disintegration method
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Record the core, polymer grade, coating composition, coat mass gain and any curing condition.
4. Inspect coating continuity and dimensions using the adopted procedure.
5. Evaluate the selected acid-stage response followed by the specified buffer-stage response, preserving exact method conditions and timing.
6. Measure drug release where required rather than substituting appearance alone for the product test.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Coat and core identity	Record the adopted method	Record	Evaluate
Acid-stage result	Record the adopted method	Record	Evaluate
Buffer-stage result	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Assay / physical observations	Record the adopted method	Record	Evaluate

Calculations

• Coat mass gain (%) = (coated mass - core mass) / core mass x 100

Worked Example

Illustrative core mass 250 mg and coated mass 270 mg give 8.0% coat mass gain.

A formal conclusion also requires the product-specific acid and buffer-stage criteria; mass gain alone does not establish enteric performance.

Result and Interpretation

• Report both stages and the supporting coating and assay evidence.

• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Use the correct polymer and method conditions.

• Control curing and coating defects.

• Keep teaching preparations identified for laboratory evaluation.

• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

Why use two stages?

The intended response differs between the defined environments.

Can coat mass alone prove function?

No; continuity, chemistry and testing matter.

Why record curing?

It can influence film formation and permeability.

Freeze-Dried Formulations

Practical 13 - Bench formulation practical

Aim

To prepare or evaluate a freeze-dried model and relate the cycle record to product attributes.

Principle

Freeze-drying removes ice by sublimation during primary drying and removes additional water during secondary drying. Freezing behaviour and product temperature relative to critical formulation limits affect structure and recovery.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved model formulation and containers
- Qualified lyophiliser operated by trained staff
- Temperature and pressure records and relevant moisture and reconstitution tests
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Characterise the model formulation and document the basis for the selected cycle and fill conditions.
4. Have the trained operator execute the approved freezing and drying cycle while retaining product, shelf and pressure data.
5. Assess cake appearance, container integrity, residual moisture by the selected method and reconstitution behaviour.
6. Compare results with the intended attribute targets and explain relevant cycle deviations.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Formulation and fill	Record the adopted method	Record	Evaluate
Cycle conditions	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Cake / moisture	Record the adopted method	Record	Evaluate
Reconstitution and recovery	Record the adopted method	Record	Evaluate

Calculations

• Solids recovery (%) = measured recovered dry solids / theoretical input solids x 100

Worked Example

Illustrative theoretical solids per unit 100 mg and recovered solids 98 mg give 98% solids recovery.
A good-looking cake still requires the specified moisture, content, integrity and stability evidence.

Result and Interpretation

• Relate the product evidence to the recorded cycle and critical formulation properties.
• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Operate vacuum and refrigeration equipment through trained staff.
• Use a cycle justified for the model rather than a universal temperature schedule.
• Control handling after drying to avoid moisture uptake.
• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

What is primary drying?

Removal of frozen solvent mainly by sublimation.

Why monitor product temperature?

It relates the cycle to product structural and thermal limits.

Does cake appearance prove stability?

Other chemical and physical evidence is required.

Spray-Dried Formulations

Practical 14 - Bench formulation practical

Aim

To evaluate a spray-dried model using process records, powder recovery and product characterisation.

Principle

Spray drying atomises a liquid feed into a drying-gas stream. Feed properties, atomisation, residence conditions and outlet behaviour influence particle formation. Inlet gas temperature is not identical to particle temperature.

A formulation comparison is meaningful when the raw-material grades, batch size and evaluation conditions are recorded. Change one planned factor at a time or use a documented experimental design, and compare independently prepared batches rather than only repeated readings from one batch.

Materials and Requirements

- Approved aqueous model feed and solids specification
- Qualified spray dryer operated by trained staff
- Powder recovery and particle, moisture and assay methods
- Calibrated balance, suitable containers and identified evaluation equipment
- Controlled batch sheet and raw-data forms

Procedure

1. Define the purpose, formula, batch size, material grades and comparison conditions. Calculate all quantities before weighing.
2. Check equipment readiness and record material identities and actual quantities. Reconcile theoretical and actual batch mass.
3. Record feed solids, viscosity condition, composition and the selected operating procedure.
4. Have the trained operator run the approved atomisation and drying conditions and retain actual operating records.
5. Recover and reconcile powder fractions, documenting wall deposits and collection losses.
6. Evaluate particle properties, moisture, content and any relevant redispersion or dissolution behaviour.
7. Evaluate the stated quality attributes on representative portions using the same method for all comparison batches. Record individual readings and any excluded observations with reasons.
8. Calculate the specified response, variability and material balance. Compare with predefined teaching or product criteria and discuss sources of variation.
9. Label retained preparations and dispose of remaining material through the laboratory procedure. Keep the complete preparation and evaluation record together.

Observations and Record

Enter actual measurements or the supplied teaching data. Record the method, material identity, conditions and units.

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Feed properties	Record the adopted method	Record	Evaluate
Operating records	Record the adopted method	Record	Evaluate

Attribute or stage	Method / conditions	Individual readings	Calculation / comment
Recovered fractions	Record the adopted method	Record	Evaluate
Powder quality	Record the adopted method	Record	Evaluate

Calculations

• Powder yield (%) = recovered powder mass / theoretical feed solids x 100

Worked Example

Illustrative feed mass 500 g at 10.0% solids contains 50.0 g theoretical solids.

Recovered powder 35.0 g gives 70.0% yield.

Discuss wall and collection losses separately from any measured chemical degradation.

Result and Interpretation

• Report yield and powder attributes with the actual feed and operating conditions.

• State the preparation conditions and the evidence supporting the result. A satisfactory physical observation alone does not establish long-term stability, clinical performance or suitability for administration.

Precautions

• Use dust, heat and equipment controls specified for the system.

• Use only approved feed and solvent conditions.

• Avoid interpreting inlet temperature as the exact material exposure temperature.

• Use the laboratory-approved formulation and equipment procedure. Teaching batches are identified for laboratory evaluation.

Viva Questions and Answers

What does atomisation influence?

Droplet size and subsequent particle-formation behaviour.

Why reconcile wall deposits?

They can explain recovery losses.

Does low yield prove degradation?

Physical recovery losses may also be responsible.

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