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Antagonism and Potentiation of an Agonist Curve

Practical 2 - Pharmacology simulation and data practical

Aim

To compare agonist curves under antagonist and potentiating conditions.

Principle

For a simple Hill model E = E0 + (Emax - E0)C^n/(EC50^n + C^n). EC50 is an operational potency measure under the experiment conditions, not automatically a binding affinity.

Materials and Requirements

- Supplied anonymised teaching traces or datasets
- Study design, controls, units and instrument calibration records
- Ethics and welfare records where the original study involved animals
- 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. Identify the study question, experimental unit, controls and original approval or data provenance. This notes exercise uses records or simulation; it is not authorisation to perform animal procedures.
3. Use supplied isolated-preparation traces or simulation and verify baseline, calibration, concentration units and viability controls.
4. Extract responses by a consistent rule and plot response against log molar concentration.
5. Fit a justified concentration-response model, assess residuals and estimate EC50, Emax and uncertainty.
6. Evaluate repeated-curve stability, desensitisation and whether the tested range supports a plateau.
7. Summarise independent experimental units, variability, exclusions and limitations; retain all original traces and data.
8. 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.

Group / preparation	Condition / time	Raw endpoint	Derived result / interpretation
Vehicle / baseline	Record	Enter	Evaluate
Reference condition	Record	Enter	Evaluate
Test condition	Record	Enter	Calculate

Calculations

- pEC50 = -log10(EC50 in mol/L)

Worked Example

Illustrative EC50 = 10^-7 mol/L gives pEC50 = 7.0. For E0 = 0, Emax = 100 and n = 1, concentration equal to EC50 gives response 50.

Curve comparison

- Compare baseline, EC50, Emax and slope on the same response basis with appropriate time controls.
- A parallel rightward shift with preserved maximum can be consistent with reversible competitive antagonism under suitable equilibrium conditions. Other mechanisms and experimental artifacts must be considered.
- Illustrative control EC50 10 nM and exposed EC50 30 nM give dose ratio 3; a left shift may indicate potentiation but requires mechanism-specific controls.

Result and Interpretation

- Provide fitted and raw curves, parameter units and the evidence supporting the model.

Precautions

- Apply replacement, reduction and refinement to study planning.
- Any live work requires the current institutional and Indian CCSEA/IAEC framework, trained staff and an approved protocol.
- Do not convert a teaching calculation into an unapproved animal or patient procedure.

Viva Questions and Answers

What is potency?

The concentration or dose associated with a defined effect under specified conditions.

Is EC50 always Kd?

System response and receptor coupling can make them differ.

Why include a plateau?

It supports estimation of the maximum response.

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