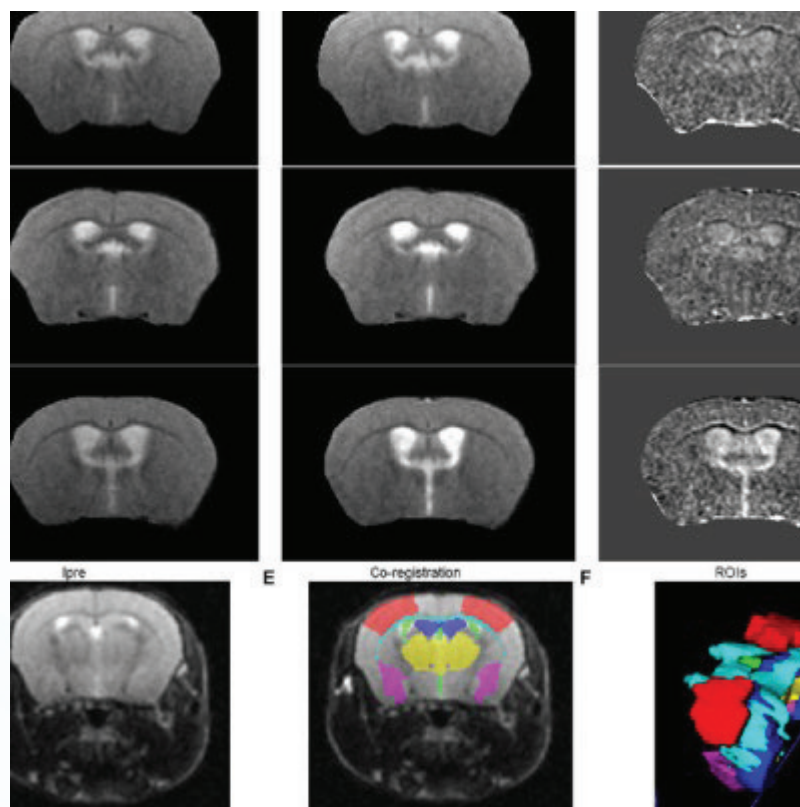




CNS Penetration Studies: Neuro PK Insights from TCGLS

Overview of CNS Penetration Studies

The primary objective of a central nervous system (CNS) penetration study in laboratory animals is to evaluate the ability of a drug or substance to cross from the bloodstream into the brain, CSF, DRGs, spinal cord, etc. This assessment is essential in the development of therapeutics targeting neurological conditions, as it determines whether a compound can access its intended site of action at concentrations necessary for pharmacological effect.

CNS Penetration Following Infusion After Bolus Administration

Brief Design

Animal: Sprague Dawley Rats

Dose & route: 30mg/kg; PO

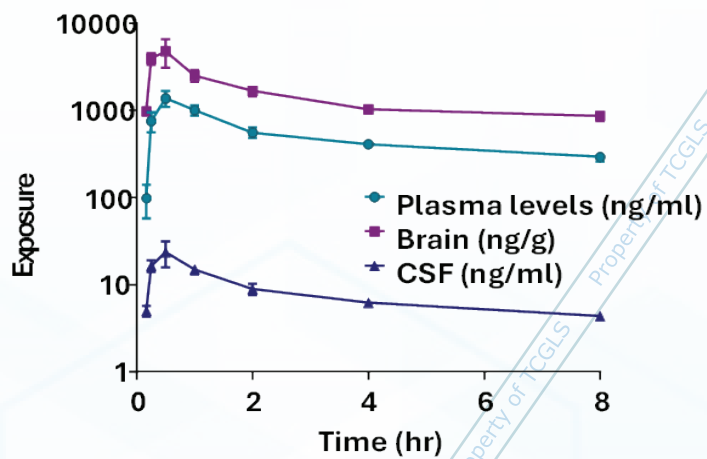
Sampling timepoints: 0.167, 0.25, 0.5, 1, 2, 4, 8 hours

Number of animals: Group sampling; n = 3/timepoint

Biological matrices: Plasma, Brain & CSF



Exposure in plasma, brain & CSF
(Dose: 30mg/kg; po)



CNS penetration following infusion after bolus administration may vary based on sampling time. To reduce variability in measured blood–brain partitioning, a steady-state infusion approach is preferred. Administering a loading dose followed by constant infusion enables faster attainment of steady-state plasma drug concentration.

Steady-State Infusion in Conscious Rats

Brief Design

Animal: Jugular vein-cannulated Sprague Dawley rats

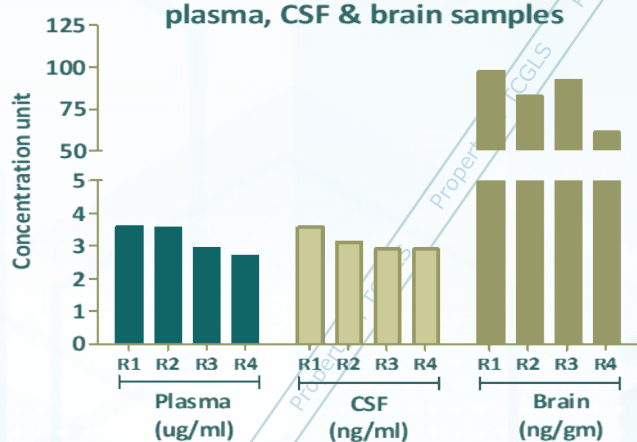
Dosing regimen: IV bolus followed by IV infusion

Infusion technique: Through jugular vein by tethered infusion system

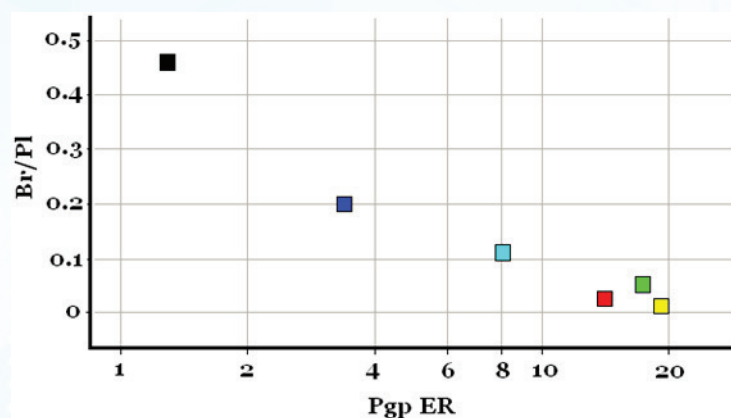
Biological matrices: Plasma, CSF & brain after 4 hours of infusion



Comparative exposure of compound in plasma, CSF & brain samples



In Vivo CNS penetration & its correlation with In Vitro PGP efflux ratio (ER)



In this model, steady-state plasma concentration is achieved through a 4-hour infusion in cannulated rats. Infusion is delivered using an infusion pump connected through a tethered assembly in conscious animals. Following the 4-hour infusion period, plasma, cerebrospinal fluid (CSF), and brain samples are collected for analysis.

Sample Collection and Concentration Measurement

This setup supports accurate evaluation of CNS penetration by measuring drug levels in plasma, cerebrospinal fluid and brain tissue at steady-state conditions.

Key Takeaway

The steady-state infusion method provides a controlled framework for evaluating CNS penetration by achieving stable plasma concentrations and enabling collection of plasma, CSF, and brain samples after defined infusion in conscious rats. This supports effective assessment of CNS drug exposure.