cyprotex
AN EVOTEC COMPANY

Matrix Binding Services

In drug discovery, a compound's pharmacological effect is driven by its free (unbound) concentration. Unbound *in vivo* blood or plasma concentrations are estimated by multiplying total levels by the fraction unbound in these matrices. Measuring a compound's unbound fraction is also crucial in other scenarios involving matrices like isolated plasma proteins, microsomes, hepatocytes, and tissues (e.g., brain). Binding to these matrices is highly dependent on physicochemical properties such as lipophilicity and pKa.

- **Advanced Screening for Tissue and Protein Binding**
  Measure the binding affinity of compounds in biological matricies to help predict drug behavior and efficacy.
- **High Throughput Screening**
  Streamline your research with rapid, large-scale screening services.
- **Accurate Data**
  Ensure reliability with precise measurements across various matricies.
- **Tailored Solutions**
  Customized assays to meet your specific research needs.

	Equilibrium Dialysis: Matrix Matched Protein Binding (MMPB) Method	**Equilibrium Dialysis: Matrix-Matched, Single Calibration (MMSC) Method**	**Blood-Plasma Ratio (BPR) Method**
Detection	▸ UPLC-MS/MS or UPLC-HRMS endpoints ▸ ~2 orders of magnitude ▸ Dynamic range: 10.00% to 99.0% bound	▸ UPLC-MS/MS or UPLC-HRMS endpoints ▸ ~4 orders of magnitude ▸ Dynamic range: ~10.00% to 99.99% bound	▸ UPLC-MS/MS
Assay Details	▸ Incubation: variable ▸ Device: RED ▸ Replicates: 3 ▸ Temperature: 37°C ▸ Matrix: variable ▸ Buffer: variable ▸ Initial form: DMSO stock ▸ Post-equilibration cassette analysis option	▸ Incubation: variable ▸ Device: RED or HTDialysis ▸ Replicates: 3 ▸ Temperature: 37°C ▸ Matrix: variable ▸ Buffer: variable ▸ Initial form: DMSO stock ▸ Calibration curve: 7-point ▸ Post-equilibration cassette analysis option	▸ Incubation: 1 hr ▸ Replicates: 3 ▸ Temperature: 37°C ▸ Matrix: variable ▸ Initial form: DMSO stock
Notes	▸ Suitable for compounds that are <=99.00% bound – designed to be a screening assay	▸ Suitable for compounds that are >99.00% bound – ideal for lead optimization	

Multiple Binding Methods Available

Plasma Protein Binding

Throughout the drug discovery process, it is often proposed that a compound's pharmacological effect is driven by its free, or unbound, concentration. Unbound *in vivo* plasma concentrations can be estimated by multiplying total levels by a measurement of the fraction of the compound that is unbound in plasma. Cyprotex provides a plasma protein binding service for a wide range of species, strains and anti-coagulants.

Microsomal and Hepatocyte Binding

Compounds can be sequestered (non-specifically) into microsomes or hepatocytes where they are presumed to be unavailable to be metabolized. Correcting for such non-specific binding in *in vitro* stability assays can improve the prediction of *in vivo* clearance and *in vivo* drug-drug interactions. Cyprotex provides a microsomal binding service and a hepatocyte binding service for a range of species.

Whole Blood Binding

Pharmacokinetic parameters are usually determined by analysis of drug concentrations in plasma rather than whole blood. Understanding the extent of whole blood binding in comparison to plasma protein binding is important in identifying if differential binding to a specific component in the blood occurs and in interpreting pharmacokinetic data. Cyprotex provides a whole blood binding service for a range of species.

Tissue Binding

Compounds can be sequestered (non-specifically) into tissue and an understanding of the free-levels therein is important for understanding the relationship between exposure and efficacy. Determination of a compound's extent to be bound to brain tissue is often considered for drugs that tend to cross into the central nervous system. For such compounds, permeability and brain to plasma ratio data can be important to understand. Cyprotex provides a brain tissue binding service as well as MDR1-MDCK permeability and plasma protein binding services.

Media Binding

Often, cell-based *in vitro* assays use media that contain components to which a compound can bind to (e.g. FCS or BSA). In doing so, the free-levels of the compound able to illicit the intended effect are lowered and it is important to adjust the observed effect proportionally. Cyprotex provides a tailorable media binding service.

Custom Services

Additional bespoke services include:

- Matrix solubility/stability testing
- Post-study matrix pH testing
- Time to equilibration testing
- Inter-assay measurements to assess biological variability
- Matrix binding specific:
  - volume-shift and protein leakage testing
  - ultrafiltration instead of equilibrium dialysis
- Higher MWCO for larger compounds (bRo5)

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