cyprotex AN EVOTEC COMPANY

In vitro **ADME & PK**

Blood to Plasma Ratio

Background Information

'RBC partitioning of a compound may be concentration-dependent if the partitioning involves not only passive diffusion, but also protein binding or active transporters.'

[1]Yu S, Li S, Yang H, Lee F, Wu J-T and Qian MG (2005) *Rapid Commun in Mass Spectrom* **19**; 250-254

- Pharmacokinetic parameters are usually determined by analysis of drug concentrations in plasma rather than whole blood.
- Parameters determined using plasma data may be misleading if concentrations of drug differ between plasma and red blood cells as a consequence of differential binding to a specific component in the blood.
- The blood to plasma ratio determines the concentration of the drug in whole blood compared to plasma and provides an indication of drug binding to erythrocytes.
- At blood to plasma ratios of greater than 1 (usually as a consequence of the drug distributing into the erythrocyte), the plasma clearance significantly overestimates blood clearance and could exceed hepatic blood flow.
- Blood to plasma ratio is an important parameter, in conjunction with other ADME and physicochemical properties, for predicting whole body pharmacokinetics.

Protocol

Typical Test Article Concentration
500 nM (additional concentrations available)

Test Article Requirements
50 µL of 10 mM DMSO solution

Positive Controls
Methazolamide (human)
Chlorthalidone (rat and mouse)
Chloroquine (dog)

Analysis Method
LC-MS/MS

Data Delivery
Mean blood to plasma ratio
Standard deviation of blood to plasma ratio

Blood to plasma ratio assists in determining the relevance of the plasma clearance and can also be used to predict or understand haemotoxicity.

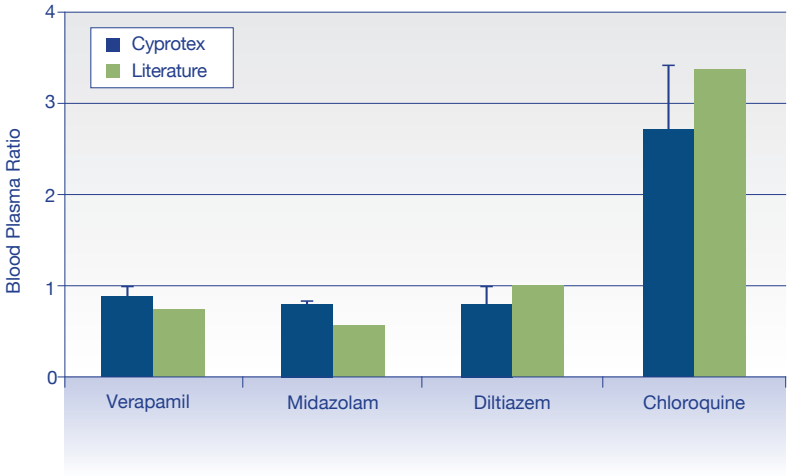

Figure 1

Comparison of Cyprotex's blood to plasma ratio values (mean ± standard deviation; n=3) with literature values[2,3].

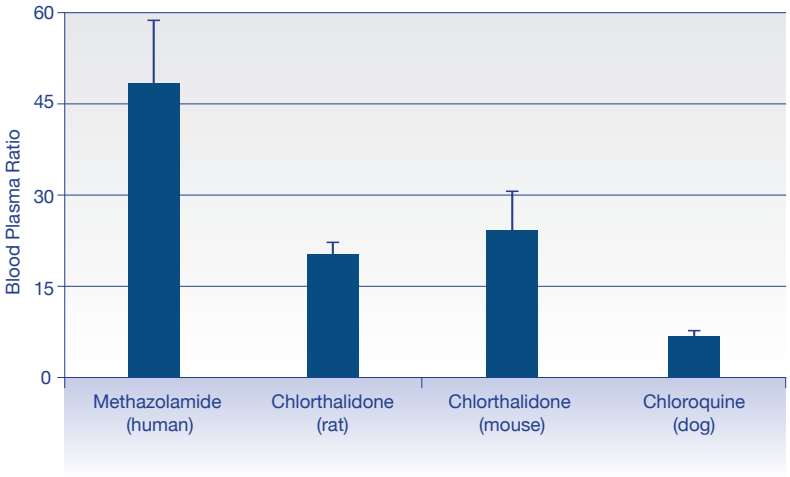

Figure 2

Graph illustrating the intra-assay reproducibility of the blood to plasma ratio values for the species-specific positive control compounds (mean ± standard deviation; n=3 replicates).

References

1 Yu S *et al.*, (2005) *Rapid Commun in Mass Spectrom* **19**; 250-254.
2 Hinderling PH (1997) *Pharmacol Rev* **49(3)**; 279-295
3 Obach RS (1999) *Drug Metab Dispos* **27(11)**; 1350-1359.