



# Cloe Select Blood to Plasma Ratio

**cyprotex**experts in **ADME**

## 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.'

<sup>1</sup>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 Compound Concentration**  
500 nM (additional concentrations available)

**Compound Requirements**  
50 µL of 10 mM solution

**Positive Control**  
Chloroquine

**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 potential haemotoxicity.

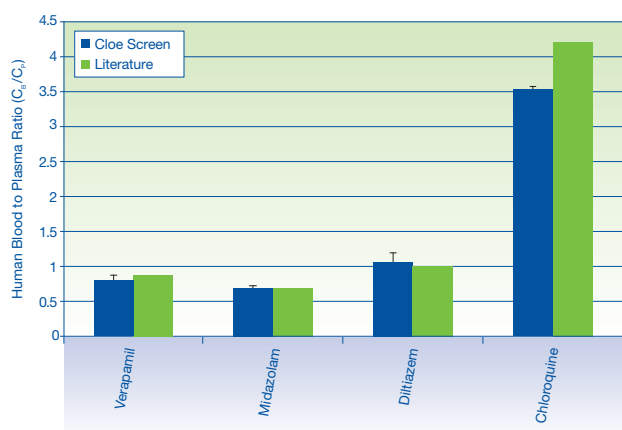


### Cloe Select Blood to Plasma Ratio

A set of 4 compounds was assessed in the Cloe Select Blood to Plasma Ratio assay in triplicate over 3 separate occasions. Data generated in the Cloe Select Blood to Plasma Ratio assay were compared with data from the literature.

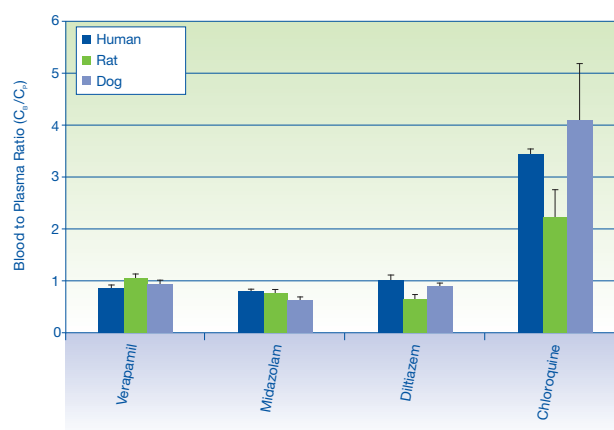
**Figure 1**

Comparison of Cloe Select Blood to Plasma Ratio ( $C_B/C_P$ ) values (mean  $\pm$  standard deviation) with literature values<sup>1,2,3</sup>.



**Figure 2**

Comparison of human, rat and dog data in the Cloe Select Blood to Plasma Ratio assay (data represents the mean  $\pm$  standard deviation).



For the 4 compounds assessed, only chloroquine exhibits a blood to plasma ratio significantly above 1 in all the species, consistent with its ability to accumulate in the red blood cells.

#### References

- <sup>1</sup> Yu S *et al.*, (2005) *Rapid Commun in Mass Spectrom* **19**; 250-254.
- <sup>2</sup> Heizmann P *et al.*, (1983) *Br J Clin Pharmacol* **16**; 43S-49S.
- <sup>3</sup> Obach RS (1999) *Drug Metab Dispos* **27** (11); 1350-1359.