BD Gentest℠ Contract Research Services

Combine our expertise and exclusive technologies to help you identify better drugs faster.

Protein Binding

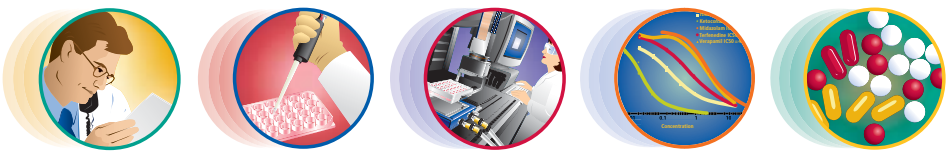
INTRODUCTION

Drug efficacy and disposition are influenced by binding of a drug to plasma proteins, primarily serum albumin and α-acid glycoprotein.[1] High drug-protein binding can both reduce the fraction of free drug available for target sites and prolong the duration of drug activity.[2] BD Biosciences provides rapid *in vitro* plasma protein binding testing, offering both ultrafiltration and equilibrium dialysis methods to determine % drug bound to plasma proteins. Blood cell partitioning testing to determine the % drug associated with blood cells is also available. A standard set of test compound concentrations and incubation times may be used. Appropriate positive controls are included. Incubations can be performed with radiolabeled and non-radiolabeled compounds, with samples analyzed by LC/MS or radiometric detection. These services are available with human, rat, mouse, monkey, dog, and rabbit plasma and blood, and can be conducted according to GLP regulations.

DRUG-PLASMA PROTEIN BINDING AND BLOOD CELL PARTITIONING VALUES OF MODEL DRUGS AND DRUG X IN HUMAN PLASMA AND BLOOD

Compound	Literature Values	BD Gentest™ Values						
		Ultrafiltration			Equilibrium Dialysis		Blood Cell Partitioning	
	% Bound to Plasma Protein	% Non-Specifically Bound	% Bound to Plasma Protein	% Mass Balance	% Bound to Plasma Protein	% Mass Balance	% Associated with Blood Cells	Cb/Cp Ratio
Testosterone	95	1.3	95.1	98.6	94.1	93.5	27.8	0.65
Salicylic Acid	82	0.2	83.0	96.6	81.9	86.6	8.7	0.49
Example Drug X	—	0.1	10.5	101.7	10.4	90.1	41.3	0.92

Validation data obtained in Ultrafiltration Equilibrium Dialysis and Blood-Cell Partitioning assay systems using testosterone and salicylic acid. Example Drug X data is from a Protein Binding Study.



EXPERIMENTAL OUTLINE

Plasma Protein Binding

Ultrafiltration Procedure

1. Ultrafiltration is performed at 37°C with plasma fortified with the test compound. Concentrations and replicate number are flexible.
2. Ultrafiltrate and retentate samples are collected for analysis by LC/MS or radiometric detection.
3. The % bound to plasma proteins and mass balance are determined.
4. Non-specific binding assessment of the test compound to the ultra-filtration device is also performed.

Plasma Protein Binding

Equilibrium Dialysis Procedure

1. Equilibrium dialysis is performed at 37°C with plasma fortified with the test compound. The time spacing, concentrations, and replicate number are flexible.
2. Donor and receptor side samples are collected for analysis by LC/MS or radiometric detection.
3. The % bound to plasma proteins and mass balance are determined.

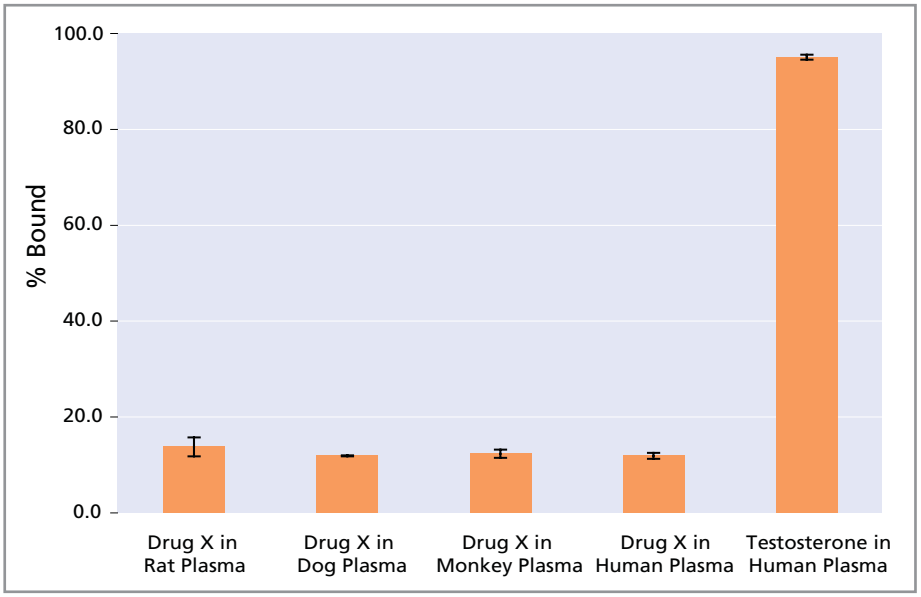
Blood Cell Partitioning

1. Hematocrit determination of the blood source is performed.
2. The test compound is incubated at one or more concentrations in the blood source.
3. At one or more time intervals, blood samples are taken for oxidation and plasma samples are prepared from the incubated blood. The time spacing and replicate number are flexible.
4. The drug bound to blood cells is determined following analysis of the samples by LC/MS or radiometric detection.
5. The % associated with blood cells and blood cell ratio (Cb/Cp) are determined.

References

1. Lin, J., et al. The role of Absorption, Distribution, Metabolism, Excretion and Toxicity in Drug Discovery. Current Topics in Med. Chem. **3**:1125 (2003).
2. Kratochwil, N.A., et al. Predicting plasma protein binding of drugs: a new approach. Biochem. Pharmacol. **64**:1355 (2002).

DRUG-PLASMA PROTEIN BINDING RESULTS OBTAINED IN MULTIPLE SPECIES PLASMA USING ULTRAFILTRATION



Drug-plasma protein binding results from Ultrafiltration assays using rat, dog, cynomolgus monkey and human plasma fortified with test drug X or testosterone. Results are the mean and standard deviation of triplicate determinations.

CONTACT INFORMATION

Call the BD Gentest℠ Contract Research Services Department at:
888.334.5229 x2246 (North America), **781.935.5115 x2246** (Worldwide)
E-mail **info_gentest@bd.com**

Your local BD Gentest™ Product and Services Sales Specialist will promptly provide you with initial study and price information. Your project will be assigned to a Study Director who will coordinate and tailor your Protein Binding Study to your total satisfaction. A finished detailed report will be provided.

BD Biosciences
Two Oak Park
Bedford, MA 01730 USA
tel: 800.343.2035
fax: 800.743.6200

Nippon BD
Akasaka DS Bldg.
5-26 Akasaka 8-chome
Minato-ku, Tokyo 107 Japan
tel: (81) 24 593 5405
fax: (81) 24 593 5761

BD
2771 Bristol Circle
Oakville, Ontario
Canada L6H 6R5
tel: 905.855.5550
fax: 905.829.5405

BD Biosciences Europe
Erembodegem-Dorp 86
9320 Erembodegem, Belgium
tel: (32) 53 720 211
fax: (32) 53 720 450
e-mail: contact_bdb@europe.bd.com

BD
BD Biosciences