

NoAb BioDiscoveries

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Plasma Protein Binding Assays

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The pharmacokinetic and pharmacodynamic properties of drugs are largely a function of the reversible binding of drugs to plasma or serum proteins. Such proteins include albumin, α_1 -acid glycoprotein, lipoproteins and α , β and γ globulins. Generally, only the unbound drug is available for diffusion or transport across cell membranes, and for interaction with a pharmacological target (e.g. receptor, ion channel, transporter, enzyme). As a result, the extent of plasma protein binding of a drug influences the drug's action as well as its distribution and elimination.

Highly plasma protein bound drugs are confined to the vascular space, thereby having a relatively low volume of distribution. In contrast, drugs that remain largely unbound in plasma are generally available for distribution to other organs and tissues, resulting in large volumes of distribution. The binding of drugs to proteins both in the vascular space and/or the extravascular space results in a decrease in drug clearance and a prolonged drug half-life. Only the unbound drug is available for glomerular filtration and, in some cases, hepatic clearance. However, for high extraction ratio drugs, clearance is relatively independent of protein binding.

NoAb BioDiscoveries offers plasma or serum protein binding assays using the equilibrium dialysis method. Equilibrium dialysis studies are offered using a 96-well microplate format or using conventional 2-chambered Teflon dialysis cells. Combined with LC/MS/MS analysis for test compound quantification, the 96-well microplate format is a rapid throughput method that is excellent for screening compound libraries to identify compounds with high, medium and low binding fractions. The Teflon dialysis cell system is commonly used to determine the time to reach equilibrium, the fraction of a compound bound and unbound to plasma proteins and the effect of concentration on the extent of binding. Test compound quantification is performed by HPLC or LC/MS/MS analysis.

NoAb BioDiscoveries offers services to assess the binding of drug candidates to plasma and serum proteins during the early discovery process. Our services will aid in the selection of drug candidates for further development, and move these new chemical entities closer to the clinic. We tailor our assays to meet our clients' needs.