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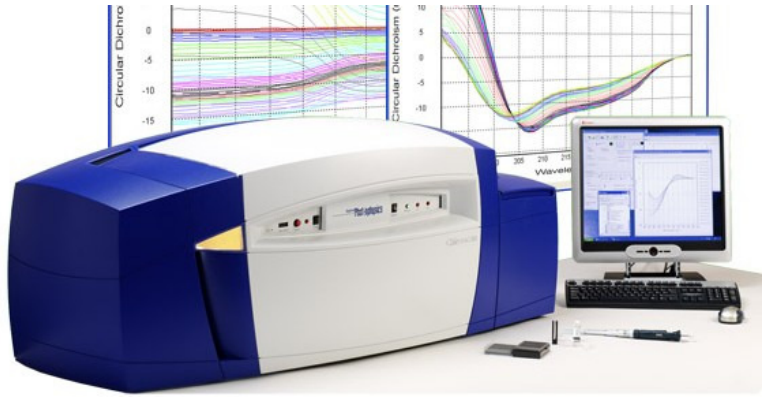
Pharmacokinetics of small molecules



The use of Chirascan to study the competitive binding of diazepam and ibuprofen to human serum albumin (HSA)

Many drug molecules bind reversibly to plasma proteins and often circulate in the body as this bound form with a small population free in solution. Two major proteins that regularly bind small molecule drugs are human serum albumin (HSA) and α1-acid glycoprotein. The binding of drug molecules to these proteins has a large impact on the pharmacokinetics of the drug, and the changes in free plasma concentrations of a drug have significant bearing on the pharmacological activity as well as the rate of breakdown and excretion.

Particular drugs, metabolites and other molecules have high affinities for certain binding sites on plasma proteins. The different affinities of different molecules for specific binding sites can result in a drug being displaced from the protein by another molecule. These complex interactions can significantly change the pharmacokinetics of a drug and is one of the mechanisms by which multi-drug interactions occur.

Monitoring changes in circular dichroism (CD) spectra of either the protein or the ligand is a very specific signal for structural changes induced in either the protein or the ligand. The ligand does not need to be chiral to produce a CD signal when bound to a protein.

In this application note, the binding interactions of two well known and characterized small molecule drugs, ibuprofen and diazepam, to HSA are studied using CD spectral changes recorded on a Chirascan spectrometer.

Download the full Application Note here.

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