Validated protein binding method used for more than 4000 drug compounds

Fast gradient HPLC method to determine compounds binding to human serum albumin. Relationships with octanol/water and immobilized artificial membrane lipophilicity

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A fast gradient HPLC method (cycle time 15 min) has been developed to determine human serum albumin binding of discovery compounds using **CHIRAL-HSA** 50x3.0 mm columns. The HSA binding values were derived from the gradient retention times that were converted using data from a calibration set of compounds.

Calibration set of compounds

Compound	Literature % prot.bind.	Measured % HSA bind.
Warfarin (peak 2)	98	98.1
Nizatidine	35	31.1
Bromazepam	60	71.2
Carbamazepine	75	76.8
Budesonide	88	84.2
Piroxicam	94.5	93.6
Nicardipine	95	97
Ketoprofen	98.7	97.3
Indomethacine	99	99.5
Diclofenac	99.8	99.5

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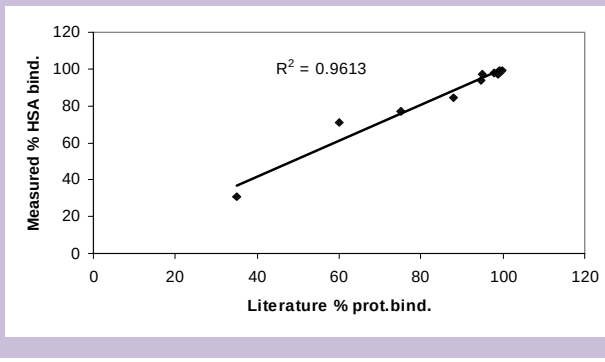
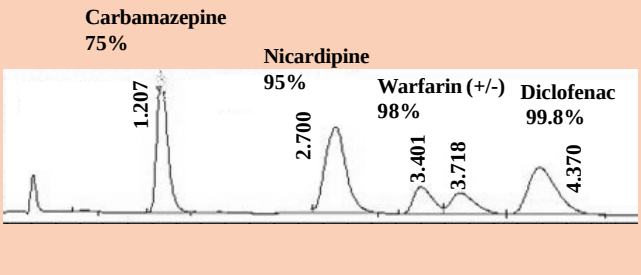


Plot of measured percentage of HSA-binding for the calibration set of compounds versus literature data on percentage proteinbinding

The method has been **validated** using literature plasma protein binding data of 68 known drug molecules. Being **fully automated**, the method has been used for more than 20 company projects. HSA binding data for more than **4000 drug compounds** have been obtained and from this it has been possible to set up quantitative structure binding relationships to help compound design in early drug discovery.

Below is a chromatogram showing some of the compounds in the calibration set.



The article is attached with the e-mail as a PDF-file.

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