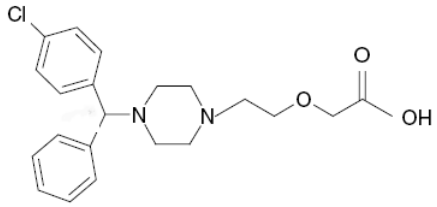
Bioanalysis of cetirizine enantiomers on CHIRAL-AGP with LC/MS/MS detection

A.Gupta et al. has published a method for the resolution of cetirizine enantiomers: Quantitative determination of cetirizine enantiomers in guinea pig plasma, brain tissue and microdialysis samples using liquid chromatography/tandem mass spectrometry (in Rapid. Commun. Mass Spectrom. 19 (2005) 1749-1757).



Cetirizine

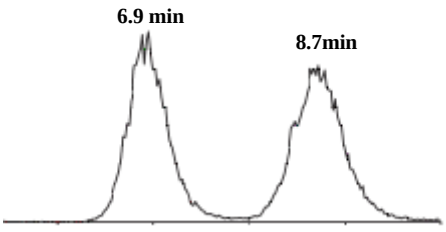
Chromatography

The article describes three methods for the analysis of cetirizine enantiomers in:

- guinea pig plasma
- guinea pig brain tissue
- guinea pig brain interstitial fluid (ISF), Ringer method, microdislysis

The same column was used for all three methods, CHIRAL-AGP 150x4.0 mm. The mobile phase used for the two first methods was 6.5% acetonitrile in 10 mM ammonium acetate ph 7.0 (pH adjusted with 1% ammonia). The column was thermostated at 30 degrees Celcius using a waterbath.

For the Ringer method the mobile phase contained 5.5% acetonitrile and was kept at room temperature.



A guinea pig plasma sample chromatographed on a CHIRAL-AGP 150x4.0 mm column
Flow rate: 0.9 ml/min
Detection: MS/MS

To avoid salt overload in the mass spectrometer, the column eluent during the first 6.5 minutes was discarded using a switching valve and an extra pump (to deliver flow through the mass spectrometer). The mobile phase flow rate was 0.9 ml/min. This flow was split to 250-270 ul/min before entering the mass spectrometer.

The mass spectrometer was a triple-quadropole instrument, used in the positive ESI mode.

An internal standard was used.

Validation

The following parameters were assessed in the validation process:

Linearity, precision, accuracy, specificity and lower limit of quantification (LLOQ).

	Plasma	**Brain**	**Ringer**
Standard curve linearity	0.25-5000 ng/ml	2.5-250 ng/ml	0.25-50 ng/ml
Intraday precision	$\leq$ 7.1%	$\leq$ 4.2%	$\leq$ 6.5%
Interday precision	$\leq$ 12.6%	$\leq$ 6.8%	$\leq$ 10%
LLOQ	0.25 ng/ml	2.51 ng/ml	0.25 ng/ml

Conclusion

The authors conclude that fast, sensitive and enantioselective methods have been developed and validated. A prerequisite was to obtain a low LLOQ using small sample volumes. Only 50 ul of plasma samples and 8 ul of microdialysis samples were needed in these methods.

The run time was not more than 14 minutes in any of the methods.

A very large amount of samples, more than 3500, were injected on the column.

The validated methods were successfully applied to a preclinical study of the BBB (blood brain barrier) transport of cetirizine enantiomers in guinea pig.

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