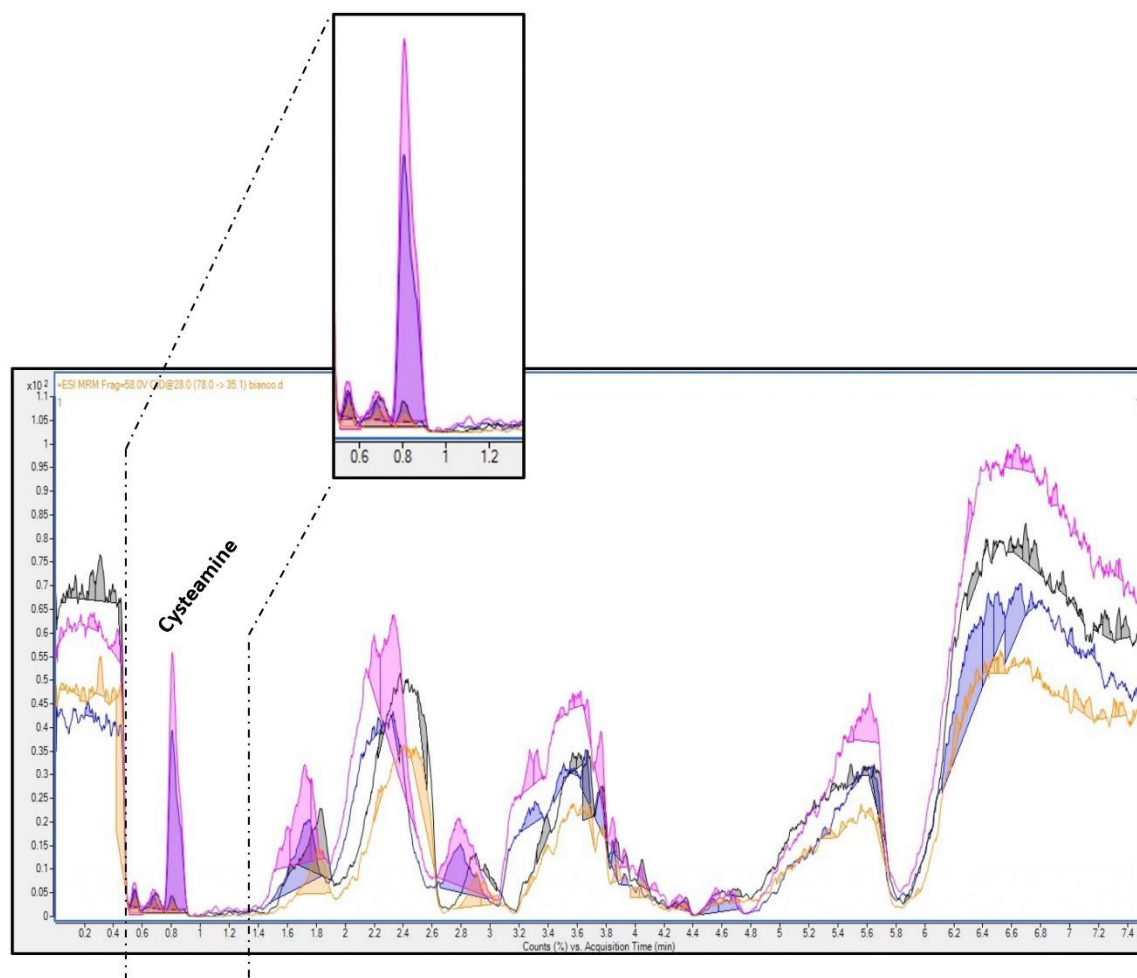
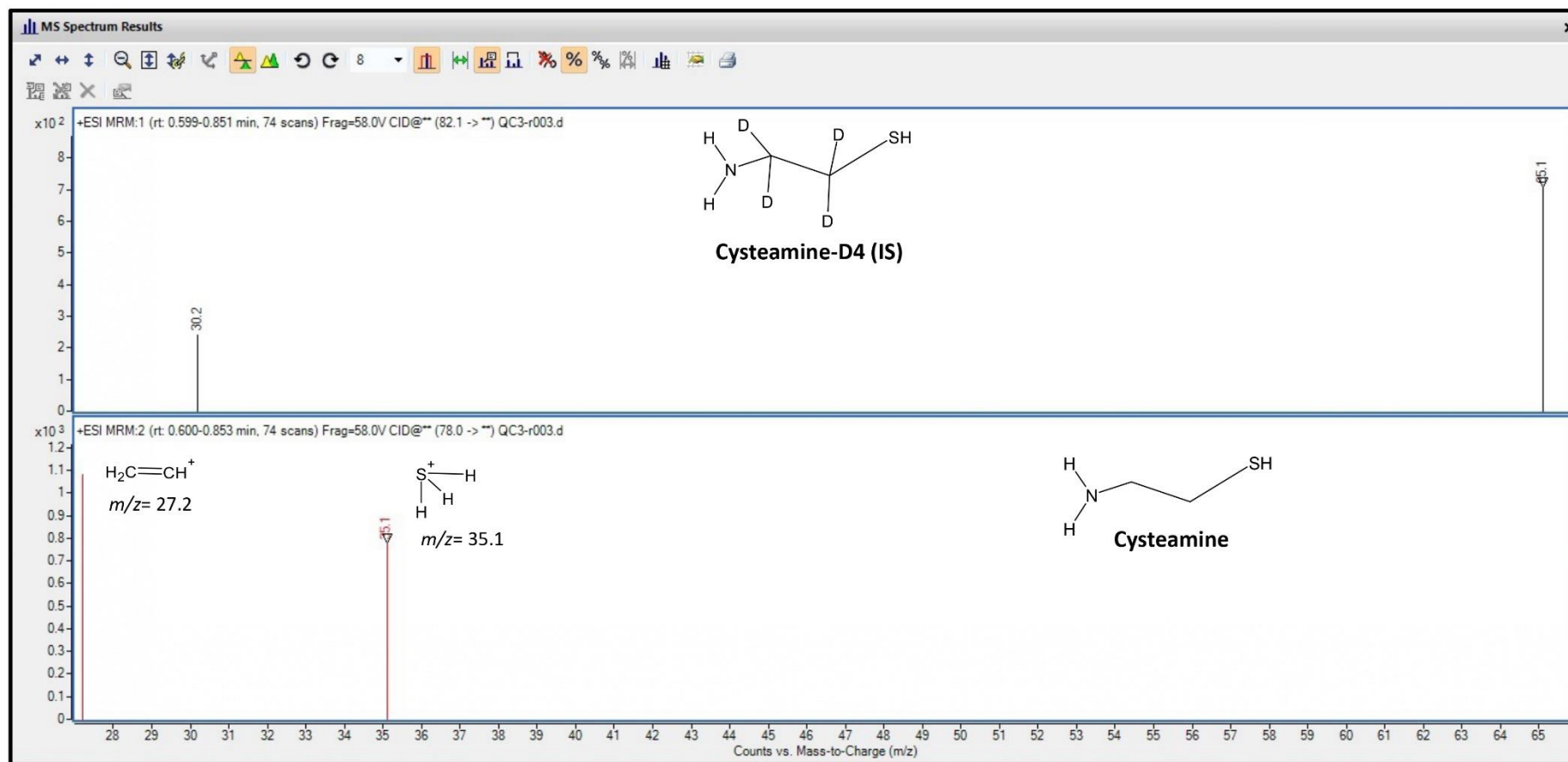


**Supplementary Figure S1 Overlaid chromatograms of blank plasma alone and spiked at LLOQ level**



## Supplementary Figure S2 Mass spectrum results



**Supplementary Table 1.** Comparison between bioanalytical method described here and previous published LC-MS/MS methods.

Bioanalytical method	Instrumentation	Chromatographic column	Elution mode and Mobile phases used	Injection volume	Flow- rate (mL/min)	Run- time	Analysed matrix (required volume)	Disulfide-Reducing Agent	Calibration range; LLOQ	Internal standard (IS) used
Method described here	UHPLC Agilent 1290 Infinity II apparatus (Agilent Technologies) coupled with 6470 Mass Spectrometry system (Agilent Technologies)	InfinityLab Poroshell 120 HILIC 1.90 $\mu\text{m}$ (100 $\times$ 2.1 mm)	Gradient elution.  Mobile phase A (0.1 % formic acid in milli-q pure water);  Mobile phase B (0.1% formic acid in acetonitrile ACN);	10.0 $\mu\text{L}$	0.5	7.50 minutes	Plasma (50 $\mu\text{L}$ )	Tris (2-carboxyethy) phosphine (TCEP)	1-2000 $\mu\text{M}$ ; 0.50 $\mu\text{M}$	D4- (deuterated) cysteamine
Dohil R. et al., 2005 [19]	API 2000 LC-MS/MS, (Applied Biosystems)	LC-CN 2 cm $\times$ 4.0 mm I.D. 3 $\mu\text{m}$ particle size (Supelco)	Isocratic elution.  Mobile phase (0.1% formic acid)	20.0 $\mu\text{L}$	0.4	Not reported	Plasma (100 $\mu\text{L}$ )	Tris (2-carboxyethy) phosphine (TCEP)	1-100 $\mu\text{M}$	2-dimethyl-ethane-aminothiol

Bouazza N. et al., 2011 [15]	Agilent 1100 system (Agilent Technologies) coupled to Applied Biosystems/MDS Sciex API3000 MSMS	XD8-C8 column 150 × 4.6 mm (Interchim)	Isocratic elution.  Mobile phase [water/acetonitrile (410/90) with 0.1% formic acid].	5.0 µL	0.6	Not reported	Plasma (200 µl)	Dithiothreitol (DTT)	Not reported	D4- (deuterated) cysteamine
Franzin M et al., 2022 [14]	SCIEX ExionLCTM AD (AB Sciex) coupled with the mass spectrometer SCIEX Triple QuadTM 6500 + LC-MS/MS System	Poroshell Agilent 120 EC-C8 150 mm × 2.1 mm, 4 µm (Agilent Technologies)	Gradient elution.  Mobile phase A (water with 0.15% formic acid and 5 mM ammonium formate).  Mobile phase B (acetonitrile: water 95:5 with 0.15% formic acid and 5 mM ammonium formate).	3.0 µL	0.4	14 minutes	Plasma (100 µL)	Dithiothreitol (DTT)	2.5-50 µM; 1.25 µM	D6- (deuterated) cystine

For reference numbers see the main manuscript.

**Supplementary Table 2.** Gradient conditions reached during the chromatographic separation.

Time (min)	Mobile Phase B (%)
0	78
1	78
4	20
4.5	20
4.6	78
7.5	78