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Quantification of thirty-one antidepressants in human serum by TurboFlow chromatography coupled to high-resolution Orbitrap mass spectrometry for clinical research

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Keywords

Antidepressants, TurboFlow, online sample preparation, serum, Orbitrap, high-resolution mass spectrometry

Application benefits

- Simple protein precipitation followed by Thermo Scientific™ TurboFlow™ online sample cleanup
- 31 antidepressants in a single quantitative method

Goal

Implementation of an analytical method for the quantification of 31 antidepressants in human serum using a Thermo Scientific™ Transcend™ II TLX-1 TurboFlow™ system coupled to a Thermo Scientific™ Q Exactive™ Focus hybrid quadrupole-Orbitrap™ high-resolution, accurate-mass (HRAM) mass spectrometer.

Introduction

An analytical method for clinical research for the quantification of 31 antidepressants in human serum is reported. Samples were prepared by offline internal standard addition and protein precipitation. Prepared samples were injected onto a Transcend II TLX-1 system for online sample cleanup using TurboFlow technology prior to LC separation. Analytes were detected using HRAM mass spectrometry on a Q Exactive Focus mass spectrometer with heated electrospray ionization. Detection was performed in full MS mode using a resolution of 70,000 (FWHM) at *m/z* 200.

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Method performance was evaluated using homemade as well as commercial quality controls from RECIPE Chemicals + Instruments GmbH (Munich, Germany) and Bio-Rad Laboratories GmbH (Munich, Germany). Precision, accuracy, recovery, matrix effect, and the stability of the extracted samples were evaluated for each analyte.

Experimental

Target analytes

The analytes and corresponding concentration ranges are reported in Table 1.

Table 1. Concentration ranges covered by calibrators

Analyte	Concentration (ng/mL)
Amitryptiline	7.07–354
Atomoxetine	20.0–2000
Citalopram	4.01–177
Clomipramine	20.6–806
Clozapine	35.0–1200
Descitalopram	4.48–197
Desfluoxetine	12.0–1000
Desipramine	10.0–600
Desmirtazapine	3.00–160
Dessertraline	35.9–215
Doxepine	4.43– 66
Duloxetine	3.00–240
Fluoxetine	10.7–895
Fluvoxamine	6.00–460
Imipramine	15.5–531
Maprotiline	6.63–230
Mianserin	1.50–140
Mirtazapine	3.00–160
Norclomipramine	23.0–900
Norclozapine	100–1200
Nordoxepine	5.00–300
Normaprotiline	10.0–400
Nortryptiline	7.02–351
Nortrimipramine	2.84–227
Norvenlafaxine	10.0–800
Paroxetin	2.64–105
Protryptiline	7.00–340
Reboxetine	5.38–627
Ritalinic acid	24.0–600
Sertraline	0.894–268
Trazodone	70.0–2000
Trimipramine	10.8–431
Venlafaxine	8.84–707

Sample preparation

Eight calibrators (including blank) and three quality controls (QCs) were prepared in-house by spiking all the analytes in water/methanol 50/50 (v/v) at the proper concentration. Commercial quality controls from RECIPE (identified as RECIPE 1 and 2) and Bio-Rad (BioRad 1 and 2) were also used. Individual concentrations are reported in Table 2 and Table 3. Samples of 50 µL (donor serum specimens, calibrators, or QCs) were subjected to protein precipitation using 150 µL of acetonitrile containing the internal standards. Precipitated samples were vortex-mixed and centrifuged, and the supernatants were transferred to a clean plate or vial.

Liquid chromatography

Online sample cleanup was achieved on a 0.5 × 50 mm Thermo Scientific™ TurboFlow™ Cyclone™ column. The LC separation was performed using a 100 × 2.1 mm (1.9 µm) Thermo Scientific™ Hypersil GOLD™ Phenyl analytical column. The mobile phases were made of 10 mM ammonium formate and 0.1% formic acid in water and methanol for both TurboFlow sample cleanup and chromatographic separation. Details of the analytical method are reported in Figure 1. Total runtime was 9.5 minutes.

Mass spectrometry

Analytes and internal standards were detected using a resolution of 70,000 (FWHM) at *m/z* 200 on a Q Exactive Focus MS system with heated electrospray ionization operated in positive mode. Data were acquired in full MS mode covering a mass range between *m/z* 215 and 375 amu. The MS conditions are summarized in Table 4.

Method evaluation

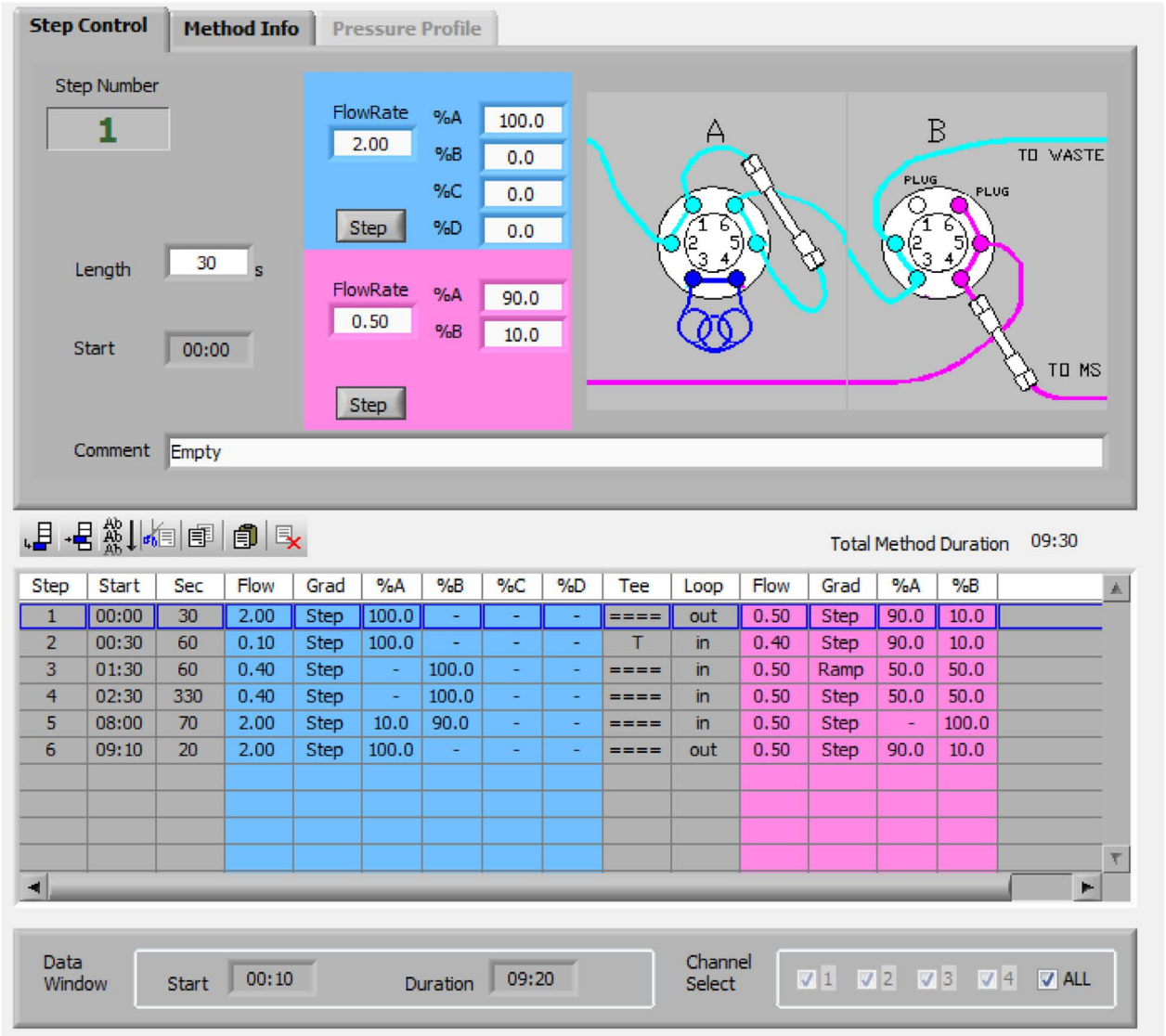
The method performance was evaluated in terms of precision, accuracy, recovery, and matrix effect for each analyte on five different validation runs. The stability of the extracted samples was also evaluated. Analytical within-run precision was evaluated for each validation run in terms of percent coefficient of variation (%CV) for each analyte on each control sample, prepared and analyzed in replicates of five.

Table 2. Individual concentrations (ng/mL) for the calibrators

Analyte	Calibrator 1	Calibrator 2	Calibrator 3	Calibrator 4	Calibrator 5	Calibrator 6	Calibrator 7
Amitryptiline	7.07	21.2	70.7	98.2	133	177	354
Atomoxetine	20.0	60.0	200	333	667	1000	2000
Citalopram	4.01	12.0	40.1	50.1	70.6	88.2	177
Clomipramine	20.6	61.8	206	258	323	403	806
Clozapine	35.0	105	350	438	480	600	1200
Descitalopram	4.48	13.4	44.8	55.9	78.8	98.5	197
Desfluoxetine	12.0	36.0	120	167	333	500	1000
Desipramine	10.0	30.0	100	167	225	300	600
Desmirtazapine	3.00	9.00	30.0	44.4	60.0	80.0	160
Dessertraline	-	-	-	35.9	71.7	108	215
Doxepine	4.43	13.3	44.3	73.7	99.6	133	266
Duloxetine	3.00	9.00	30.0	66.7	90.0	120	240
Fluoxetine	10.7	32.2	107	149	298	448	895
Fluvoxamine	6.00	18.0	60.0	128	173	230	460
Imipramine	15.5	46.5	155	194	212	266	531
Maprotiline	6.63	19.9	66.3	82.1	91.9	115	230
Mianserin	1.50	4.50	15.0	23.3	46.7	70.0	140
Mirtazapine	3.00	9.00	30.0	44.4	60.0	80.0	160
Norclomipramine	23.0	69.0	230	288	360	450	900
Norclozapine	-	-	100	200	400	600	1200
Nordoxepine	5.00	15.0	50.0	83.3	113	150	300
Normaprotiline	10.0	30.0	100	125	160	200	400
Nortryptiline	7.02	21.1	70.2	97.6	132	176	351
Nortrimipramine	2.84	8.52	28.4	63.2	85.2	114	227
Norvenlafaxine	10.0	30.0	100	222	300	400	800
Paroxetin	2.64	7.91	26.4	33.0	42.2	52.7	105
Protryptiline	7.00	21.0	70.0	94.4	128	170	340
Reboxetine	5.38	16.1	53.8	105	209	314	627
Ritalinic acid	-	24.0	80.0	167	225	300	600
Sertraline	0.894	2.68	8.94	44.7	89.4	134	268
Trazodone	70.0	210	700	556	750	1000	2000
Trimipramine	10.8	32.4	108	135	173	216	431
Venlafaxine	8.84	26.5	88.4	196	265	354	707

Table 3. Individual concentrations (ng/mL) for the controls

Analyte	Control 1	Control 2	Control 3	RECIPE 1	RECIPE 2	BioRad 1	BioRad 2
Amitryptiline	21.2	88.4	177	–	–	85.6	298
Atomoxetine	60.0	500	1000	404	969	–	–
Citalopram	12.0	44.1	88.2	43.5	102	–	–
Clomipramine	61.8	202	403	–	–	–	–
Clozapine	150	300	600	–	–	–	–
Descitalopram	13.4	49.2	98.5	–	–	–	–
Desfluoxetine	36.0	250	500	107	256	–	–
Desipramine	30.0	150	300	–	–	89.6	302
Desmirtazapine	9.00	40.0	80.0	32.7	78.3	–	–
Dessertraline	–	53.8	108	–	84.6	–	–
Doxepine	13.3	66.4	133	–	–	–	–
Duloxetine	9.00	60.0	120	47.3	111	–	–
Fluoxetine	32.2	224	448	102	247	–	–
Fluvoxamine	18.0	115	230	98.2	229	–	–
Imipramine	46.5	133	266	–	–	86.2	300
Maprotiline	19.9	57.5	115	–	–	–	–
Mianserin	4.50	35.0	70.0	29.5	70.9	–	–
Mirtazapine	9.00	40.0	80.0	33.1	79.1	–	–
Norclomipramine	69.0	225	450	–	–	–	–
Norclozapine	30.0	300	600	–	–	–	–
Nordoxepine	15.0	75.0	150			94.5	313
Normaprotiline	30.0	100	200	–	–	–	–
Nortryptiline	21.1	87.8	176			91.7	311
Nortrimipramine	8.52	56.8	114	–	–	–	–
Norvenlafaxine	30.0	200	400	102	238	–	–
Paroxetin	7.91	26.4	52.7	46.8	111	–	–
Protryptiline	21.0	85.0	170	–	–	–	–
Reboxetine	16.1	157	314	143	338	–	–
Ritalinic acid	24.0	150	300	66.7	158	–	–
Sertraline	2.68	67.1	134	26	62	–	–
Trazodone	210	500	1000	534	1284	–	–
Trimipramine	32.4	108	216	–	–	–	–
Venlafaxine	26.5	177	354	61.7	146	–	–



Step	Start	Sec	Flow	Grad	%A	%B	%C	%D	Tee	Loop	Flow	Grad	%A	%B
1	00:00	30	2.00	Step	100.0	-	-	-	====	out	0.50	Step	90.0	10.0
2	00:30	60	0.10	Step	100.0	-	-	-	T	in	0.40	Step	90.0	10.0
3	01:30	60	0.40	Step	-	100.0	-	-	====	in	0.50	Ramp	50.0	50.0
4	02:30	330	0.40	Step	-	100.0	-	-	====	in	0.50	Step	50.0	50.0
5	08:00	70	2.00	Step	10.0	90.0	-	-	====	in	0.50	Step	-	100.0
6	09:10	20	2.00	Step	100.0	-	-	-	====	out	0.50	Step	90.0	10.0

Figure 1. LC method description

Table 4. MS settings

Ion source type:	Heated electrospray ionization (HESI)
Vaporizer temperature:	320 °C
Capillary temperature:	320 °C
Spray voltage (positive mode):	3500 V
Sheath gas:	45 AU
Sweep gas:	1 AU
Auxiliary gas:	10 AU
Data acquisition mode:	Full MS at R=70,000 (FWHM) @ *m/z* 200
Mass range:	*m/z* 215–375 amu

Between-run precision was evaluated on the same controls including all 25 replicates in the five runs. Within-run accuracy was evaluated for run #4 as the percentage ratio between average experimental and nominal concentrations at each level using the same set of controls (five replicates per run). Between-run accuracy was evaluated on the same controls including all 25 replicates in the five runs. Recovery was calculated for each analyte in terms of percentage ratio between the concentration when spiked in serum and extracted and the concentration when spiked in extracted serum. Matrix effect was calculated for each analyte as the percentage ratio between the concentration when spiked in extracted serum and the concentration when spiked in solvent and processed following the extraction procedure.

Each analyte was spiked and analyzed in replicates of five using a mid-range concentration to evaluate recovery and matrix effect. Extracted sample stability was evaluated for each analyte by comparison between freshly prepared control samples and the same samples kept for 48 hours in the autosampler tray at 10 °C.

Data analysis

Data were acquired and processed using Thermo Scientific™ TraceFinder™ 4.1 software. An extraction window of 5 ppm was used to extract the individual chromatograms.

Results and discussion

Baseline chromatographic separation was achieved for the three sets of isobaric compounds (imipramine/nortrimipramine, maprotiline/amitryptiline, protryptiline/normaprotiline/nortyptiline) that could not otherwise be distinguished and properly quantified using a full MS approach. Representative chromatograms are reported in Figure 2.

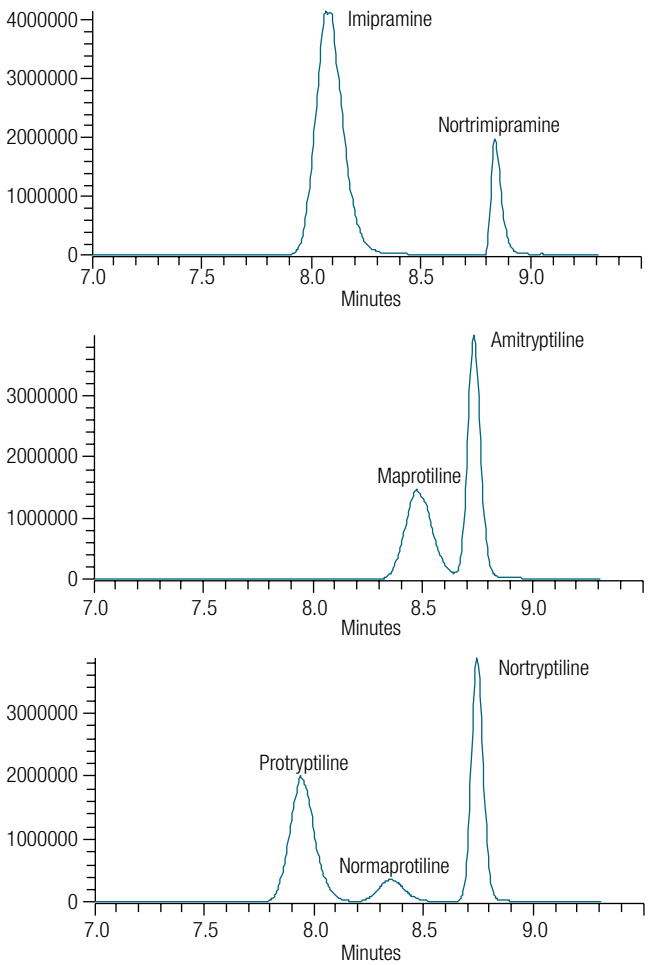


Figure 2. Representative chromatograms of the separation obtained for the three sets of isobaric compounds

The method proved to be linear for each analyte in the calibration ranges covered by the calibrators. Representative chromatograms of the lowest calibrator for citalopram, mianserin, and sertraline are reported in Figure 3.

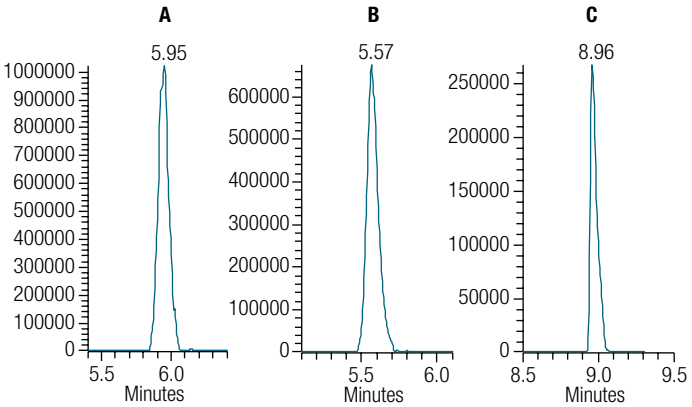


Figure 3. Representative chromatograms of the lowest calibrator for (A) citalopram, (B) mianserin, and (C) sertraline

The data demonstrated outstanding within- and between-run precisions of the method. The maximum %CV for within-run precision was 6.0% (Table 4). The %CV for between-run precision was always below 9.9% (Table 5).

Excellent results were also obtained for both within- and between-run accuracies, with only four out of 131 control samples outside the 80%–120% range. Results are reported in Tables 6 and 7.

Non-significant matrix effect was measured for all the analytes, with values between 85.8% and 108% (Table 8). A matrix effect of 191% was obtained for ritalinic acid.

Excellent recovery values were obtained for all the analytes with a minimum value of 88.0%.

All analytes proved to be stable in the extracted samples left 48 hours at 10 °C in the autosampler tray, with a maximum loss of signal of 7.4% for fluvoxamine.

Table 4. Within-run precision results (run #4)

Analyte	Control 1	Control 2	Control 3	RECIPE 1	RECIPE 2	BioRad 1	BioRad 2
Amitryptiline	1.1	0.9	0.8	–	–	1.7	1.5
Atomoxetine	0.8	0.6	1.1	1.8	1.6	–	–
Citalopram	0.9	0.8	0.8	1.2	1.2	–	–
Clomipramine	0.7	0.8	1.1	–	–	–	–
Clozapine	2.5	1.3	2.3	–	–	–	–
Descitalopram	0.9	1.1	1.0	–	–	–	–
Desfluoxetine	1.7	1.7	1.8	1.4	1.5	–	–
Desipramine	0.7	1.2	1.1	–	–	1.6	0.9
Desmirtazapine	1.3	1.8	1.5	2.2	2.0	–	–
Dessertraline	–	4.0	2.6	–	3.5	–	–
Doxepine	0.8	0.7	0.9	–	–	–	–
Duloxetine	1.9	2.1	2.0	1.2	2.0	–	–
Fluoxetine	1.1	1.2	1.5	1.5	1.4	–	–
Fluvoxamine	1.2	1.4	2.2	1.5	1.8	–	–
Imipramine	1.9	1.1	0.8	–	–	2.2	1.0
Maprotiline	1.4	1.4	1.6	–	–	–	–
Mianserin	1.7	0.9	1.0	1.4	1.1	–	–
Mirtazapine	0.7	1.0	0.7	1.2	1.1	–	–
Norclomipramine	0.7	1.3	1.3	–	–	–	–
Norclozapine	3.2	2.7	1.8	–	–	–	–
Nordoxepine	1.2	1.0	1.0	–	–	1.6	1.2
Normaprotiline	2.5	1.7	3.0	–	–	–	–
Nortryptiline	0.9	0.8	0.8	–	–	1.7	1.0
Nortrimipramine	1.9	1.5	1.3	–	–	–	–
Norvenlafaxine	4.0	2.5	4.5	2.5	2.6	–	–
Paroxetin	1.3	1.2	1.2	1.4	1.5	–	–
Protryptiline	2.1	2.2	3.4	–	–	–	–
Reboxetine	1.6	1.7	1.8	1.7	1.3	–	–
Ritalinic acid	2.1	2.8	3.6	4.9	6.0	–	–
Sertraline	2.4	1.1	1.0	1.1	1.6	–	–
Trazodone	2.1	2.0	2.9	1.8	2.6	–	–
Trimipramine	1.1	1.3	1.3	–	–	–	–
Venlafaxine	1.7	1.6	2.1	1.6	1.5	–	–

Table 5. Between-run precision (average %CV on five runs)

Analyte	Control 1	Control 2	Control 3	RECIPE 1	RECIPE 2	BioRad 1	BioRad 2
Amitryptiline	1.1	1.2	1.3	–	–	2.8	2.1
Atomoxetine	1.0	0.7	1.3	2.1	2.2	–	–
Citalopram	1.0	0.9	1.0	1.5	1.4	–	–
Clomipramine	1.1	1.1	1.1	–	–	–	–
Clozapine	3.1	1.5	2.3	–	–	–	–
Descitalopram	1.4	1.2	1.3	–	–	–	–
Desfluoxetine	1.7	2.1	2.0	2.9	2.5	–	–
Desipramine	1.5	1.2	1.2	–	–	2.5	1.1
Desmirtazapine	1.7	1.8	1.7	2.6	2.6	–	–
Dessertraline	–	8.5	7.0	–	9.9	–	–
Doxepine	1.2	0.9	1.1	–	–	–	–
Duloxetine	2.2	2.3	2.1	1.4	2.6	–	–
Fluoxetine	1.5	2.0	2.4	1.9	2.9	–	–
Fluvoxamine	1.4	2.0	2.2	2.6	3.4	–	–
Imipramine	2.4	1.3	0.9	–	–	3.0	1.0
Maprotiline	1.8	2.4	2.3	–	–	–	–
Mianserin	1.7	1.0	1.1	1.8	1.4	–	–
Mirtazapine	1.4	1.0	1.0	1.3	1.4	–	–
Norclomipramine	1.2	1.3	1.4	–	–	–	–
Norclozapine	3.0	3.1	3.3	–	–	–	–
Nordoxepine	1.6	1.1	1.2	–	–	2.9	1.5
Normaprotiline	7.5	4.7	5.3	–	–	–	–
Nortryptiline	1.1	1.0	1.1	–	–	2.4	1.1
Nortrimipramine	2.2	1.4	1.8	–	–	–	–
Norvenlafaxine	4.1	2.8	4.4	3.8	3.2	–	–
Paroxetin	1.4	1.3	1.5	1.6	2.0	–	–
Protryptiline	3.6	3.7	4.3	–	–	–	–
Reboxetine	1.7	1.9	2.6	1.8	2.1	–	–
Ritalinic acid	3.2	5.8	5.7	6.8	7.5	–	–
Sertraline	2.6	1.4	1.2	1.4	2.2	–	–
Trazodone	2.4	2.4	3.1	1.9	2.5	–	–
Trimipramine	1.4	1.2	1.4	–	–	–	–
Venlafaxine	1.8	1.6	2.1	1.7	1.6	–	–

Table 6. Within-run accuracy results (average % accuracy on five runs)

Analyte	Control 1	Control 2	Control 3	RECIPE 1	RECIPE 2	BioRad 1	BioRad 2
Amitryptiline	102	98.2	99.2	–	–	102	100
Atomoxetine	106	95.1	93.8	93.7	89.5	–	–
Citalopram	100	96.1	97.2	113	108	–	–
Clomipramine	97.9	102	103	–	–	–	–
Clozapine	104	107	99.0	–	–	–	–
Descitalopram	104	97.4	94.6	–	–	–	–
Desfluoxetine	102	99.5	100	73.6	70.3	–	–
Desipramine	103	93.1	96.3	–	–	89.6	92.5
Desmirtazapine	105	98.6	97.1	114	98.9	–	–
Dessertraline	–	110	109	–	107	–	–
Doxepine	98.5	100	103	–	–	–	–
Duloxetine	94.8	93.5	102	86.8	84.1	–	–
Fluoxetine	103	98.2	98.4	93.3	85.9	–	–
Fluvoxamine	103	95.9	97.8	73.9	72.1	–	–
Imipramine	99.6	94.9	94.9	–	–	91.2	90.8
Maprotiline	102	90.7	90.2	–	–	–	–
Mianserin	99.3	99.4	100	90.5	86.2	–	–
Mirtazapine	99.7	98.9	100	106	101	–	–
Norclomipramine	98.7	98.1	99.9	–	–	–	–
Norclozapine	102	106	97.2	–	–	–	–
Nordoxepine	97.2	95.8	102	–	–	93.7	99.2
Normaprotiline	88.7	86.9	100	–	–	–	–
Nortryptiline	103	96.0	97.6	–	–	98.5	99.8
Nortrimipramine	105	99.4	96.9	–	–	–	–
Norvenlafaxine	107	96.7	95.1	112	102	–	–
Paroxetin	101	94.8	95.8	93.6	88.4	–	–
Protryptiline	94.4	95.2	108	–	–	–	–
Reboxetine	102	98.0	94.9	110	101	–	–
Ritalinic acid	110	90.6	104	118	107	–	–
Sertraline	97.1	102	102	103	97.7	–	–
Trazodone	109	102	101	113	101	–	–
Trimipramine	101	94.0	95.3	–	–	–	–
Venlafaxine	105	95.5	95.8	106	100	–	–

Table 7. Between-run accuracy (average % accuracy on five runs)

Analyte	Control 1	Control 2	Control 3	RECIPE 1	RECIPE 2	BioRad 1	BioRad 2
Amitryptiline	102	96.8	99.2	–	–	101	100
Atomoxetine	106	94.6	93.7	91.8	87.7	–	–
Citalopram	101	95.5	96.6	112	108	–	–
Clomipramine	98.9	102	103	–	–	–	–
Clozapine	104	106	98.6	–	–	–	–
Descitalopram	104	97.0	94.5	–	–	–	–
Desfluoxetine	103	101	101	72.7	70.3	–	–
Desipramine	105	93.2	96.0	–	–	89.5	92.5
Desmirtazapine	106	98.1	95.4	112	99.0	–	–
Dessertraline	–	101	102	–	93.1	–	–
Doxepine	99.2	100	102	–	–	–	–
Duloxetine	95.0	93.3	102	86.7	84.4	–	–
Fluoxetine	104	99.3	98.9	93.4	87.4	–	–
Fluvoxamine	103	97.0	97.3	74.4	71.8	–	–
Imipramine	101	94.6	95.2	–	–	90.9	90.6
Maprotiline	103	89.0	89.3	–	–	–	–
Mianserin	100	99.2	99.8	90.6	86.3	–	–
Mirtazapine	101	98.6	100	106	102	–	–
Norclomipramine	99.9	98.5	99.7	–	–	–	–
Norclozapine	102	109	103	–	–	–	–
Nordoxepine	97.6	95.7	101	–	–	93.6	98.7
Normaprotiline	92.9	90.3	103	–	–	–	–
Nortryptiline	104	95.0	97.0	–	–	97.8	98.9
Nortrimipramine	105	99.4	96.6	–	–	–	–
Norvenlafaxine	107	98.6	97.0	111	101	–	–
Paroxetin	102	94.9	96.0	93.2	88.9	–	–
Protryptiline	95.9	96.1	107	–	–	–	–
Reboxetine	102	97.9	96.0	110	103	–	–
Ritalinic acid	112	87.7	99.7	114	103	–	–
Sertraline	98.2	101	102	102	98.7	–	–
Trazodone	109	101	101	112	100	–	–
Trimipramine	101	94.3	95.3	–	–	–	–
Venlafaxine	105	96.4	96.0	106	101	–	–

Table 8. Matrix effect, recovery, and stability of the extracted samples after 48 hours in the autosampler at 10 °C

Analyte	Spiking Concentration (ng/mL)	Matrix Effect (%)	Recovery (%)	Extracts Stability (%)
Amitryptiline	88.4	97.5	91.1	99.1
Atomoxetine	500	98.5	92.5	100
Citalopram	44.1	97.3	91.9	100
Clomipramine	202	98.2	90.4	99.4
Clozapine	300	87.8	91.5	99.4
Descitalopram	49.2	98.1	90.9	97.7
Desfluoxetine	250	88.4	88.9	95.0
Desipramine	150	98.2	90.4	101
Desmirtazapine	40.0	94.7	89.9	96.0
Dessertraline	53.8	106	88.0	147
Doxepine	66.4	98.6	91.0	99.2
Duloxetine	60.0	97.7	91.6	100
Fluoxetine	224	96.6	90.3	99.3
Fluvoxamine	115	85.8	89.2	92.6
Imipramine	133	98.6	90.6	99.0
Maprotiline	57.5	99.1	90.5	99.5
Mianserin	35.0	97.4	90.7	99.8
Mirtazapine	40.0	97.6	91.8	100
Norclomipramine	225	96.5	89.0	99.6
Norclozapine	300	99.1	89.3	99.4
Nordoxepine	75.0	98.6	90.3	102
Normaprotiline	100	99.8	89.9	97.5
Nortryptiline	87.8	98.3	89.7	99.7
Nortrimipramine	56.8	96.2	90.1	100
Norvenlafaxine	200	102	89.2	101
Paroxetin	26.4	96.4	89.2	99.5
Protryptiline	85.0	99.3	90.1	104
Reboxetine	156	99.0	91.6	102
Ritalinic acid	150	191	88.3	105
Sertraline	67.1	98.7	89.0	101
Trazodone	500	108	91.0	93.1
Trimipramine	108	97.1	90.4	100
Venlafaxine	177	98.2	90.0	99.5

Conclusions

A liquid chromatography – Orbitrap HRAM mass spectrometry method for clinical research for the quantification of 31 different antidepressants in human serum was implemented. The use of TurboFlow online sample cleanup offers improved robustness and sensitivity, while the full MS acquisition in high resolution gives the flexibility to expand the panel of analytes without modifying the method. The described method meets research laboratory requirements in terms of sensitivity, linearity of response, accuracy, and precision.

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