Electronic Supplementary Material (ESI) for Analyst.

Liquid chromatography-miniature mass spectrometry (LC-Mini MS) method for quantitative analysis of risperidone and 9-hydroxyrisperidone in plasma

Supporting information

Hao Gu,[#,*,a] Guoxin Dai,[#,a] Zhongqiu Teng,[b] Lina Geng [a] and Wei Xu [a]

[a] School of Life Science, Beijing Institute of Technology, Beijing 100081, China

[b] The State Key Laboratory of Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, Beijing 100081, China

Table of contents

1. ESI interface setup

The LC-Mini MS system included a compact LC, an ESI interface setup and a home-built miniature mass spectrometer. The ESI interface setup is shown in Fig. S1, which has a splitter valve, a metal joint and a capillary needle. In order to minimize the footprint of LC-Mini MS system, the ESI interface was not equipped with sheath gas system. Instead, the splitter valve between the LC system and the Mini-MS system was used to adjust the flow rate from the C18 column. The flow rate of the C18 column was set at 0.25 mL/min, and the flow rate at the nozzle of the capillary was adjusted to microliters per minute by the splitter valve.

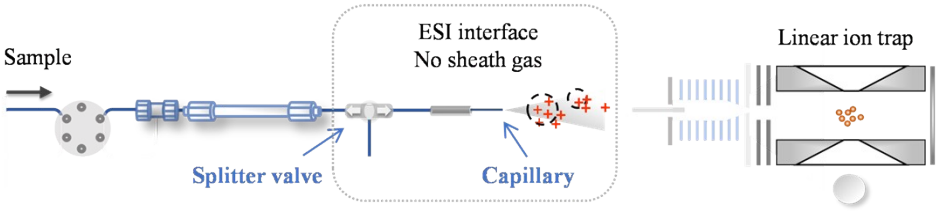

Fig. S1 Instrumentation of the ESI interface with a split valve, a metal joint and a capillary spray needle.

2. Liquid chromatography method

As shown in Fig. S2, methanol and acetonitrile were used as mobile phase of phase B. In the experiments, 80%, 85%, 90% and 95% methanol solvent were used as mobile phase of phase B at 1.0-3.5 min. Different elution durations of 1.0-3.0 min, 1.0-3.5 min, 1.0-4.0 min and 1.0-4.5 min were tested. The liquid chromatography method was set as following: mobile phase of phase A: water containing 0.1% formic acid and mobile phase of phase B: methanol containing 0.1% formic acid. The gradient elution method was 50%-15% of phase A at 0.0-1.0 min, 15% of phase A at 1.0-3.5 min, 15%-50% of phase A at 3.5-4.5 min and 50% of phase A at 4.5-7.0 min, and the run time was 14.0 min. The repeatability of the experimental method was tested. 50% of phase A was used at the beginning of the gradient elution method. This was due to the fact that the higher proportion of aqueous phase was less favorable for desolvation when there was no sheath gas at the nozzle of the interface.

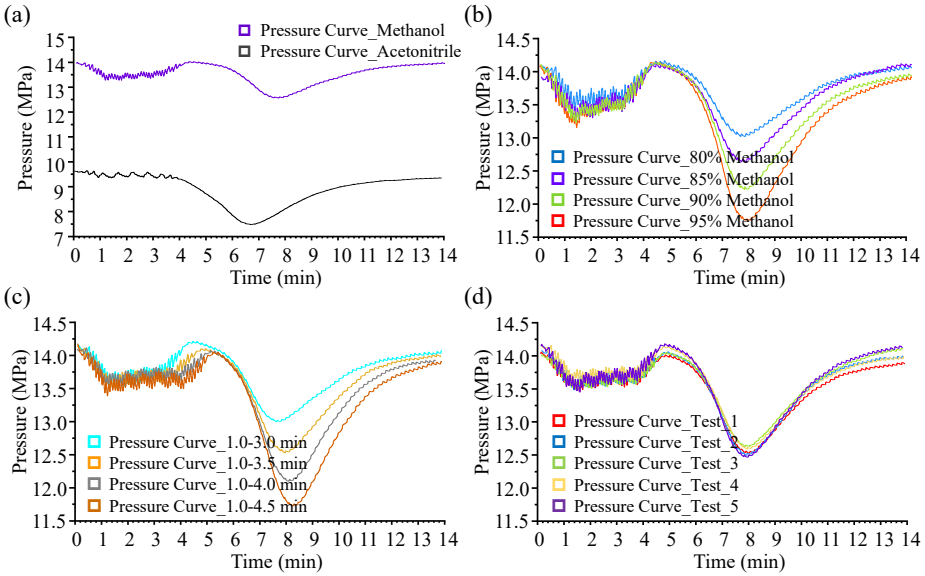

Fig. S2 Pressure lines of gradient elution methods with (a) different solvents, (b) methanol ratios in elution interval, (c) different elution durations and (d) repeatability.

3. Chemical structure and mass spectrum

The chemical structures of risperidone, 9-hydroxyrisperidone and their isotope internal standards are shown in Fig. S3. By the miniature mass spectrometer, the mass spectra of risperidone and 9-hydroxyrisperidone in methanol/water (5:5, v/v; 0.1% formic acid) at 100 ng/mL are shown in Figs. S4 and S5. The precursor ions and fragment ions of risperidone/risperidone-d_4 and 9-hydroxyrisperidone/9-hydroxyrisperidone-d_4 were used for qualitative and quantitative analysis.

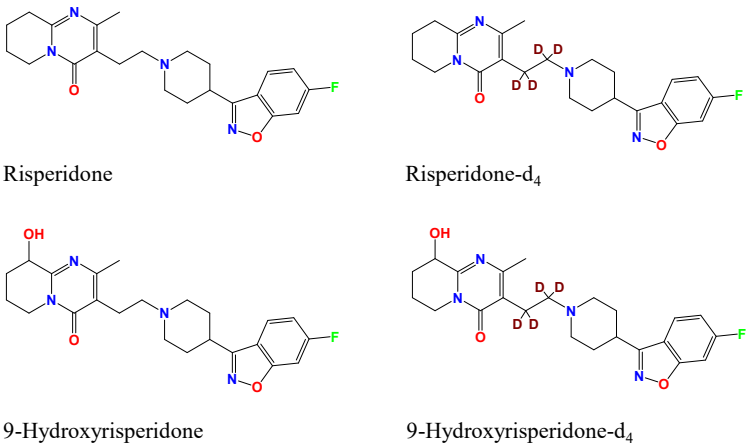

Fig. S3 Chemical structures of risperidone, risperidone-d_4, 9-hydroxyrisperidone and 9-hydroxyrisperidone-d_4.

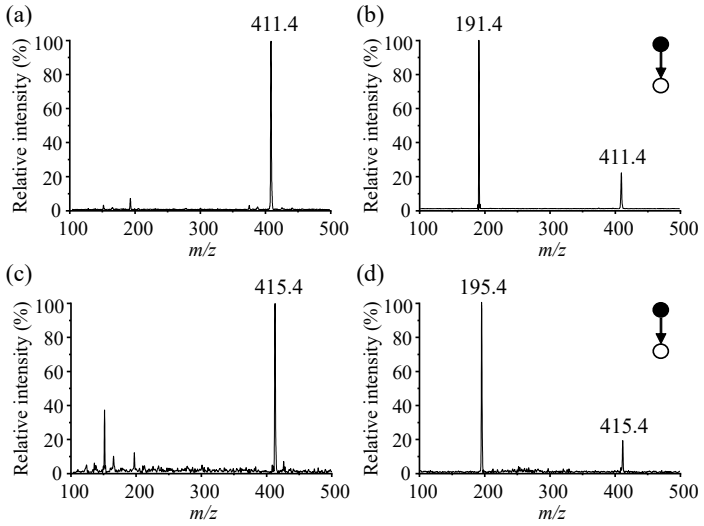

Fig. S4 Mass spectra of (a) risperidone and (c) risperidone-d_4, and fragment ion spectra of (b) risperidone (m/z 411.4 → 191.4) and (d) risperidone-d_4 (m/z 415.4 → 195.4).

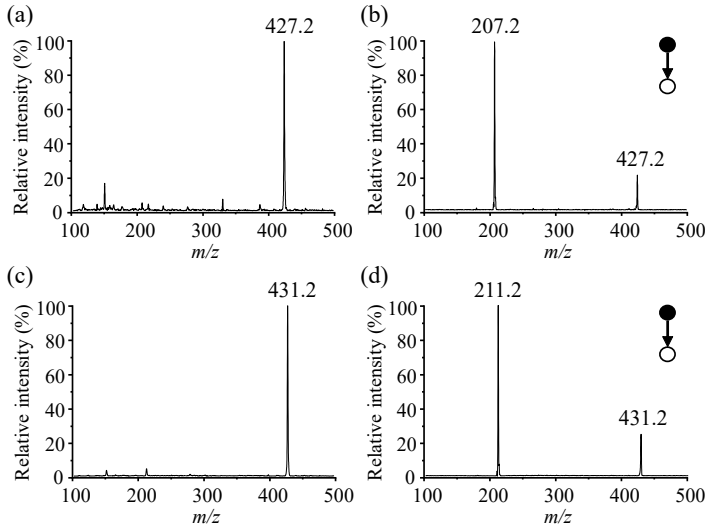

Fig. S5 Mass spectra of (a) 9-hydroxyrisperidone and (c) 9-hydroxyrisperidone-d_4, and fragment ion spectra of (b) 9-hydroxyrisperidone (m/z 427.2 → 207.2) and (d) 9-hydroxyrisperidone-d_4 (m/z 431.2 → 211.2).

4. Capillary needle

The images of the capillary needles with inner diameters (I.D.) of 30 μm, 50 μm and 75 μm and outer diameter (O.D.) of 150 μm are shown in Fig. S6. The experiments were performed by a DXX-N2000A microscope (Shanghai, China). The objective lens of microscope was 10x and the magnification was 3.5x.

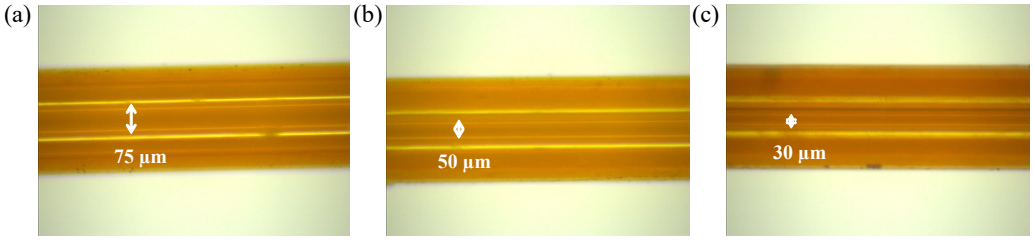

Fig. S6 Capillary needles with different inner diameters of (a) 30 μm, (b) 50 μm and (c) 75 μm and outer diameter of 150 μm.

5. ESI interface setting

The electrospray was tested using different capillary needles with inner diameters (I.D.) of 30 μm, 50 μm and 75 μm and outer diameter (O.D.) of 150 μm. When the splitter ratio was set to 95:1 (v/v) and the length of these capillary needles was 4 cm, the flow rate and ion source voltage were shown in Table S1. Different splitter ratios were tested when using the capillary with I.D. of 30 μm. In the experiments, the electrospray effect was related to the flow rate and ion source voltage. Different flow rate and ion source voltage were shown in Table S2.

Table S1 Flow rate and ion source voltage with different capillaries.

I.D. (μm)	O.D. (μm)	Flow rate (μL/min)	Ion source voltage (kV)
75	150	2.6	5000
50	150	2.1	5000
30	150	0.8	5000

Table S2 Flow rate and ion source voltage with different splitter ratios.

I.D. (μm)	Splitter ratios (v/v)	Flow rate (μL/min)	Ion source voltage (kV)
30	95:1	0.8	2100
30	89:1	1.4	2800
30	60:1	2.0	3500
30	37:1	3.0	4500
30	25:1	3.5	5000