Electronic Supplementary Material (ESI) for Analytical Methods.

Electronic Supplementary Information

Facile preparation of different materials coated paper substrates and their applications in paper spray mass spectrometry

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Experimental Section

The configuration of the coating procedure based on vacuum filtration is shown in Figure 1. The commercially available materials such as silica and metal oxides were dispersed in 100 mL deionized water containing 0.2 g starch as the bonding agent. After sonication for 15 min, the obtained suspension solution was directly transferred to a Buchner funnel covered by a blank filter paper with a diameter of 11 cm for coating. When the aqueous solution was completely penetrated through the filter paper, 20 mL absolute ethanol was applied for wash in order to get rid of the remaining water at the surface of the coated paper. The papers were then hung in a hood to dry for hours and were pressed between glass plates overnight for use. The papers can be safely stored in a ziplock bag for months.

All experiments on paper spray were carried out with a TSQ Quantum Access Max mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA). Mass spectra were recorded in the positive ion mode with a capillary temperature of 270 ^{o}C. The identification of analyte ions was confirmed by tandem mass spectrometry (MS/MS) using collision-induced dissociation (CID). The used bovine whole blood was purchased from Lanzhou Institute of Biological Products Co., Ltd. (Lanzhou, China). The urine sample was collected from a volunteer. The irregular silica, zirconia, titania, magnesium oxide, aluminum oxide and zinc oxide with diameters of around 1 μm and copper powder with diameters of 70-90 nm were purchased from Shanghai ST-Nano Science & Technology Co. Ltd. (Shanghai, China). Organic silicone balls with a diameter of 2 μm were from Guiyang Constant Micro-Materials Co., Ltd. (Guiyang, China). NH_2 bonded silica microspheres with a diameter of 3 μm were from BaseLine ChromTech Research Centre (Tianjin, China). Multi-walled carbon nanotubes (MWCNTs) with diameters below than 8 nm and lengths of 10-30 μm were from Beijing Boyu Gaoke New Material Technology Co., Ltd. (Beijing, China), and soluble starch from Tianjin Kemiou Chemical Reagent Co. (Tianjin, China). The used filter paper was from Hangzhou Special Paper Co. (Fuyang, China). The SEM images were taken by using a JEOL JSM-6390A scanning electron microscope.

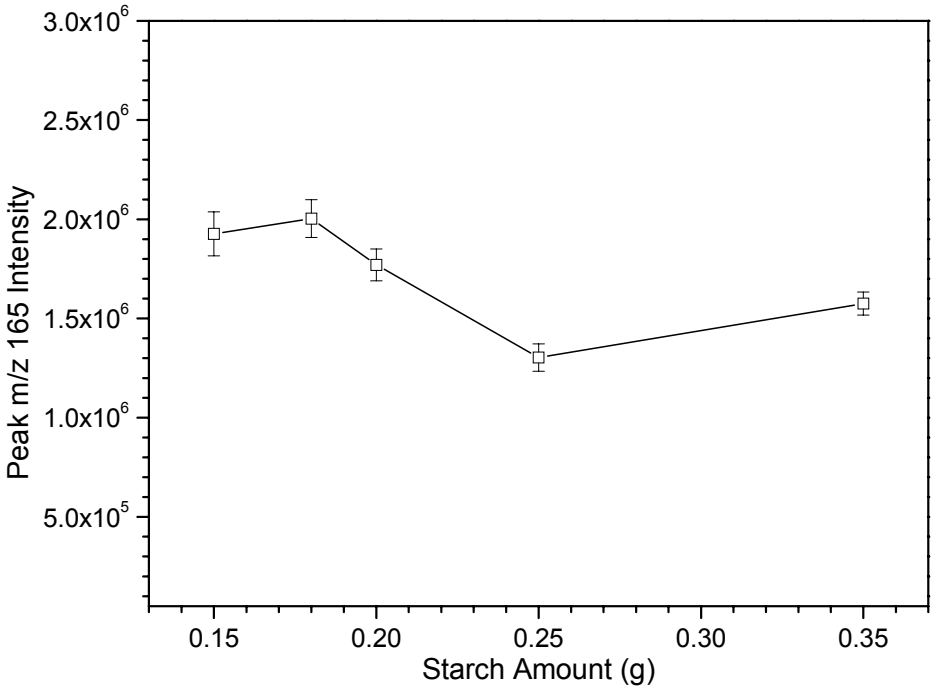

Fig. S-1 Effect of starch amount added into the 0.6 silica coating solution on the ionization efficiency of paper spray. For the paper spray analysis, a drop of 2.0 μL whole blood containing 1.0 μg mL^{-1} verapamil was deposited to the metal oxides coated papers. After drying, a 3.5 kV DC voltage is applied directly to the coated paper wetted with 20 μL acetonitrile. The quantitation analysis was evaluated by the peak intensity of the fragment ion m/z 165 from protonated verapamil m/z 455 in the SRM mode.

For optimizing the optimal starch amount added into the coating solution, different amounts of starch were used to the coating solution containing 0.6 g silica particles in 100 mL aqueous solution. When the starch amount was below than 0.10 g, the silica coated papers demonstrated most of the powdery nature. Therefore, we systematically investigated the starch amount from 0.15 g to 0.35 g. As can be seen in Fig. S-1, the ionization efficiency of paper spray was comparable when the starch amount was between 0.15 – 0.20 g. Further increasing the starch amount leads to the decrease of analysis performance in mass spectrometry. Based on the above reason, 0.20 g starch was regarded as the optimal value for the coating solution.

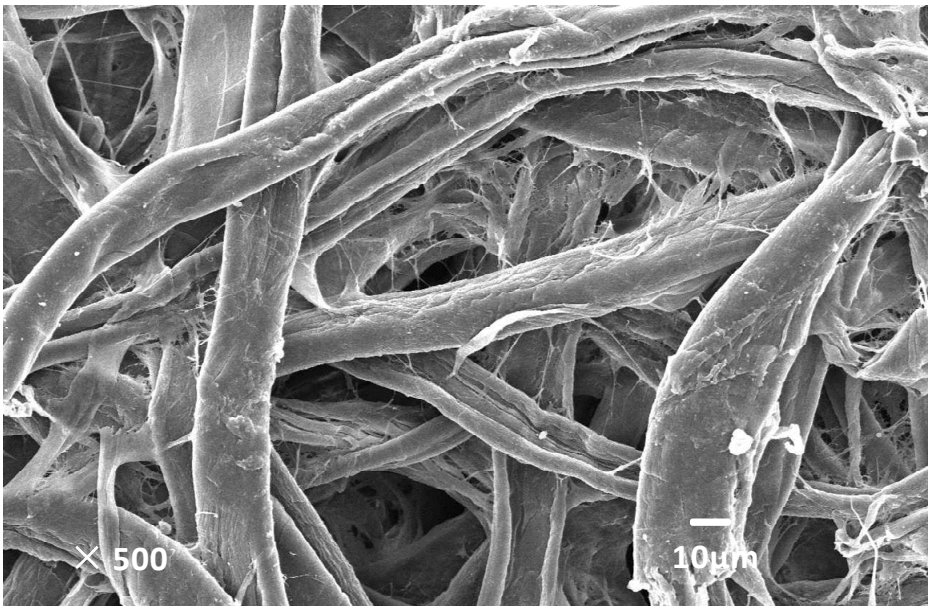

Fig. S-2 SEM image of commercially available filter paper.

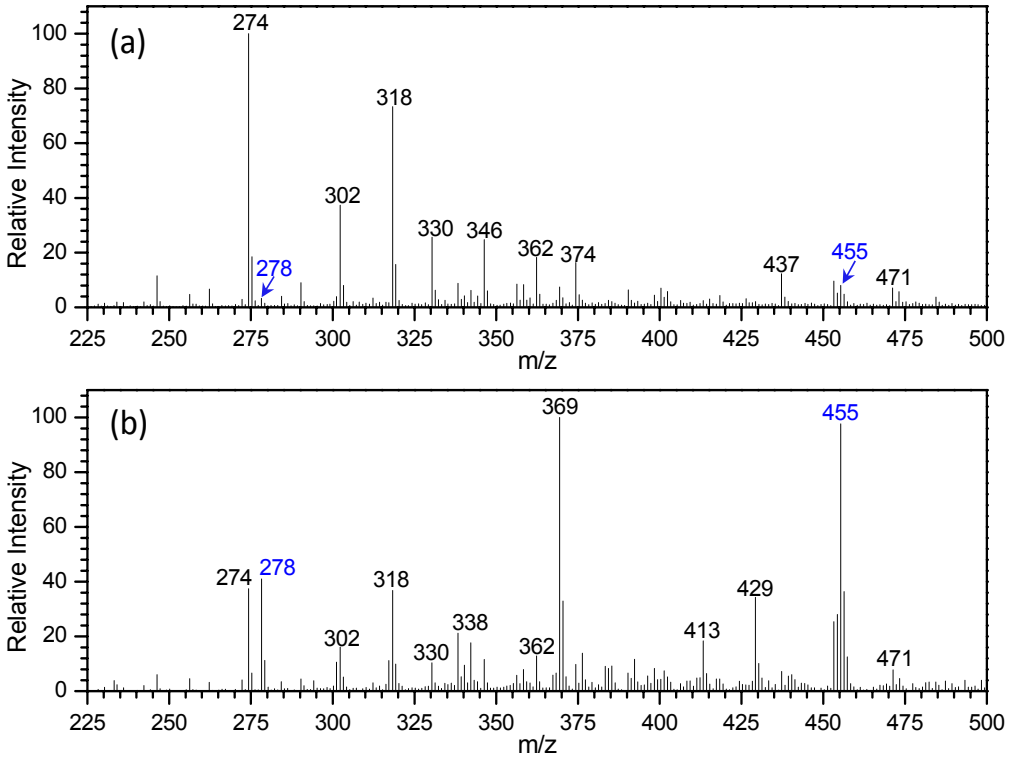

Fig. S-3 Full mass spectrum of dried blood spot containing 1μg mL^{-1} amitriptyline (m/z 278) and verapamil (m/z 455) by using (a) commercially availalbe fitler paper and (b) silica coated paper. Acetonitrile was used as the spray solvent, and spray voltage of 3.5 kV was applied for paper spray.

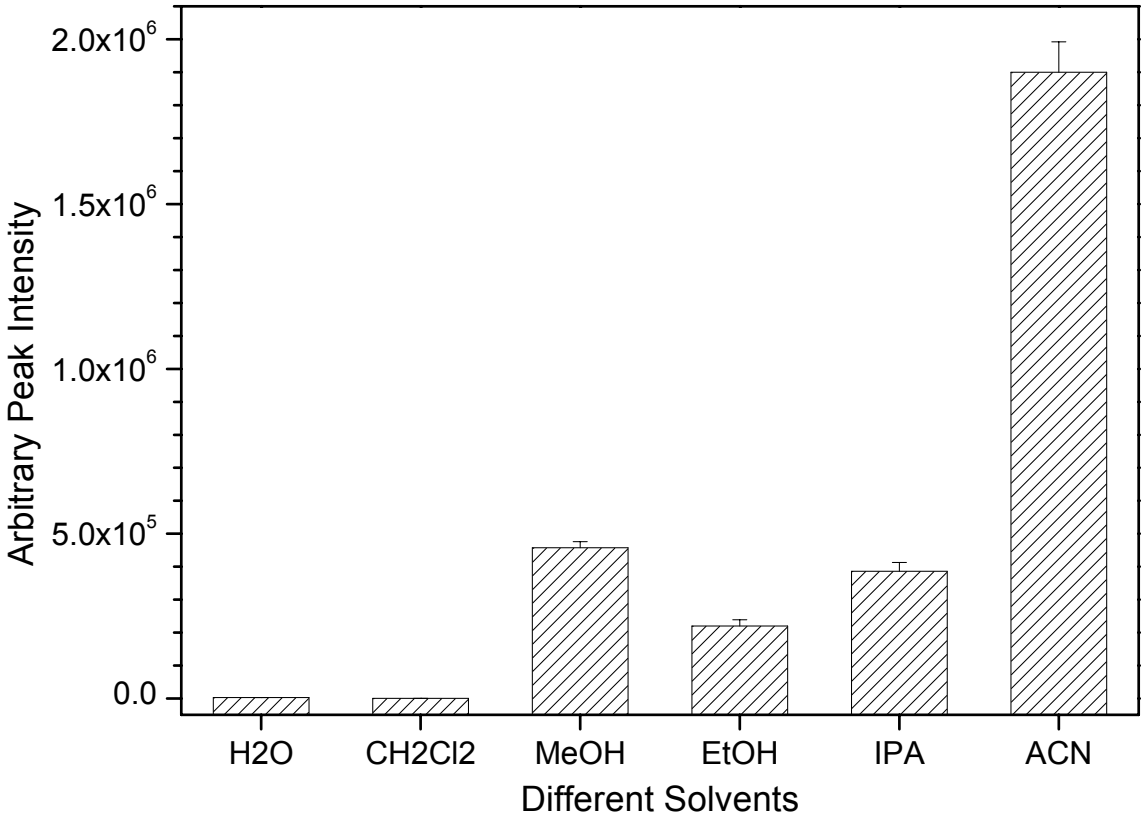

Fig.S-4 Effect of spray solvent on the ionization efficiency of paper spray using silica coated paper. For the paper spray analysis, a drop of 2.0 µL whole blood containing 1.0 µg mL^{-1} verapamil was deposited to the metal oxides coated papers. After drying, a 3.5 kV DC voltage is applied directly to the coated paper wetted with 20 µL acetonitrile. The quantitation analysis was evaluated by the peak intensity of the fragment ion m/z 165 from protonated verapamil m/z 455 in the SRM mode. (H2O means water, CH2Cl2 means dichloromethane, MeOH means methanol, EtOH means ethanol, IPA means isopropanol, and ACN means acetonitrile.)

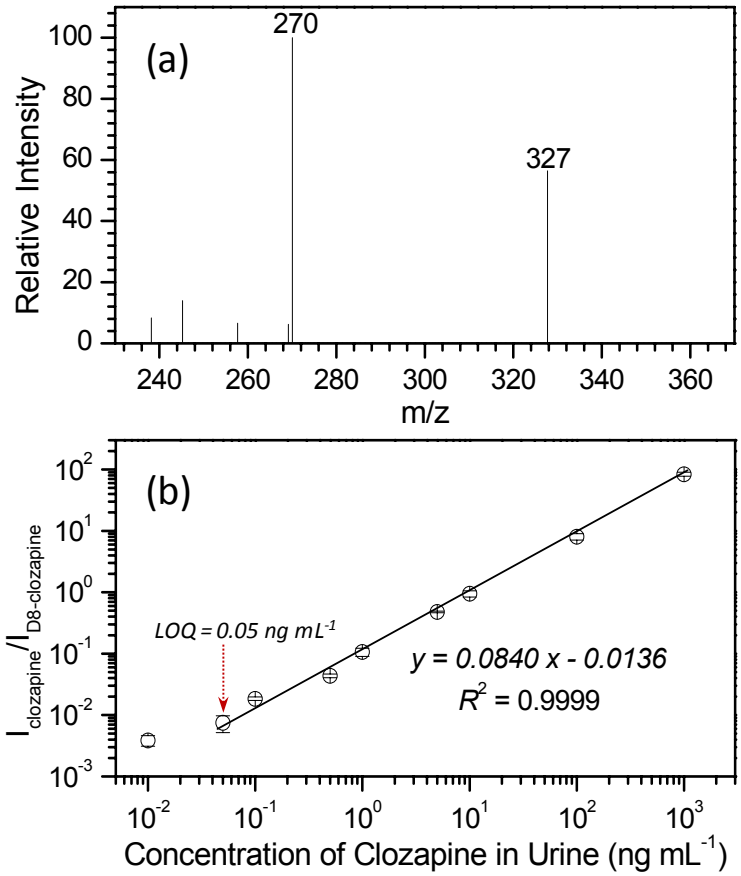

Fig. S-5 (a) MS/MS spectrum for 10 ng mL^{-1} clozapine in 2.0 µL raw urine using silica coated paper for paper spray. (b) Quantitation analysis of raw urine spiked clozapine (0.01 - 1,000 ng mL^{-1}) and its isotopomer [D_8]clozapine (10 ng mL^{-1}). The analysis was carried out by applying 3.5 kV DC voltage and 20 µL acetonitrile.

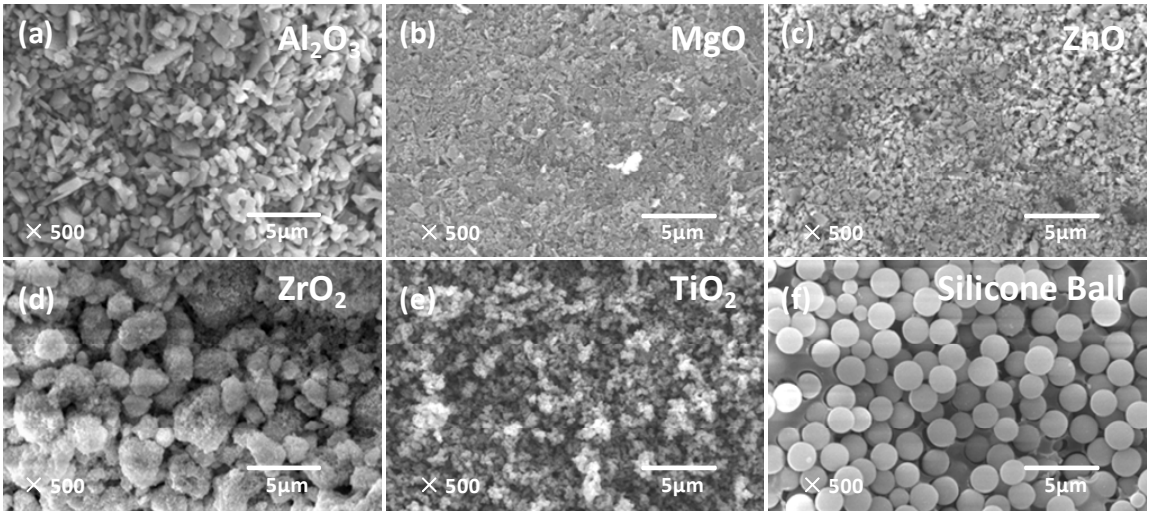

Fig. S-6 SEM images of (a) Al_2O_3, (b) MgO, (c) ZnO, (d) ZrO_2, (e) TiO_2 and (f) silicone ball coated paper. Similar to the silica particles coating procedure, the coating process for the different metal oxides coated paper is as below: The commercially available metal oxides (0.6 g) was dispersed in 100 mL deionized water containing 0.2 g starch as the bonding agent. After sonication for 15 min, the obtained suspension solution was directly transferred to a Buchner funnel covered by a blank filter paper with a diameter of 11 cm for coating. When the aqueous solution was completely penetrated through the filter paper, 20 mL absolute ethanol was applied for wash in order to get rid of the remaining water at the surface of the coated paper. The papers were then hung in a hood to dry for hours and were pressed between glass plates overnight for use. The papers can be safely stored in a ziplock bag for months. Different from the metal oxides coating procedure, the silicone ball coated paper followed the below process: The commercially available silicone ball (0.2 g) was dispersed in 100 mL deionized water/ethanol solution (1:1, v/v) containing 0.15 g starch as the bonding agent. Other steps were same as the procedure for metal oxides coating.

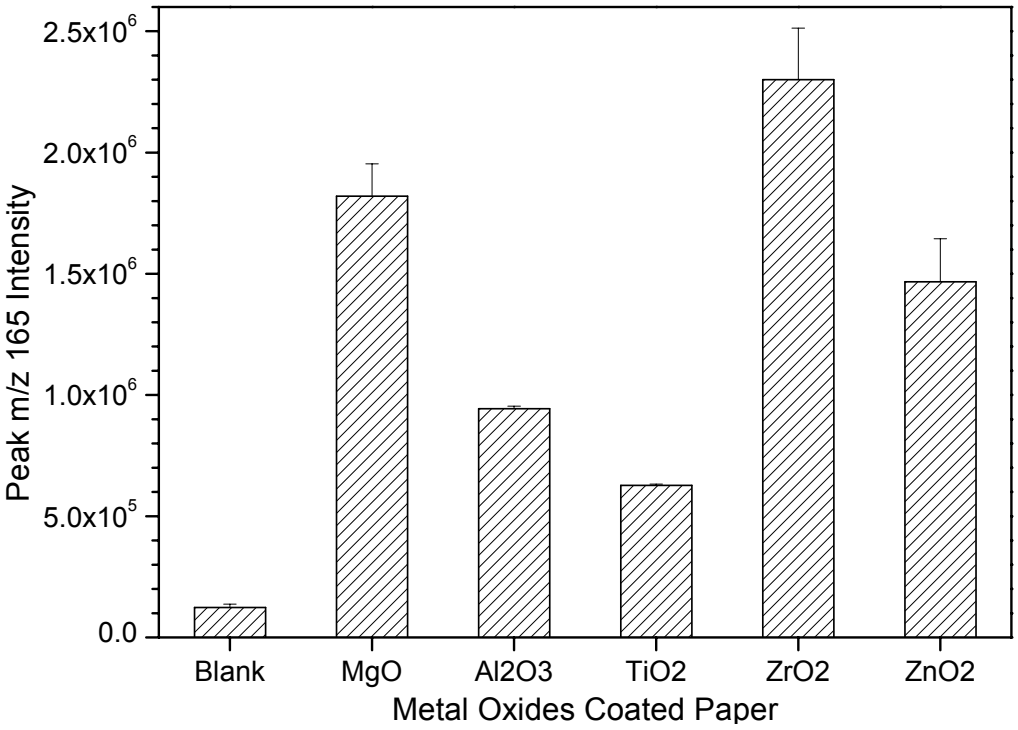

Fig. S-7 Effect of metal oxides coated papers on the ionization efficiency of paper spray. For the paper spray analysis, a drop of 2.0 µL whole blood containing 1.0 µg mL^{-1} verapamil was deposited to the metal oxides coated papers. After drying, a 3.5 kV DC voltage is applied directly to the coated paper wetted with 20 µL acetonitrile. The quantitation analysis was evaluated by the peak intensity of the fragment ion m/z 165 from protonated verapamil m/z 455 in the SRM mode. (Note: Blank means the commerically availalbe filter paper.)

To investigate the performance of metal oxides coated paper in paper spray ionization, different commercially available materials such as MgO, Al_2O_3, TiO_2, ZrO_2 and ZnO_2 were, respectively, coated on the surface of filter paper for spray. As illustrated in Fig. S-7, ZrO_2 demonstrates the superior performance to others, and MgO and ZnO are comparable in analysis of therapeutic drug verapamil in dried blood spots. The improvement in MS sensitivity using Al_2O_3 and TiO_2 coated papers is not high enough relative to the uncoated filter paper (Blank in Figure S-7).

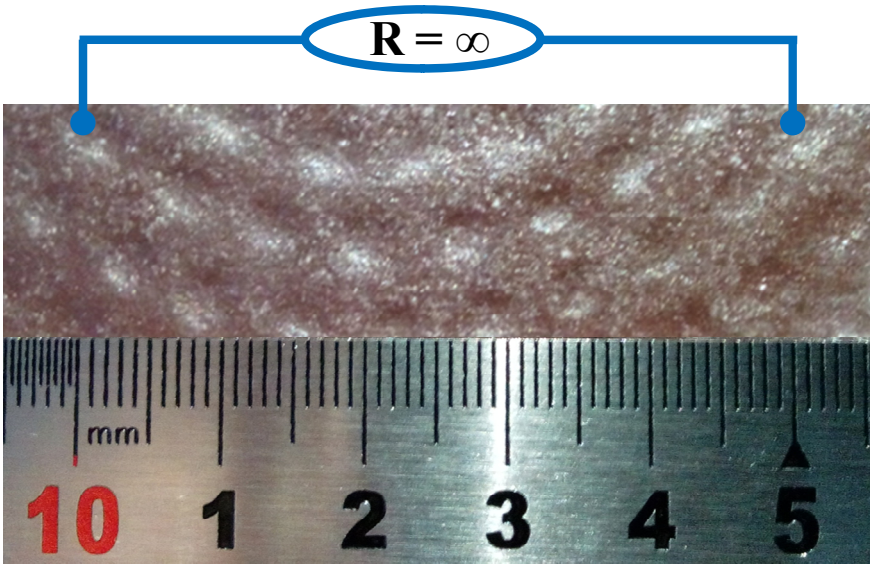

Fig. S-8 Photograph image of copper powder coated paper. The resistance value could not be determined with a multimeter between 5 mm length of coated paper. Similar to the CNTs coating procedure, the coating process for the copper powder coated paper is as below: The commercially available copper powder (0.1 g) was dispersed in 100 mL deionized water/ethanol solution (1:1, v/v) containing 0.4 g starch as the bonding agent. After sonication for 15 min, the obtained suspension solution was directly transferred to a Buchner funnel covered by a blank filter paper with a diameter of 11 cm for coating. When the aqueous solution was completely penetrated through the filter paper, 20 mL absolute ethanol was applied for wash in order to get rid of the remaining water at the surface of the coated paper. The papers were then hung in a hood to dry for hours and were pressed between glass plates overnight for use. The papers can be safely stored in a ziplock bag for months.

Table 1. Selected reaction monitoring (SRM) conditions

Number	Analyte	Parent Ion (*m/z)*	Fragment Ion (*m/z)*	Tube Lens (V)	Q2 Offset (V)
1	Amitriptyline	278	233	16	66
2	Clozapine	327	270	22	75
3	[D_8]Clozapine	335	275	24	76
4	Amisulpride	370	242	26	73
5	Quetiapine	384	253	22	77
6	Risperidone	411	191	26	84
7	Aripiprazole	448	285	25	94
8	Verapamil	455	165	26	87

Applied voltage: 3.5 kV; Solvent: Acetonitrile.