A Small Footprint and Robust Interface for Solid Phase Microextraction and Mass Spectrometry based on Vibrating Sharp-edge Spray Ionization

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Frequency (kHz)	**Amplitude (V_{pp})**	**Volume (μL)**	**Flow Rate (μL/min)**
93	7	6	0.46±0.02
93	9	6	0.58±0.03
93	11	6	0.70±0.02

Table S1 Spray flow rates of the cVSSI for a 15 μm pulled-tip capillary under different input voltage.

Analyte	Spiked Concentration (ng/mL)	Found Concentration (ng/mL)	(%) Recovery (±SD)
metoprolol	0.267	0.24(±0.01)	91(±4)
	6.675	5.54（±0.20）	83(±3)
	13.36	10.69（±0.20）	80(±2)
	20.25	17.62（±0.91）	87(±5)
	26.7	21.89（±0.99）	82(±4)

Table S2 Recovery test for spiked metoprolol samples at different concentrations.

Analyte	Dynamic Range (ng/mL)	Linear Curve	R^2
Metoprolol	0.267-26.7	Y=0.038X-0.007	0.9968
Pindolol	0.249-24.9	Y=0.006X+0.040	0.9701
Irinotecan	0.585-58.5	Y=0.016-0.045	0.9856
Capecitabine	0.360-36.0	Y=0.010X+0.082	0.9918
Acebutolol	0.337-33.7	Y=0.010X-0.040	0.9920
Oxprenolol	0.266-26.6	Y=0.010X+0.054	0.9924

Table S3 Calibration curves for all the compounds tested.

Analyte	Therapeutic Concentration (ng/mL)	Limit of Detection of the present method (ng/mL)	Reference
Metoprolol	14 to 212	0.27	[1]
Pindolol	100	0.25	[2]
Irinotecan	1600	0.59	[3]
Capecitabine	2700 to 4000	0.36	[4]
Acebutolol	200 to 2000	0.34	[5]
Oxprenolol	680	0.27	[6]

Table S4 Typical Therapeutic concentrations of drugs tested.

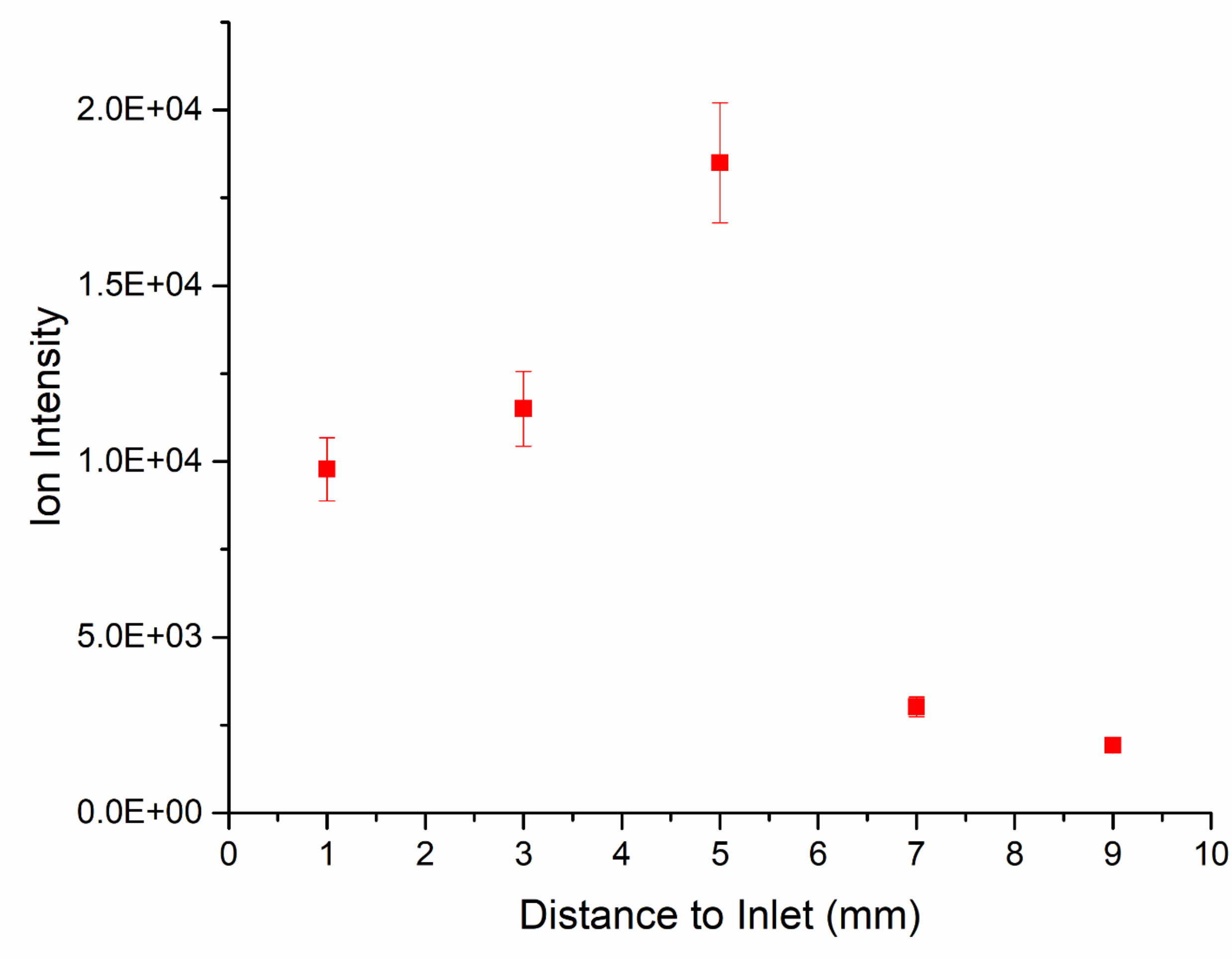


Figure S1: The relationship between ion intensity and the distance to the mass spectrometer inlet. The optimal distance to the inlet was determined to be 5 mm.

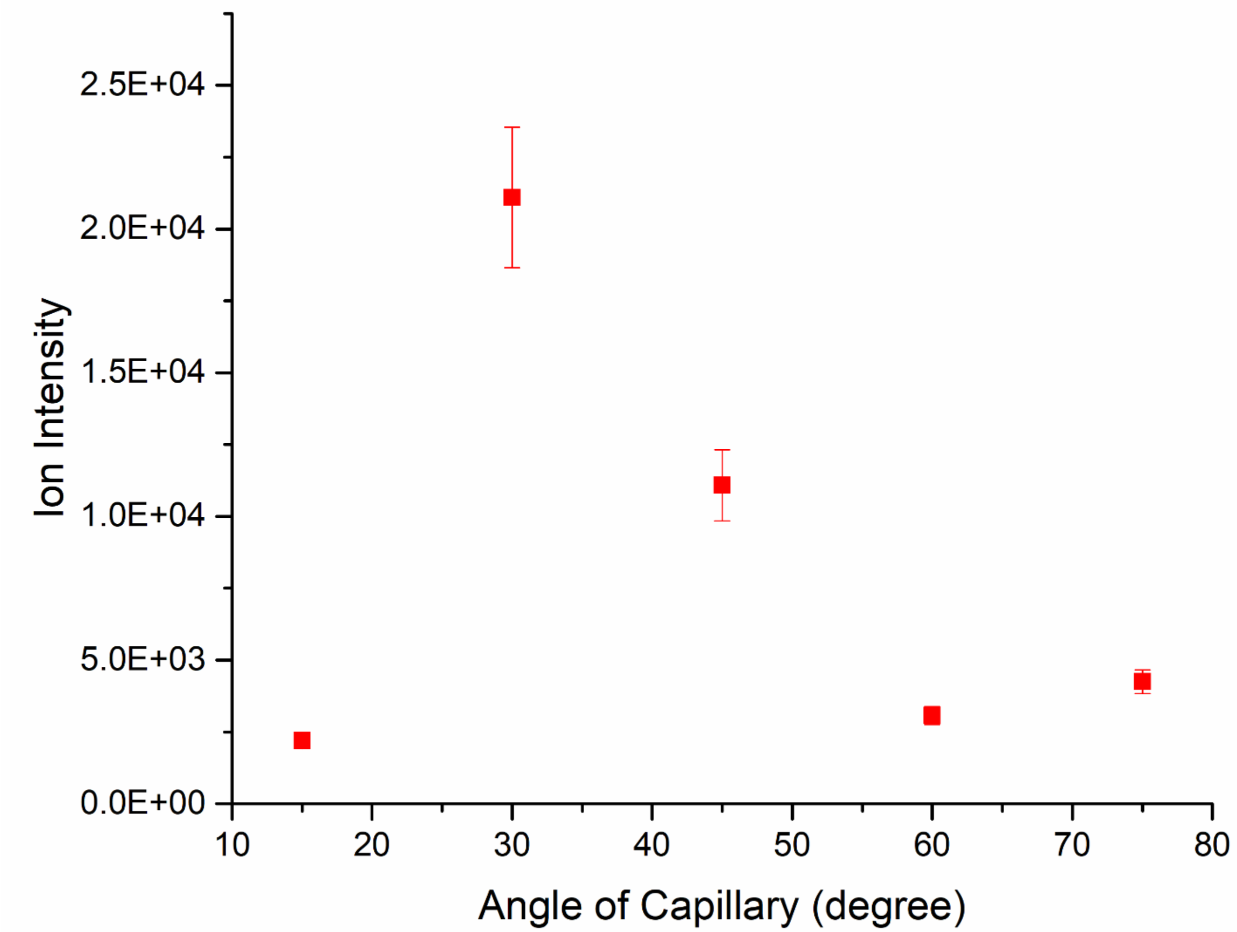


Figure S2: The relationship between ion intensity and the angle to the mass spectrometer inlet. The optimal distance to the inlet was determined to be 30 degree.

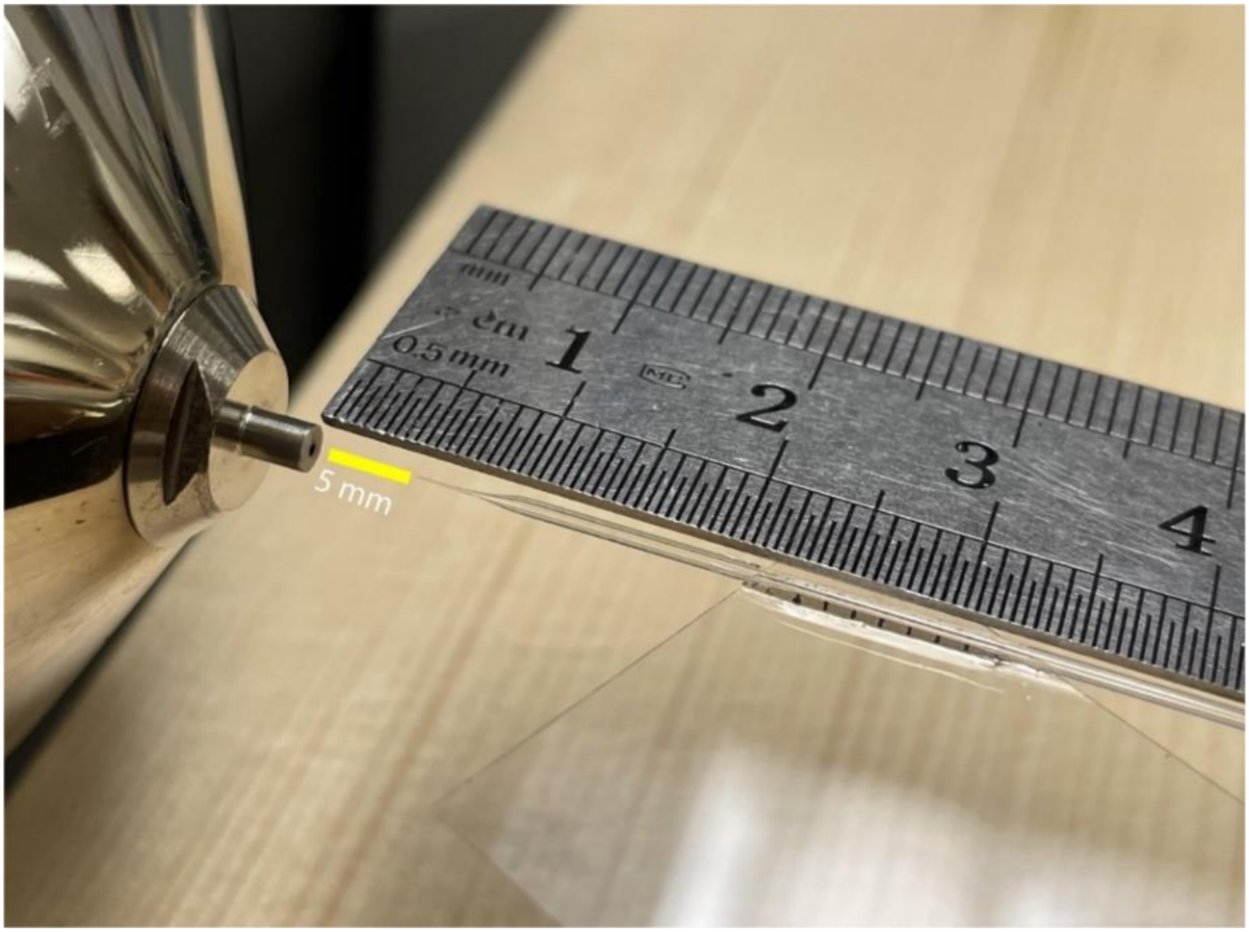


Figure S3 A close up picture of the cVSSI-MS setup

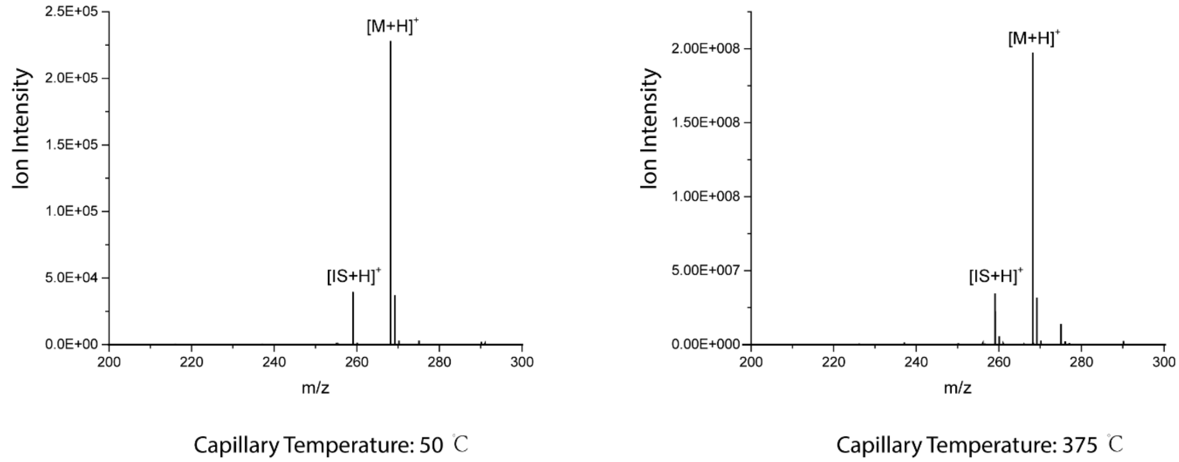


Figure S4 Comparison of mass spectra of 10 µM metoprolol with different capillary temperatures. Left: 50 ℃; Right: 375 ℃

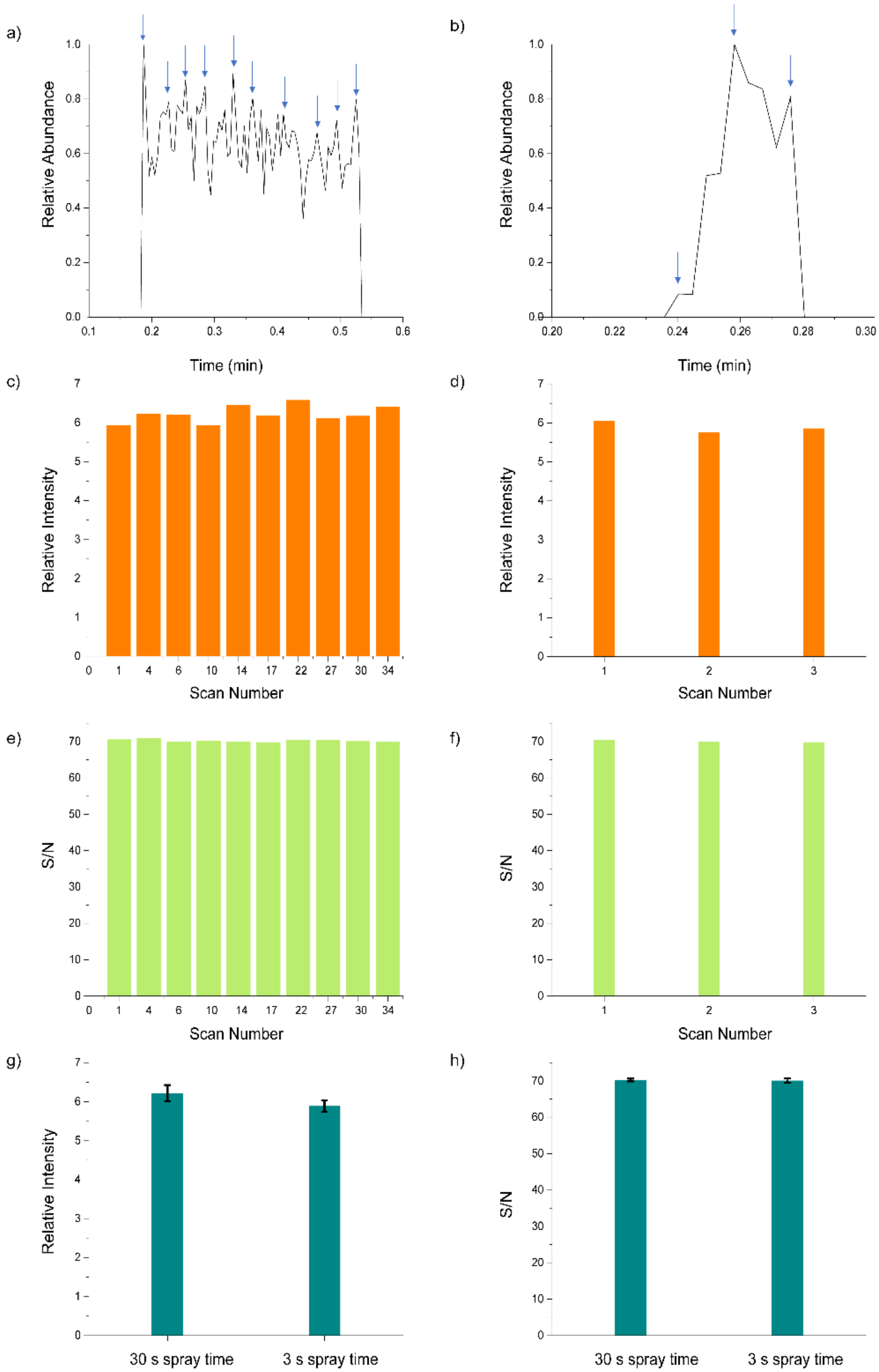
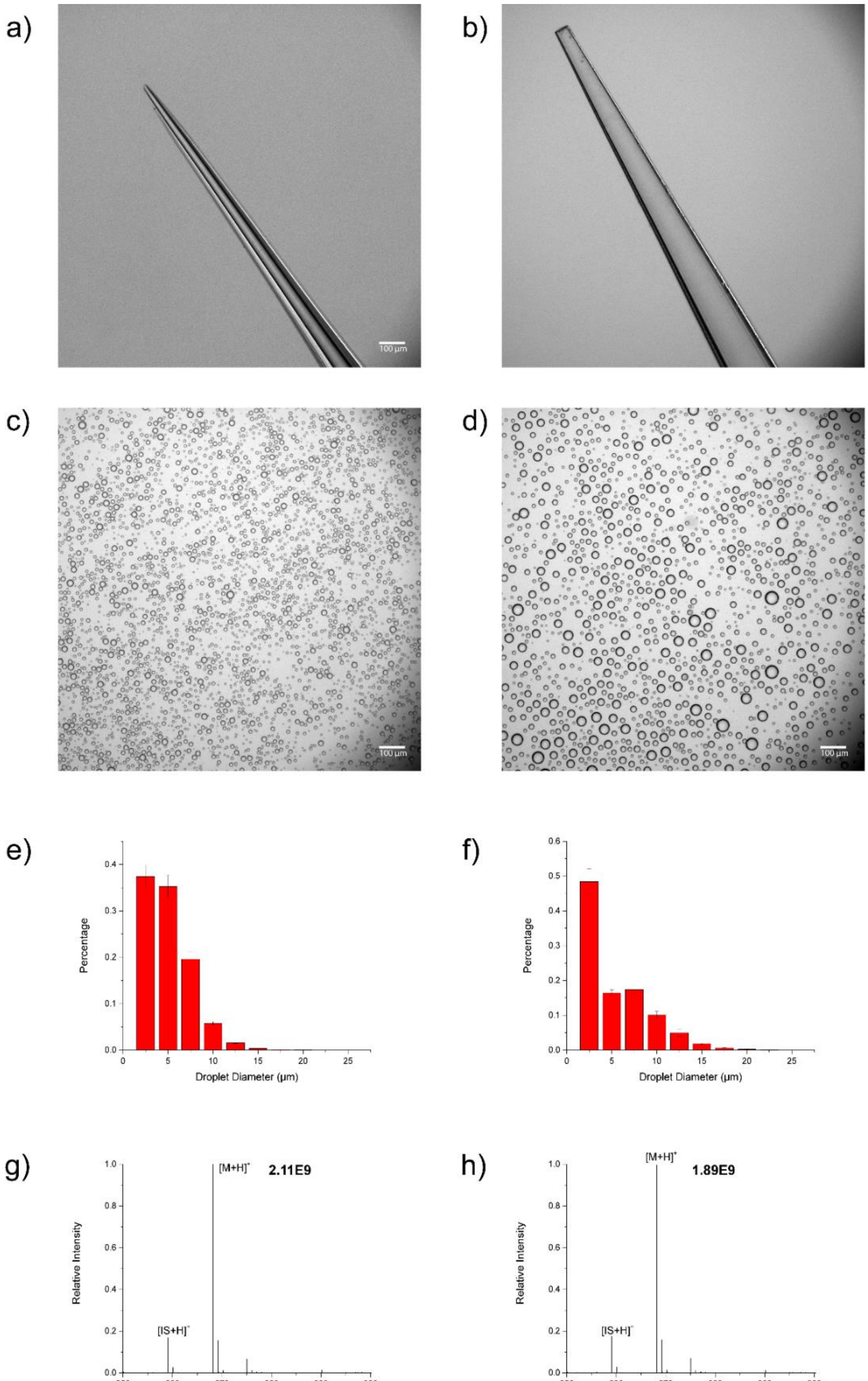

a)
b)
Relative Abundance
Time (min)
c)
d)
Relative Intensity
Scan Number
e)
f)
S/N
Scan Number
g)
h)
Relative Intensity
S/N
30 s spray time
3 s spray time

Figure S5 Comparison of MS signals with different spray time using 10 µM metoprolol. a) and b) ion chronograms of a 30 s spray and a 3 s spray, respectively. c) and d) Relative intensity of each scan of a 30 s spray and a 3 s spray, respectively. e) and f) S/N of each scan of a 30 s spray and a 3 s spray, respectively. g) and h) comparison of average relative intensity and S/N of a 30 s spray and a 3 s spray, respectively.



a)
100 µm
b)
c)
100 µm
d)
100 µm
e)
Percentage
Droplet Diameter (µm)
f)
Percentage
Droplet Diameter (µm)
g)
[M+H]+
2.11E9
[IS+H]+
Relative Intensity
m/z
h)
[M+H]+
1.89E9
[IS+H]+
Relative Intensity
m/z

Figure S6 Comparison of capillaries with 15 µm and 50 µm tip size. a) and b) microscopy images of a 15 µm tip and a 50 µm tip, respectively. c) and d) microscopy images of droplets generated by a 15 µm tip and a 50 µm tip, respectively. e) and f) size distribution of droplets generated by a 15 µm tip and a 50 µm tip, respectively. g) and h) comparison of mass spectra of 10 µM metoprolol generated by a 15 µm tip and a 50 µm tip, respectively.

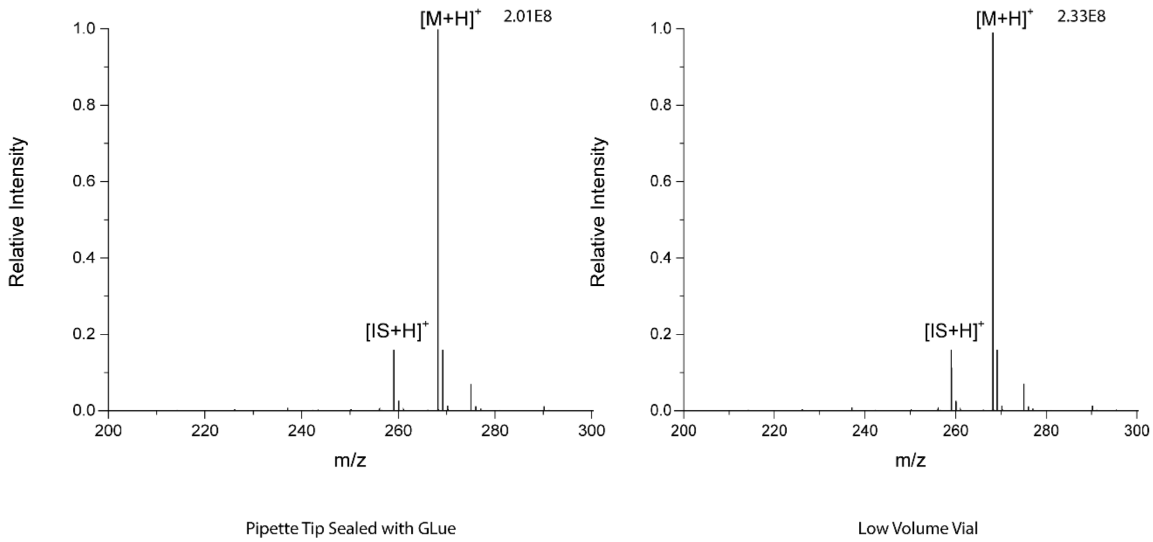


Figure S7 Comparison of mass spectra 10 µM metoprolol obtained with glue seal (left) and without glue (right).

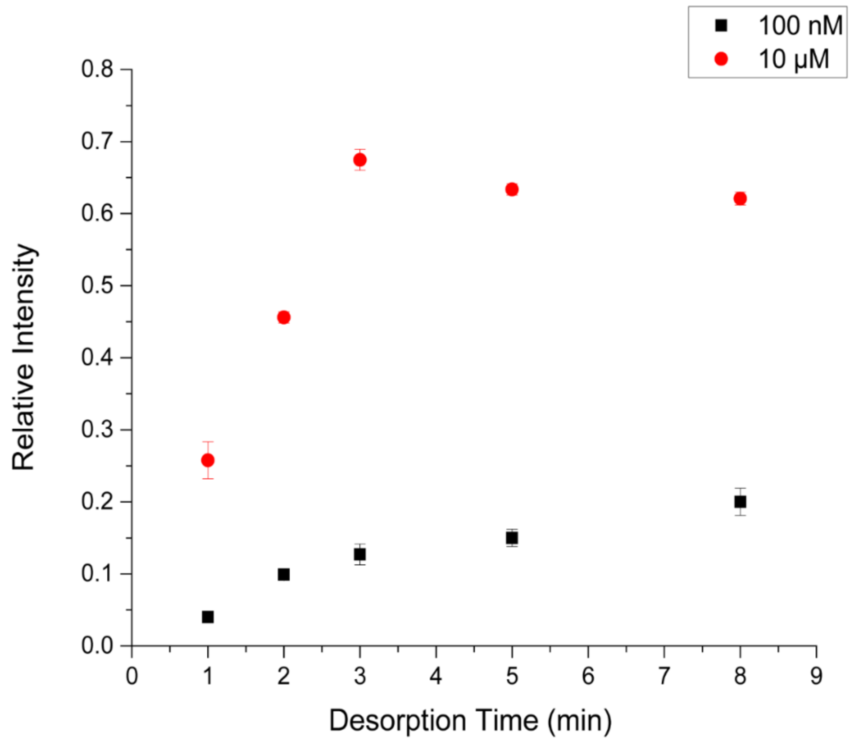


Figure S8 The relationship between the signal response and the desorption time with 500 μL extraction volume, 24 min extraction time, and 6 μL desorption volume for 100 nM and 10 μM metoprolol samples.

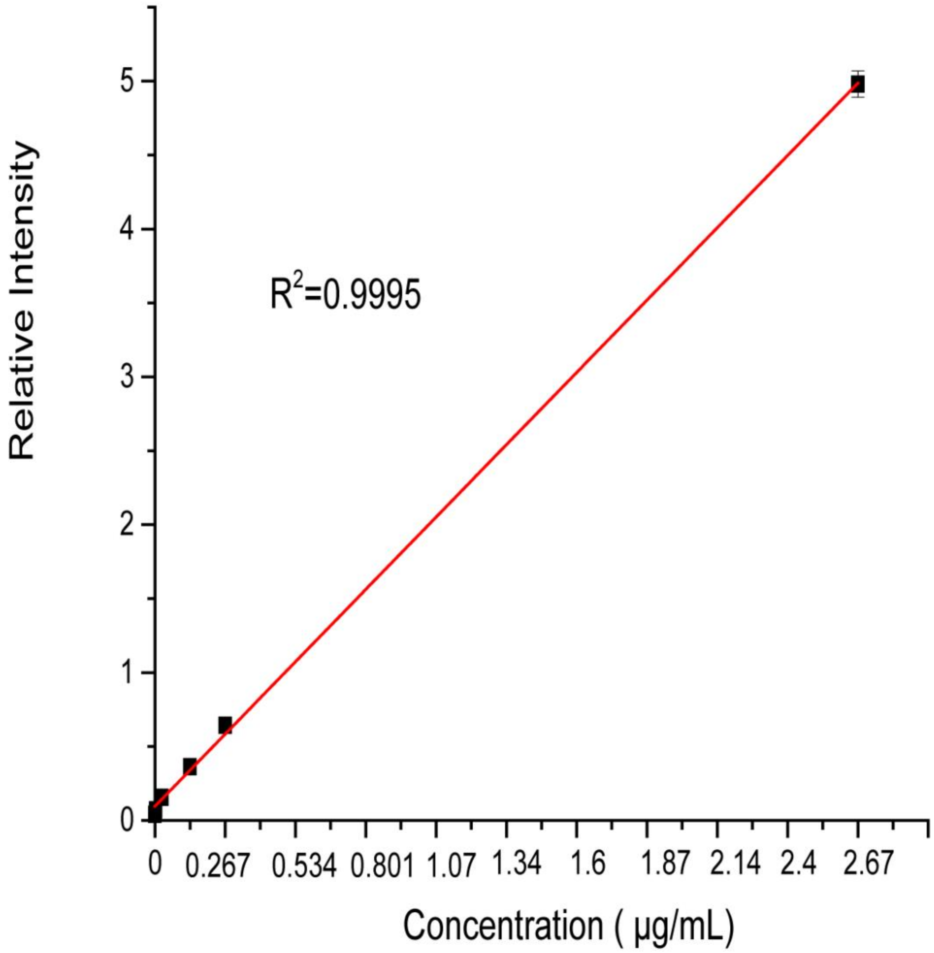


Figure S9: The calibration curve for metoprolol in serum samples obtained using SPME-cVSSI-MS.

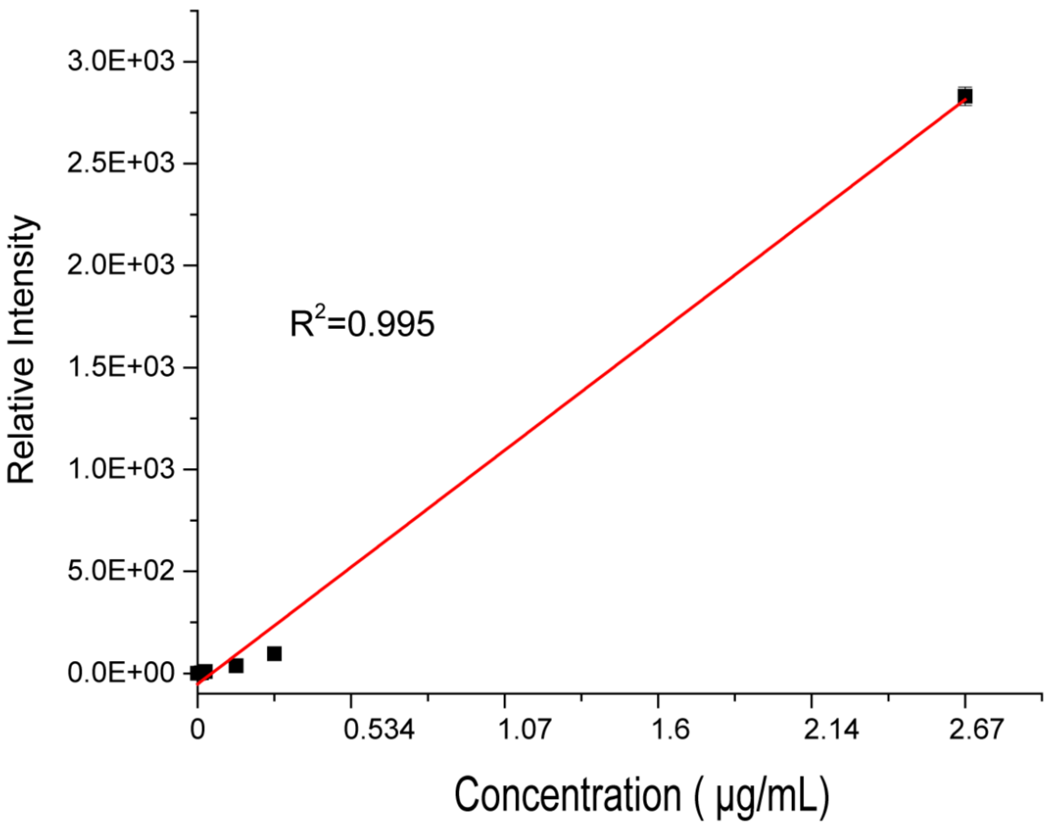


Figure S10: The calibration curve for metoprolol in serum samples obtained using SPME-nESI-MS.

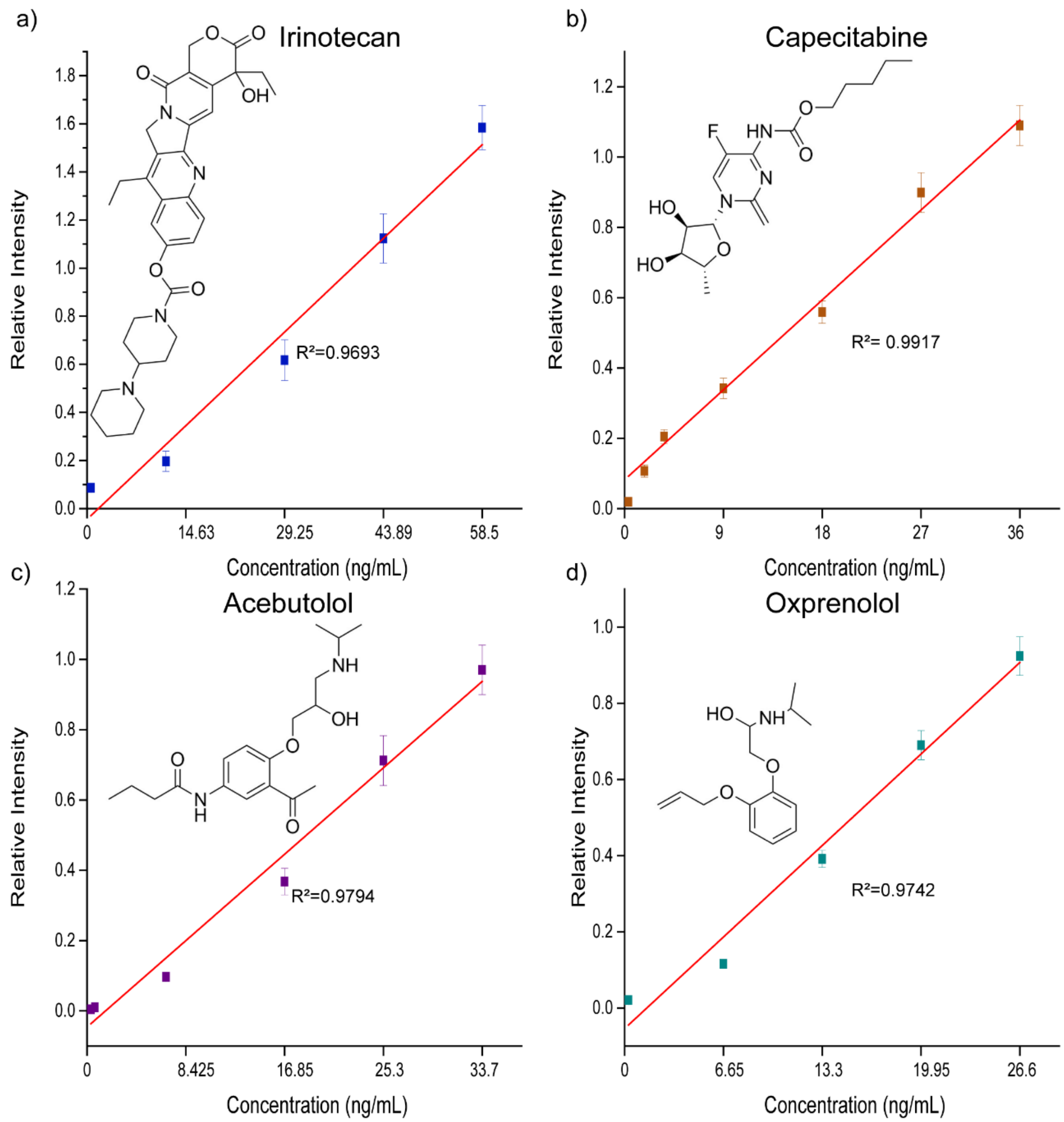


Figure S11: Calibration curves for 4 different drug compounds from serum samples. (a)-(d) irinotecan, capecitabine, acebutolol, and oxprenolol, respectively.

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