

Electronic Supplementary Material

Direct in situ labeling of target drugs with a fluorophore probe to improve MALDI-MS detection sensitivity in micro-liter plasma

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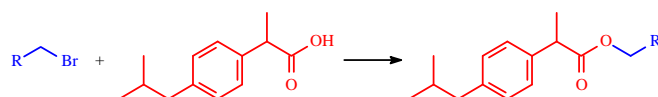
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Table S1. Effects of fluorophore probes on the formation of ibuprofen derivative



Probe	Structure	Relative response (%)
Br-MBT		100
Br-MQ		6
Br-DMC		< 1
Br-MAC		< 1
Br-MA		< 1
Br-AC		no signal
Br-AP		no signal

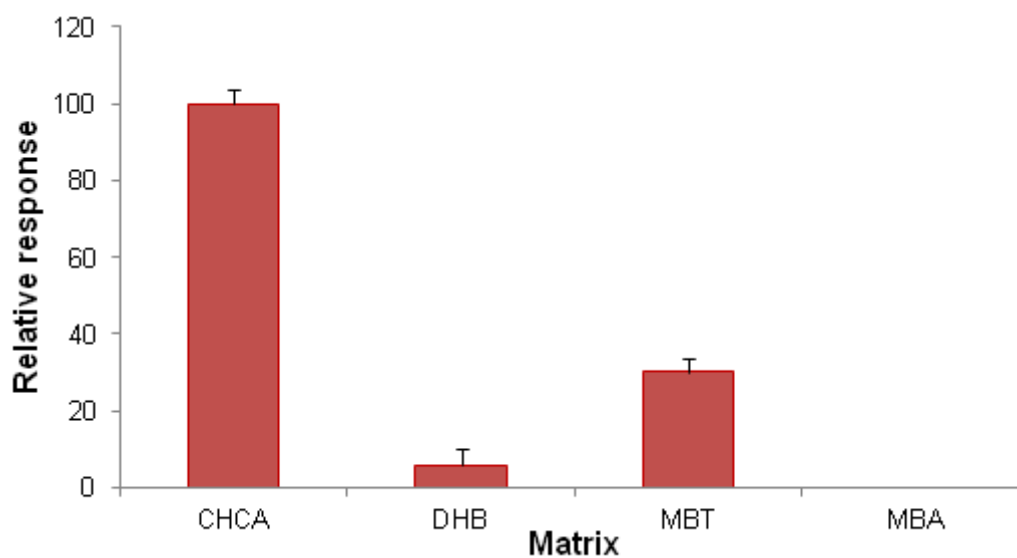


Figure S1 Effects of the matrix on detection of ibuprofen derivative signal in human plasma.

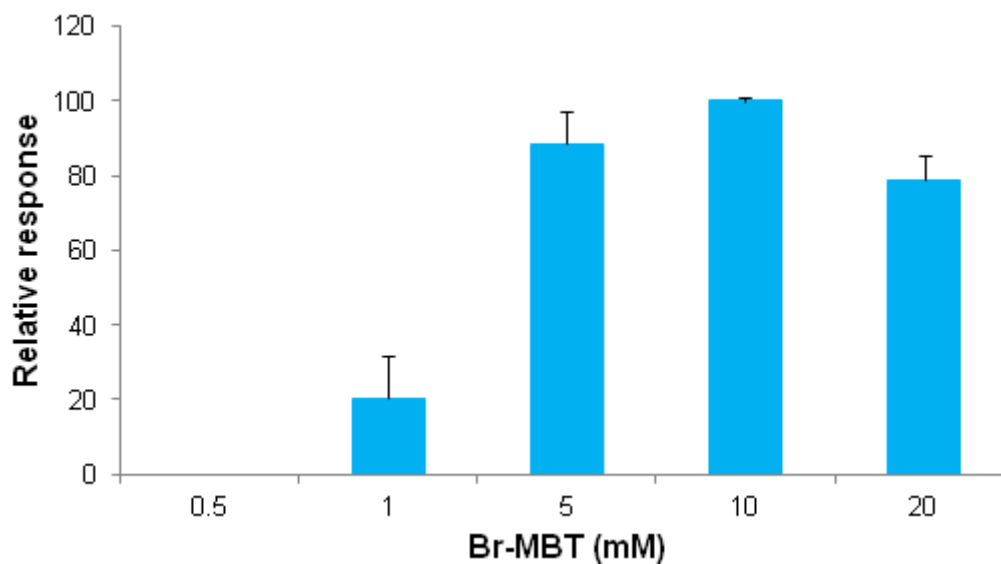


Figure S2 Effect of Br-MBT concentration on formation of the ibuprofen derivative.

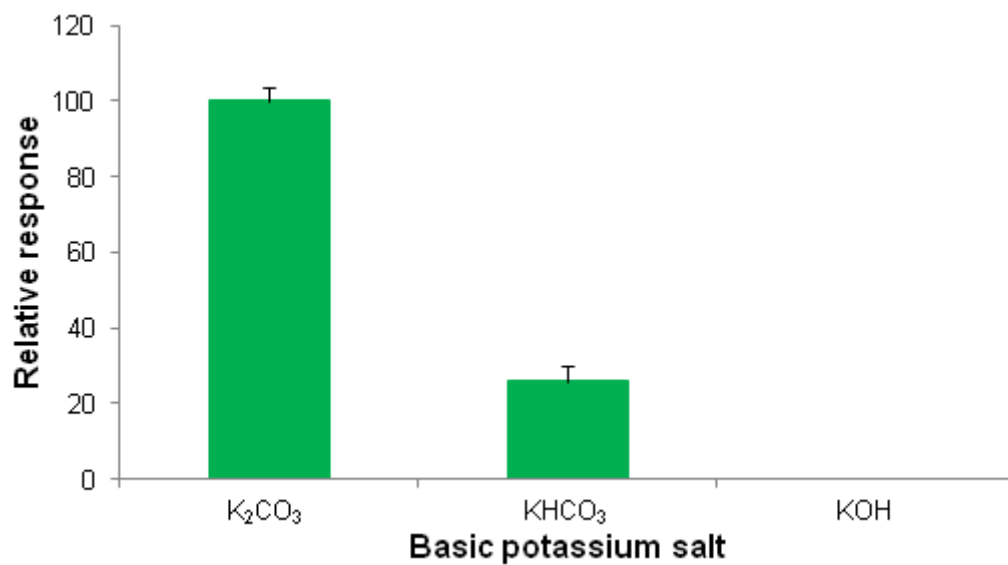


Figure S3 Effects of basic potassium salts on the formation of the ibuprofen derivative.

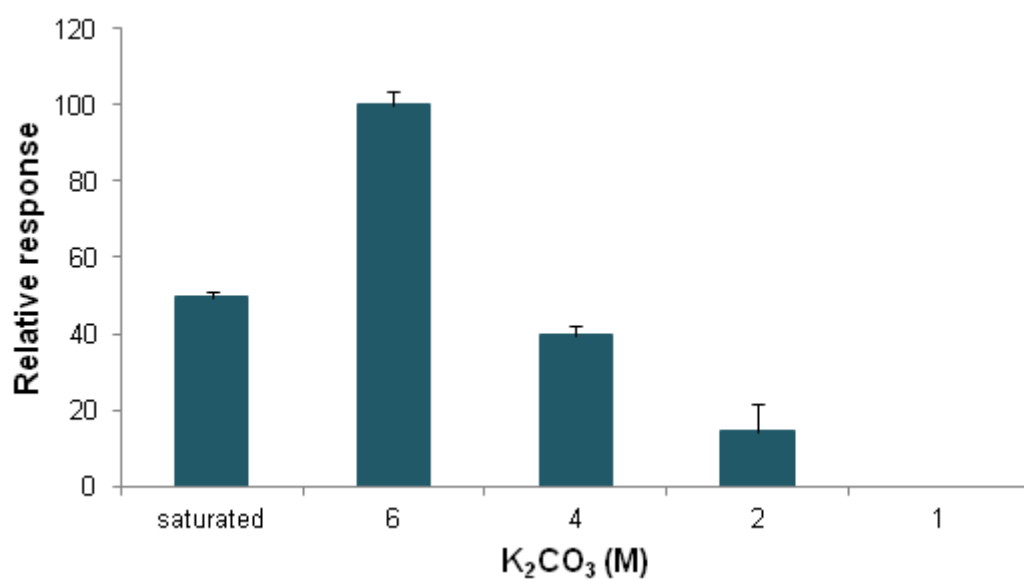


Figure S4 Effects of K_2CO_3 concentration on the formation of the ibuprofen derivative.

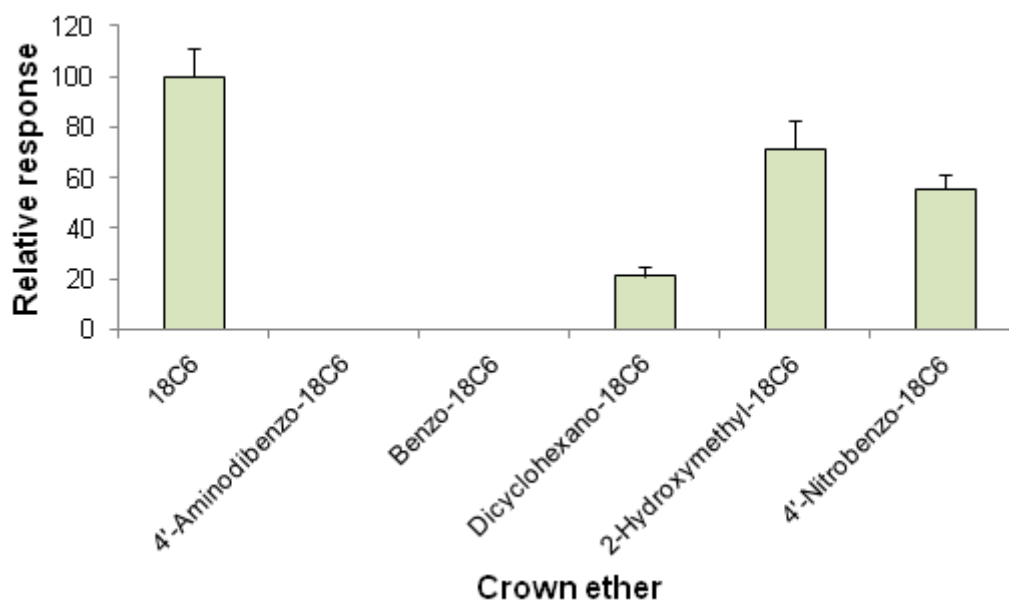


Figure S5 Effect of the different 18-crown-6 (18C6) crown ethers on the formation of the ibuprofen derivative.

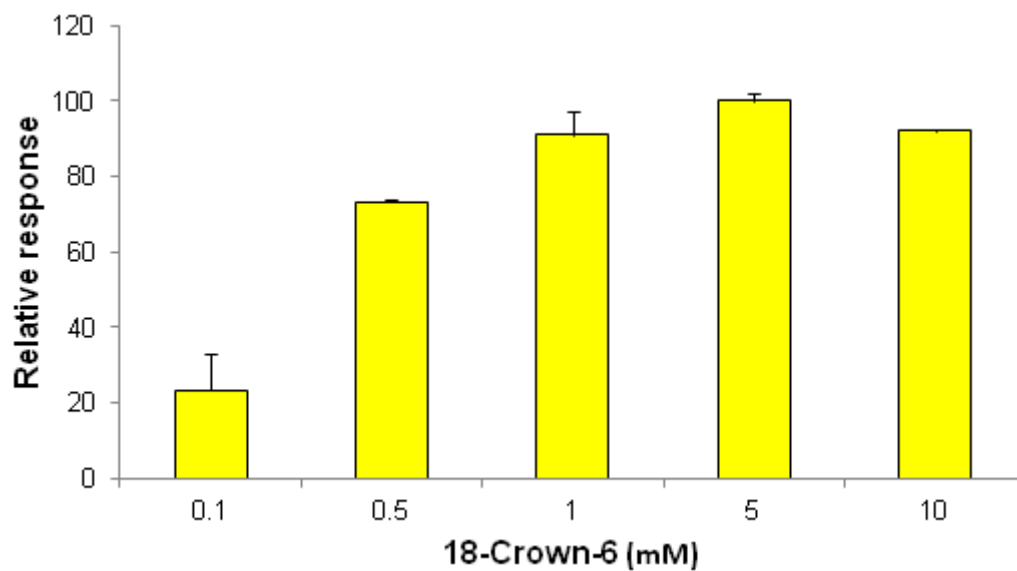


Figure S6 Effect of 18-crown-6 concentration on the formation of the ibuprofen derivative.

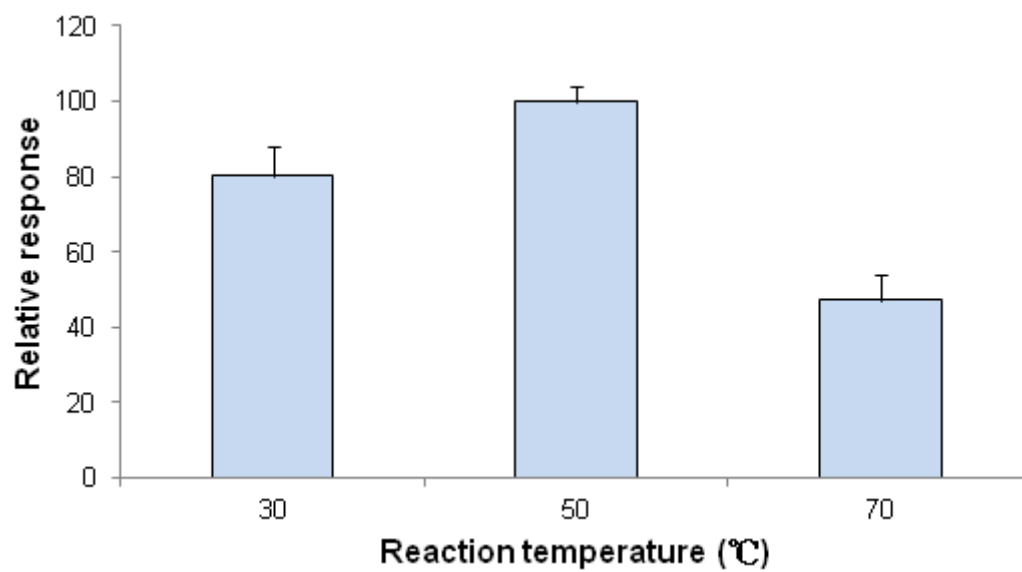


Figure S7 Effect of the reaction temperature on the formation of the ibuprofen derivative.

Table S2. Comparison of current methods for analysis of ibuprofen

Analytical method	Sample	Sample volume (µL)	Sample preparation	Analytical time (min)	LOD (µg/mL)	Mobile phase/ carrier gas	Ref.
LC-UV	human plasma	1000	LLE	3.5	0.04	acetonitrile, phosphoric acid	[1]
LC-FLD	human plasma	500	LLE	20	0.1	acetonitrile, acetic acid, triethylamine	[2]
LC-UV	human plasma	50	SPE	5	-	acetonitrile, phosphoric acid	[3]
LC-UV	human plasma	100	protein precipitation	12.5	1	methanol, potassium hydrogen phosphate	[4]
LC-MS/MS	human plasma	100	LLE	1.5	-	methanol, acetonitrile, ammonium formate buffer	[5]
LC-MS/MS	human plasma	50	LLE SPE	13	0.02	methanol, acetic acid	[6]
LC-MS/MS	human plasma	20	LLE	8	0.02	methanol, formic acid	[7]
LC-UV	human plasma	1000	direct injection	14	0.07	sodium dodecyl sulfate, n-propanol, triethylamine, orthophosphoric acid	[8]
GC-MS/MS	human plasma	10	LLE	8	-	helium	[9]
MALDI-TOF MS	human plasma	5	micro-labeling	< 1	0.1	-	This work

Abbreviations: UV, ultraviolet; FLD, fluorescence detector; MS, mass spectrometry; LC, liquid chromatography; GC, gas chromatography; LLE, liquid-liquid extraction; SPE, solid phase extraction; LOD, limit of detection; Ref., reference.

References

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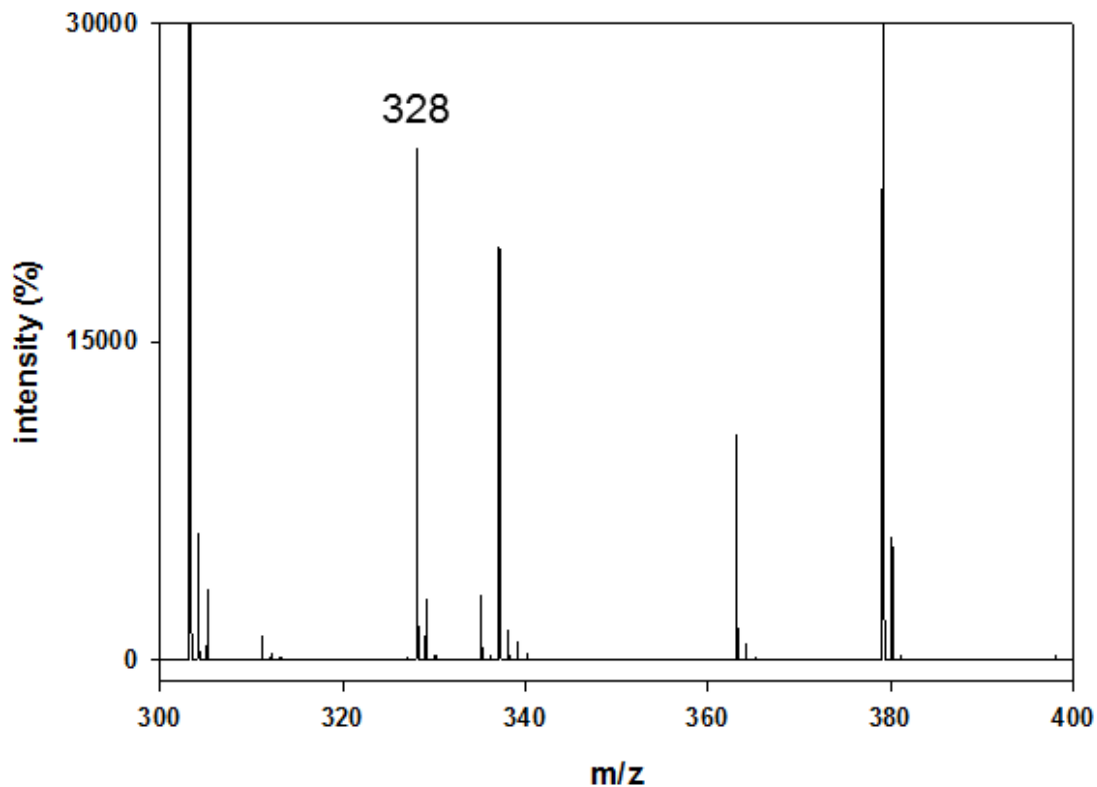


Figure S8-1 Mass spectrum for the analysis of aspirin spiked in human plasma, $[M+H]^+$ signal appears at m/z 328.

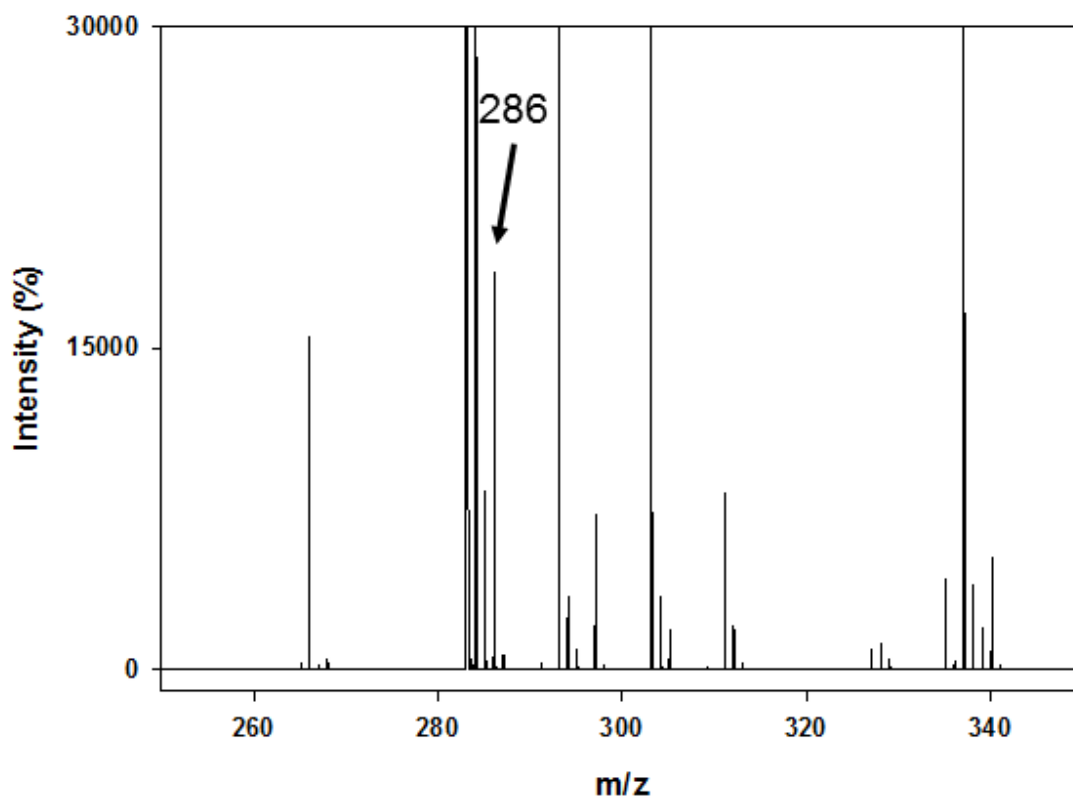


Figure S8-2 Mass spectrum for the analysis of salicylic acid spiked in human plasma, $[M+H]^+$ signal appears at m/z 286.

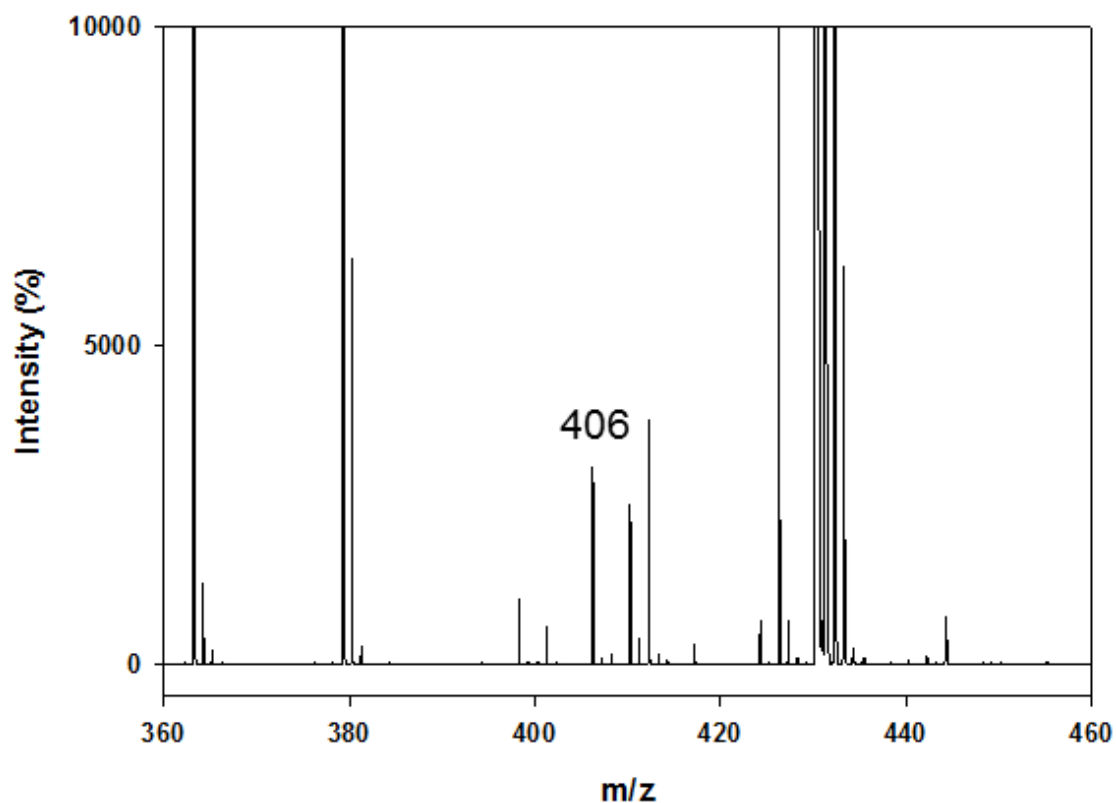


Figure S8-3 Mass spectrum for the analysis of salsalate spiked in human plasma, $[M+H]^+$ signal appears at m/z 406.

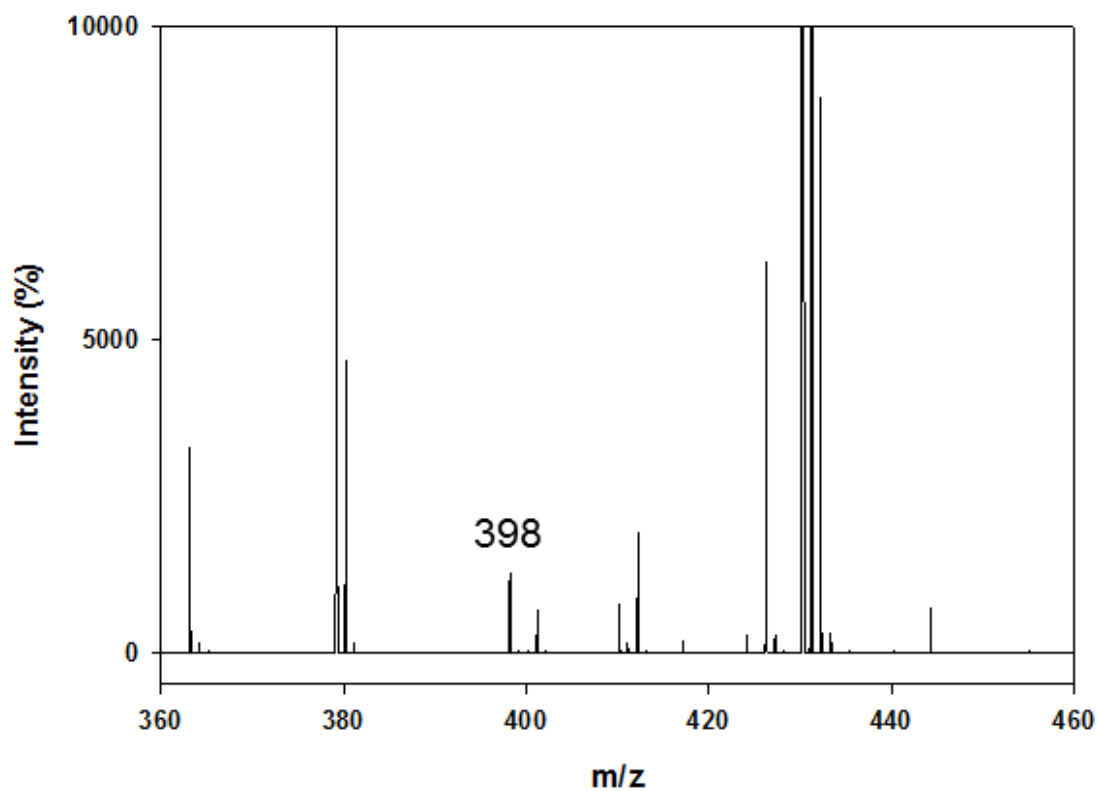


Figure S8-4 Mass spectrum for the analysis of diflunisal spiked in human plasma, $[M+H]^+$ signal appears at m/z 398.

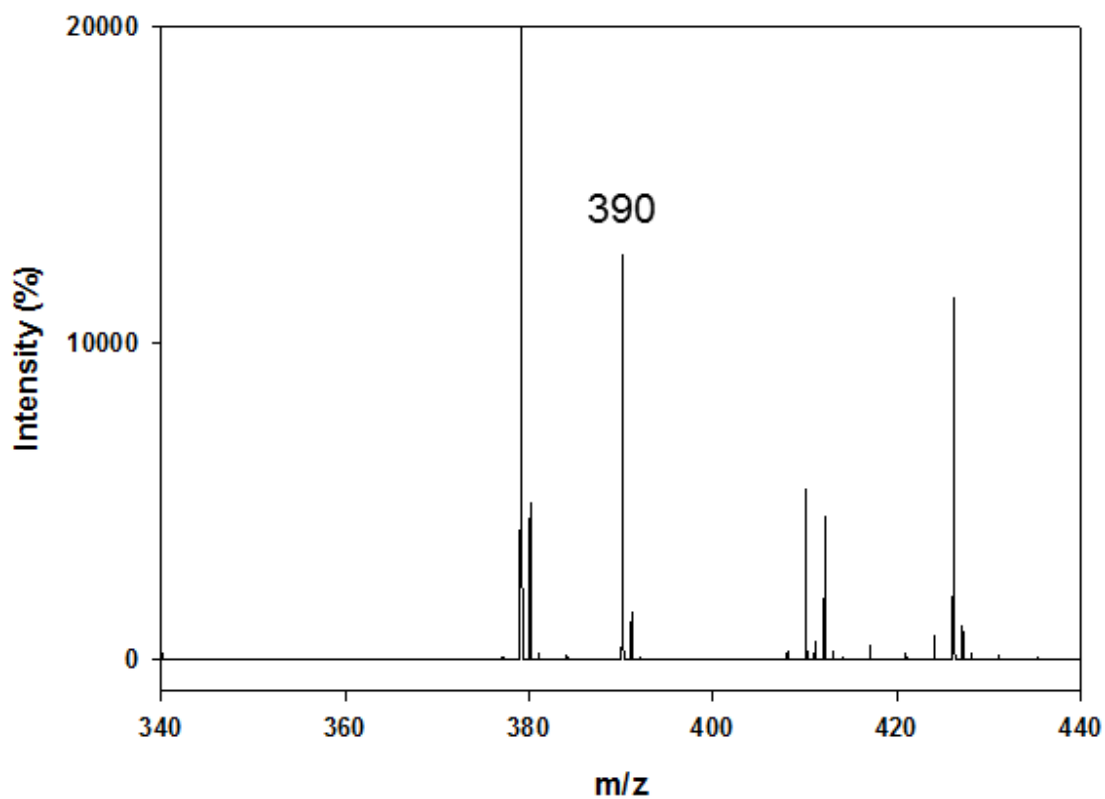


Figure S8-5 Mass spectrum for the analysis of fenopropfen spiked in human plasma, $[M+H]^+$ signal appears at m/z 390.

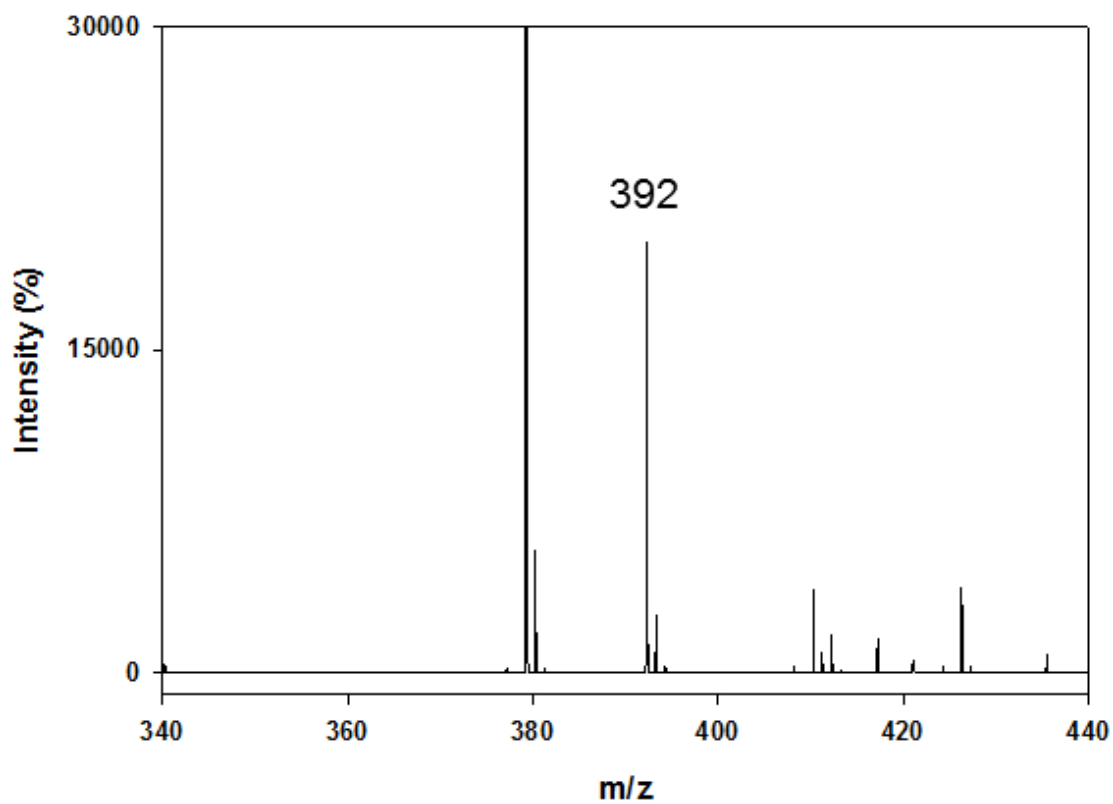


Figure S8-6 Mass spectrum for the analysis of flurbiprofen spiked in human plasma, $[M+H]^+$ signal appears at m/z 392.

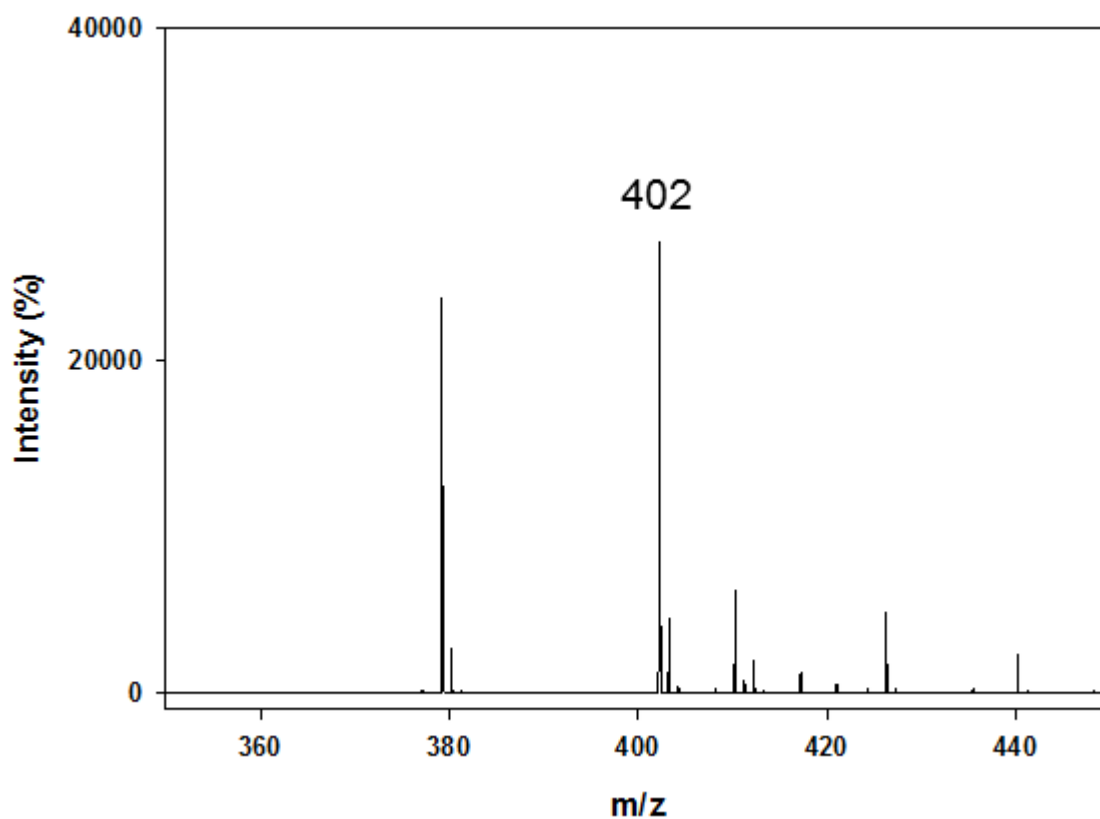


Figure S8-7 Mass spectrum for the analysis of ketoprofen spiked in human plasma, $[M+H]^+$ signal appears at m/z 402.

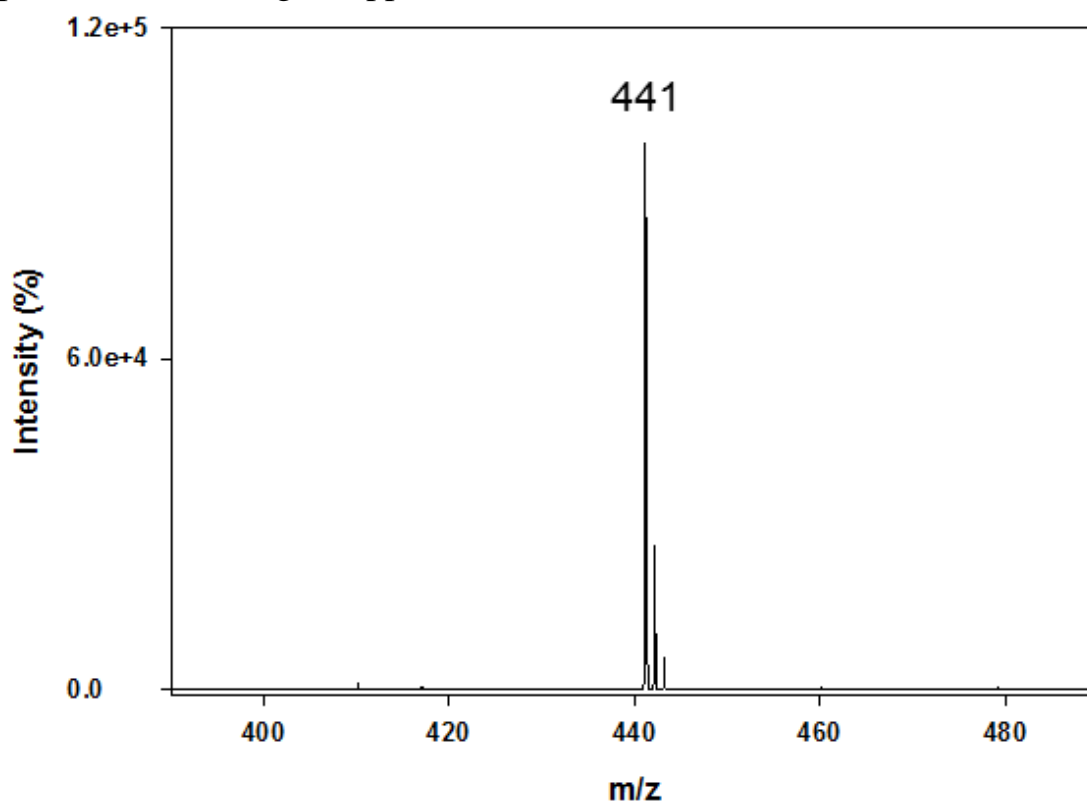


Figure S8-8 Mass spectrum for the analysis of oxaprozin spiked in human plasma, $[M+H]^+$ signal appears at m/z 441.

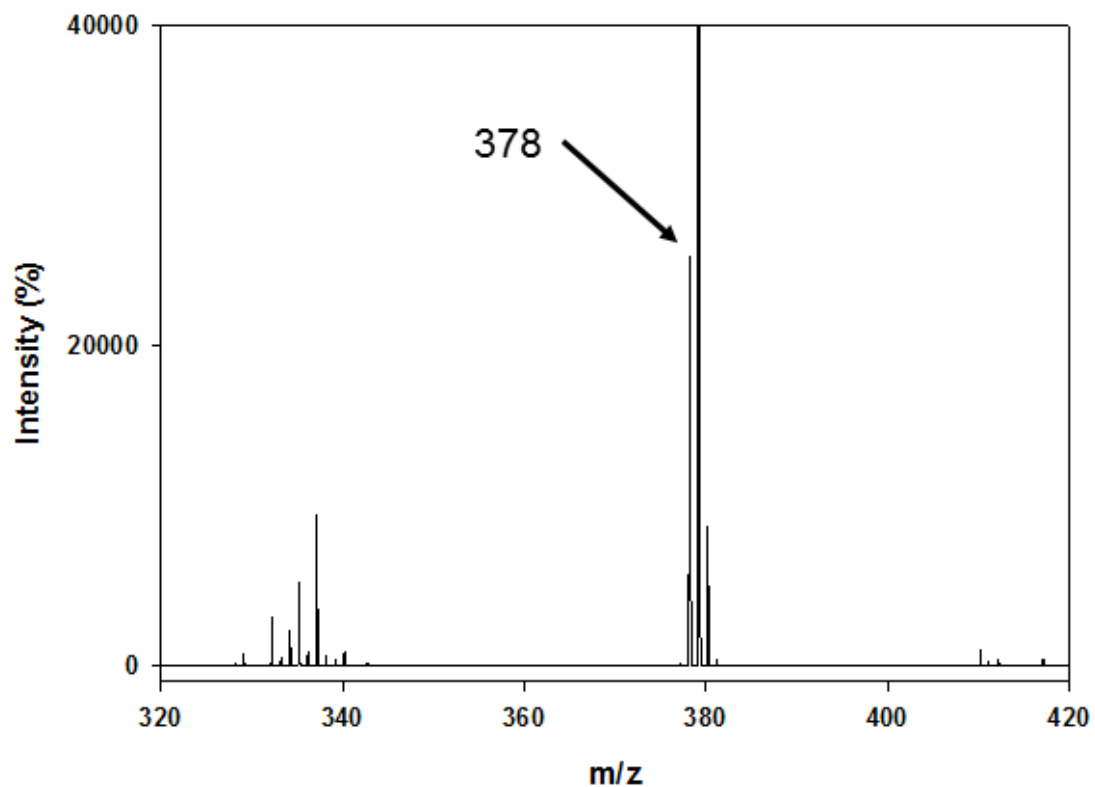


Figure S8-9 Mass spectrum for the analysis of naproxen spiked in human plasma, $[M+H]^+$ signal appears at m/z 378.

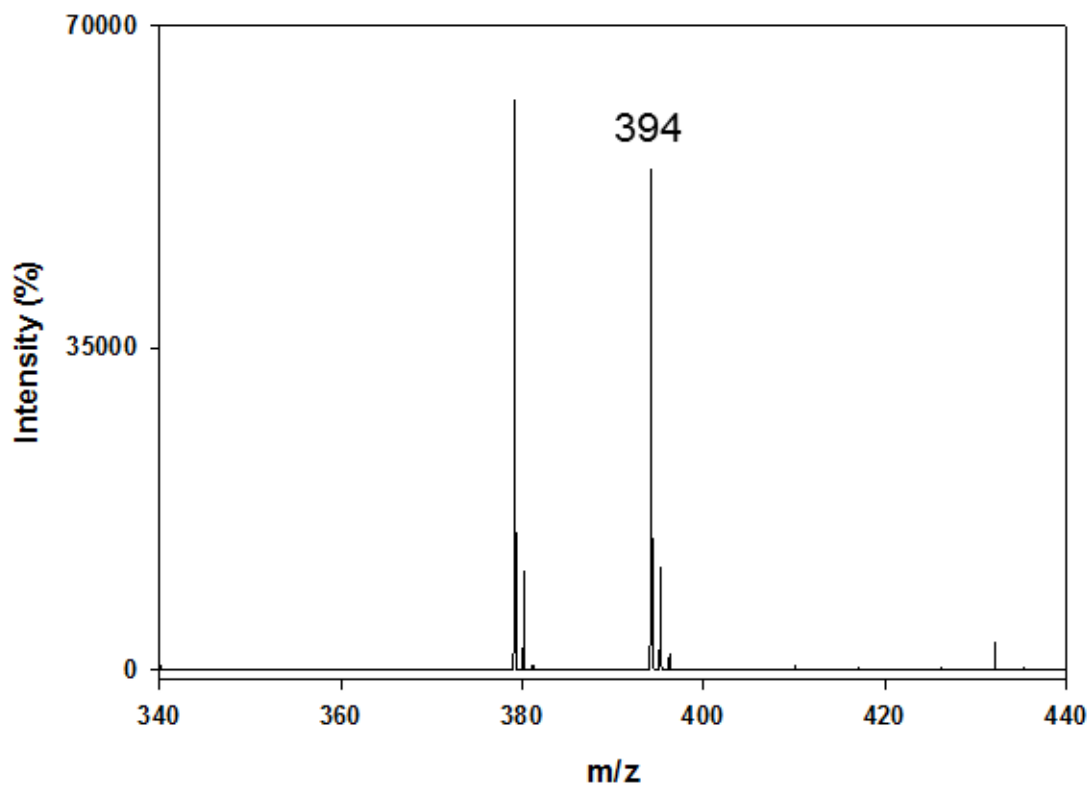


Figure S8-10 Mass spectrum for the analysis of loxoprofen spiked in human plasma, $[M+H]^+$ signal appears at m/z 394.

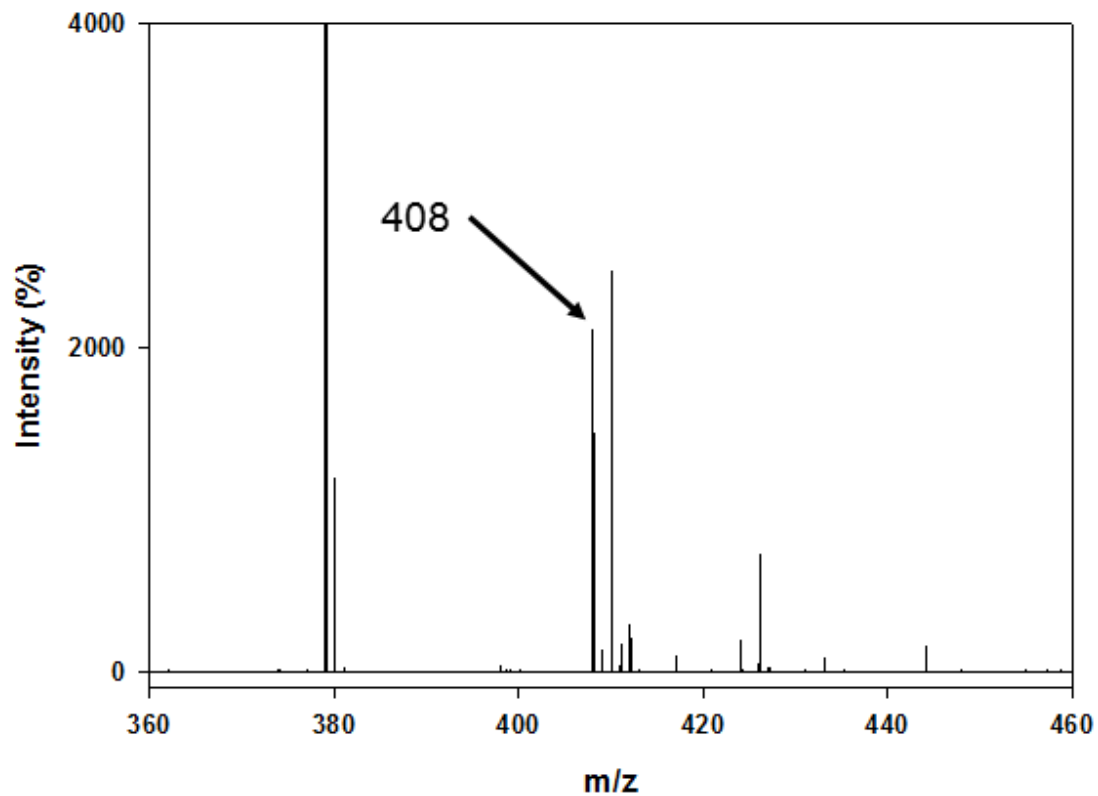


Figure S8-11 Mass spectrum for the analysis of tiaprofenic acid spiked in human plasma, $[M+H]^+$ signal appears at m/z 408.

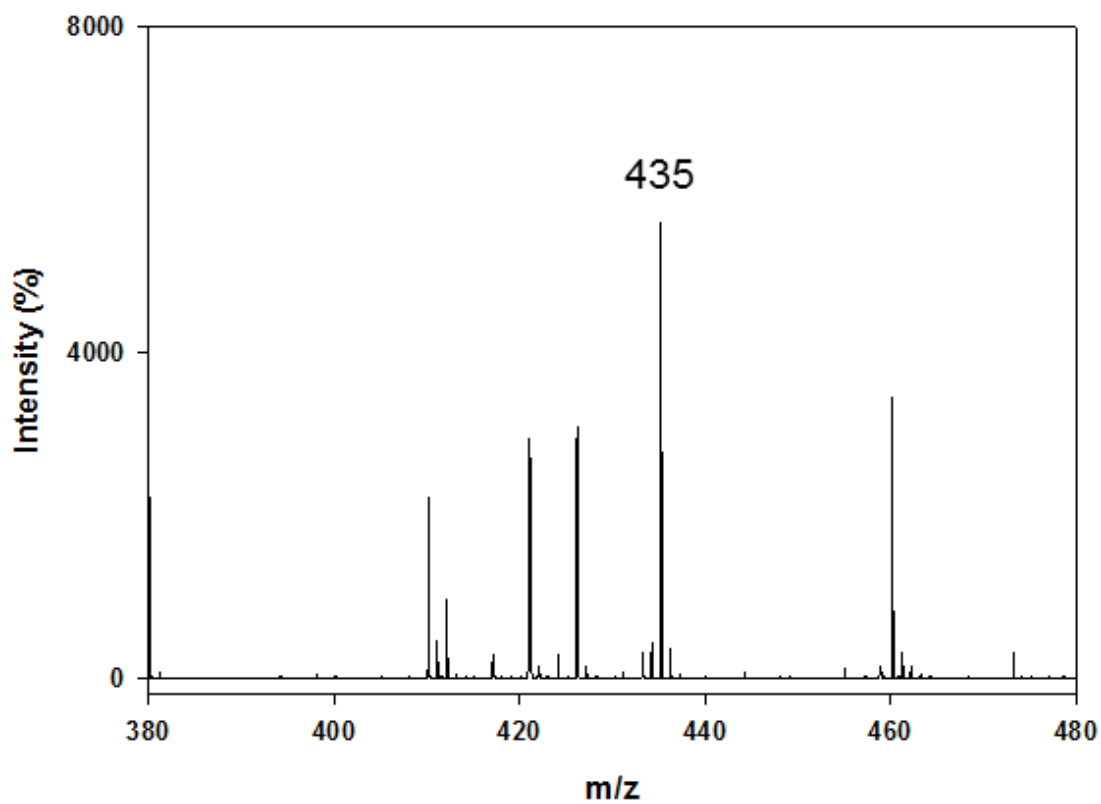


Figure S8-12 Mass spectrum for the analysis of etodolac spiked in human plasma, $[M+H]^+$ signal appears at m/z 435.

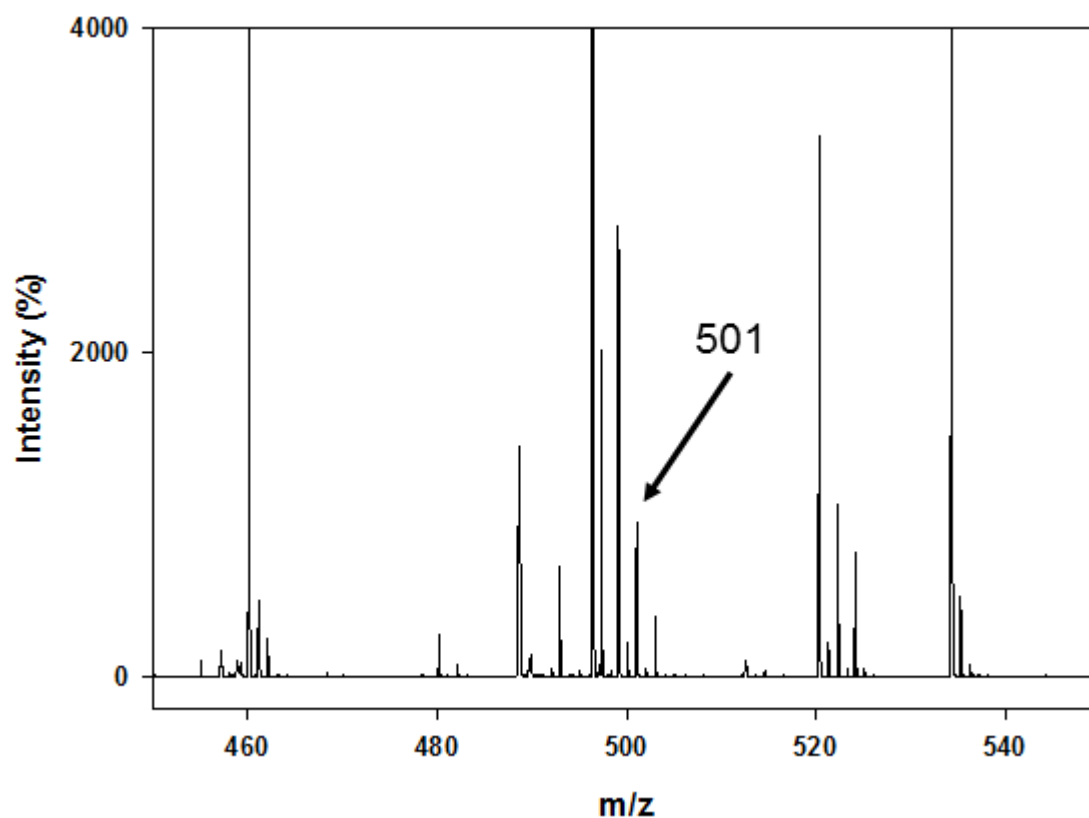


Figure S8-13 Mass spectrum for the analysis of aceclofenac spiked in human plasma, $[M+H]^+$ signal appears at m/z 501.

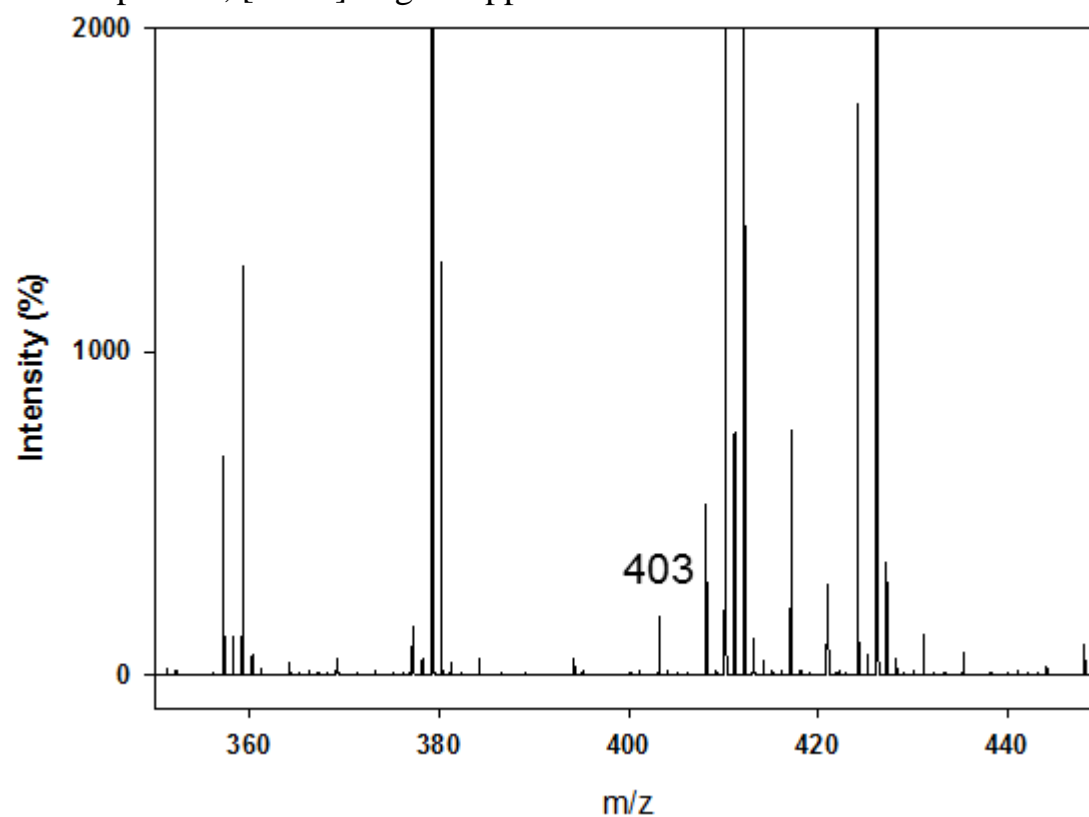


Figure S8-14 Mass spectrum for the analysis of ketorolac spiked in human plasma, $[M+H]^+$ signal appears at m/z 403.

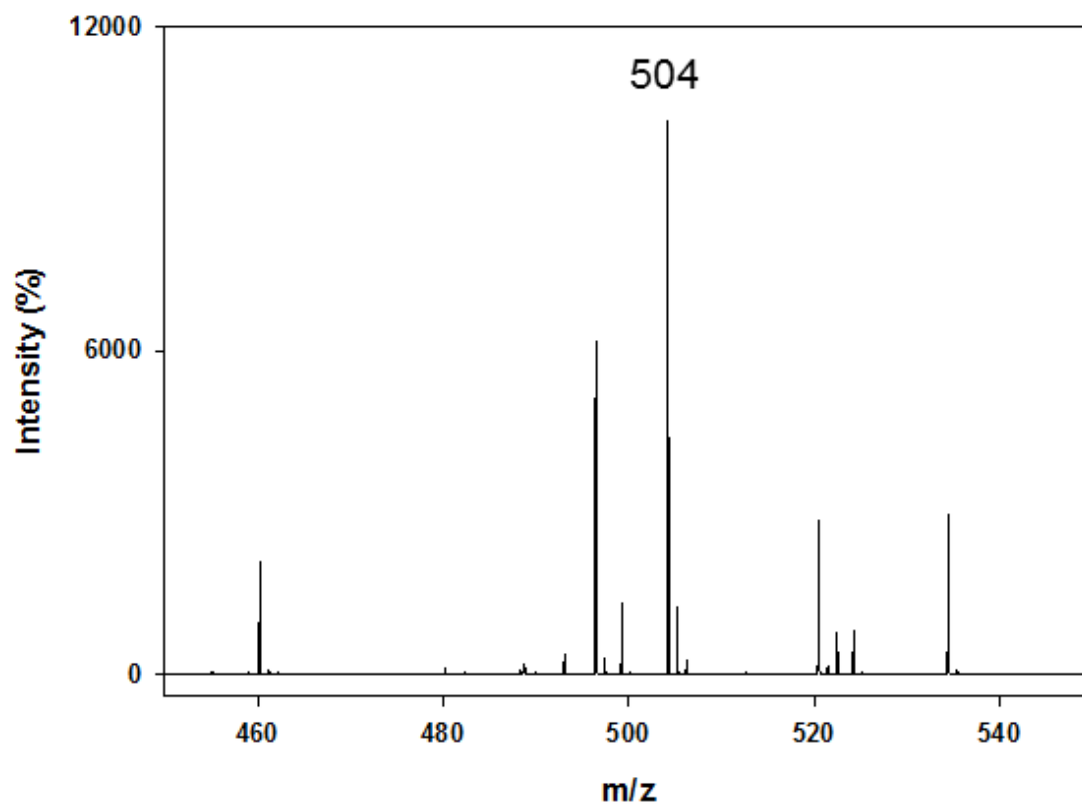


Figure S8-15 Mass spectrum for the analysis of sulindac spiked in human plasma, $[M+H]^+$ signal appears at m/z 504.

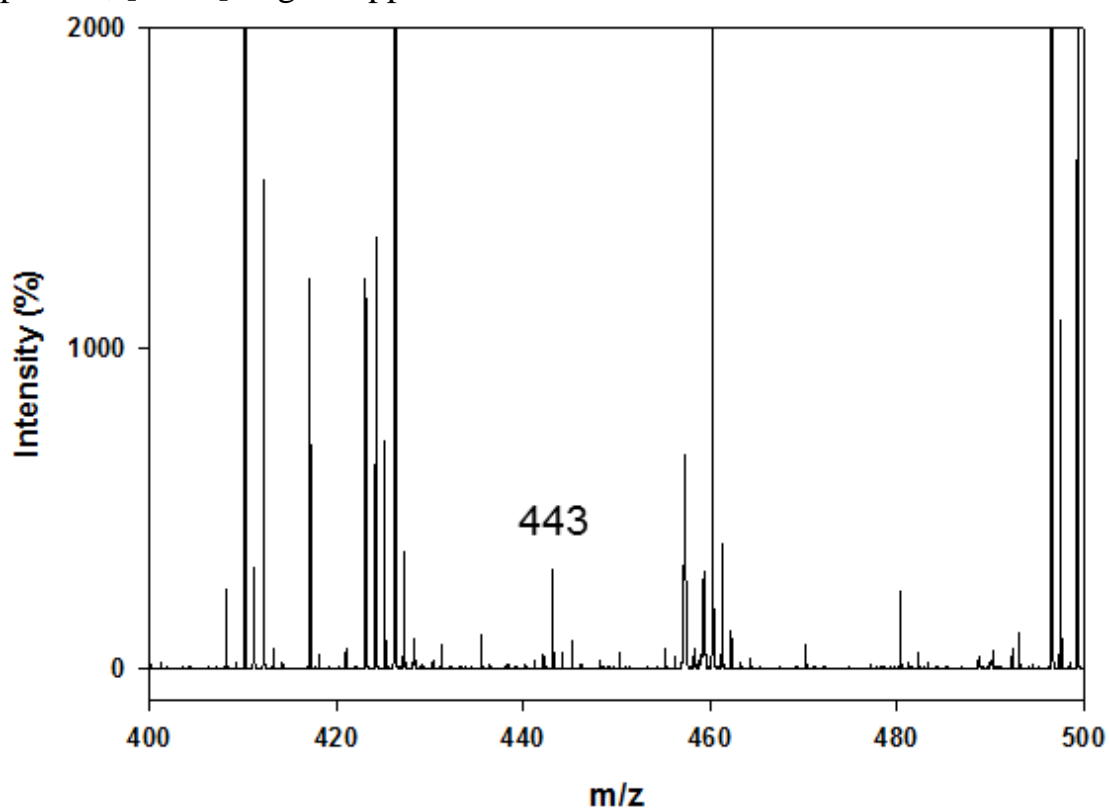


Figure S8-16 Mass spectrum for the analysis of diclofenac spiked in human plasma, $[M+H]^+$ signal appears at m/z 443.

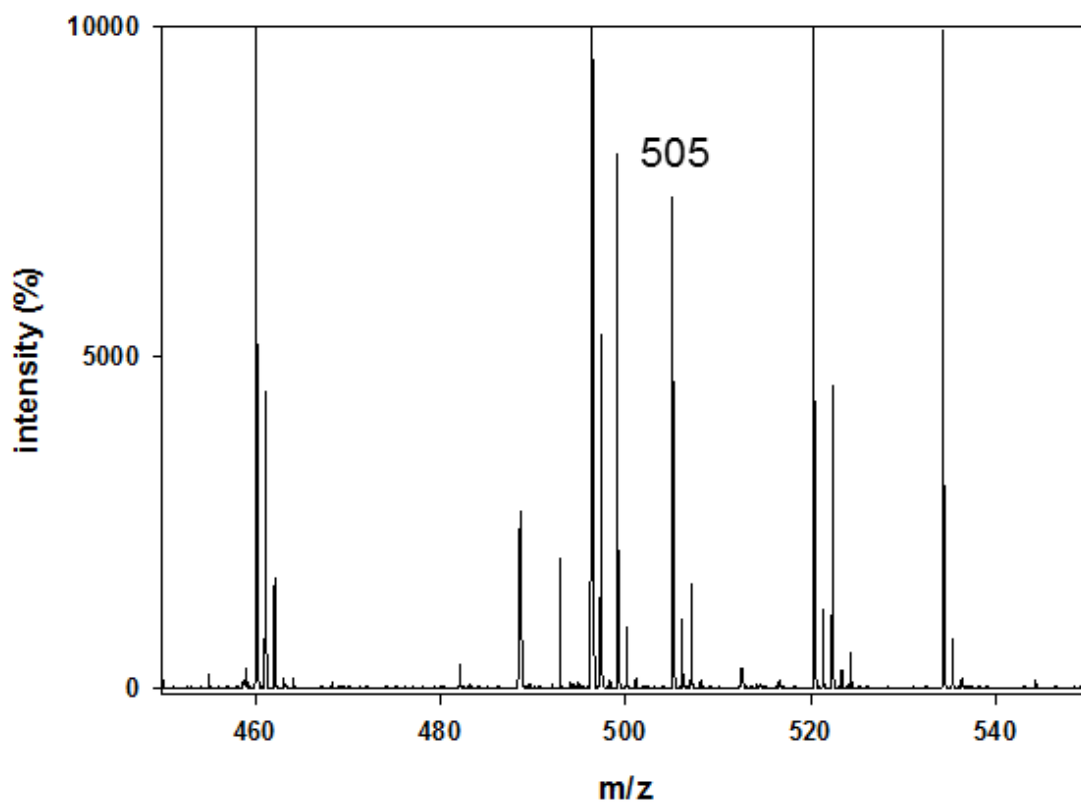


Figure S8-17 Mass spectrum for the analysis of indometacin spiked in human plasma, $[M+H]^+$ signal appears at m/z 505.

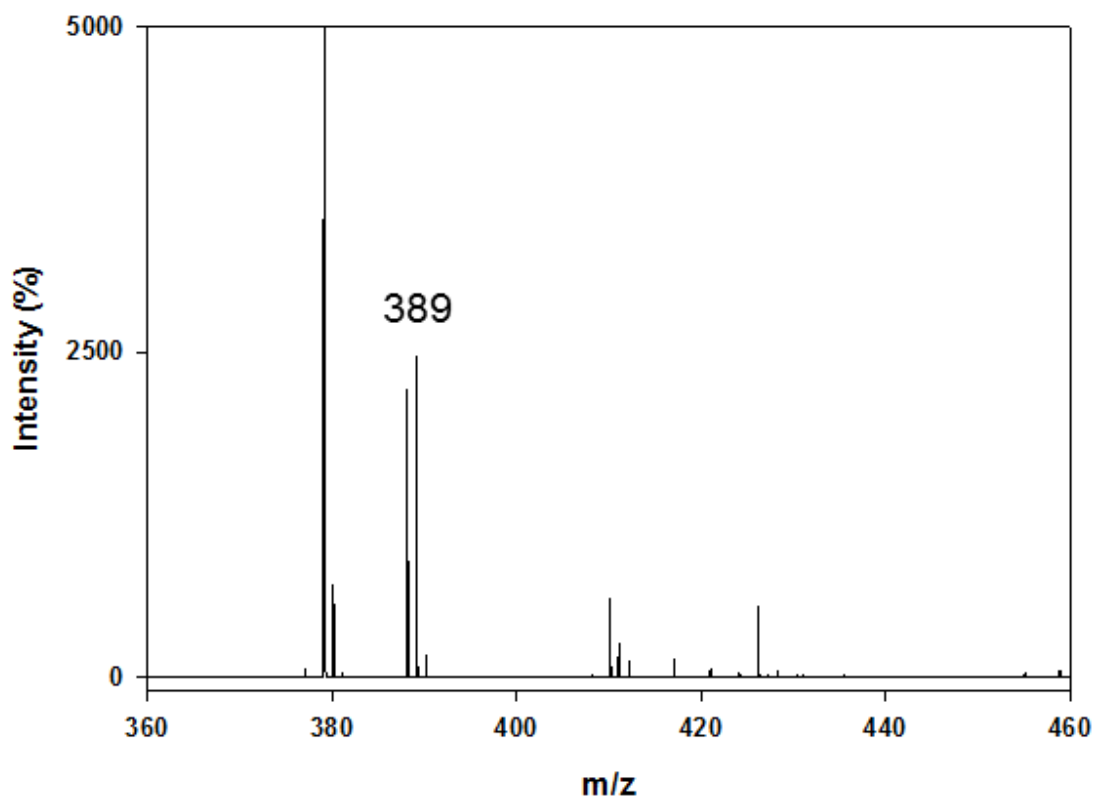


Figure S8-18 Mass spectrum for the analysis of mefenamic acid spiked in human plasma, $[M+H]^+$ signal appears at m/z 389.

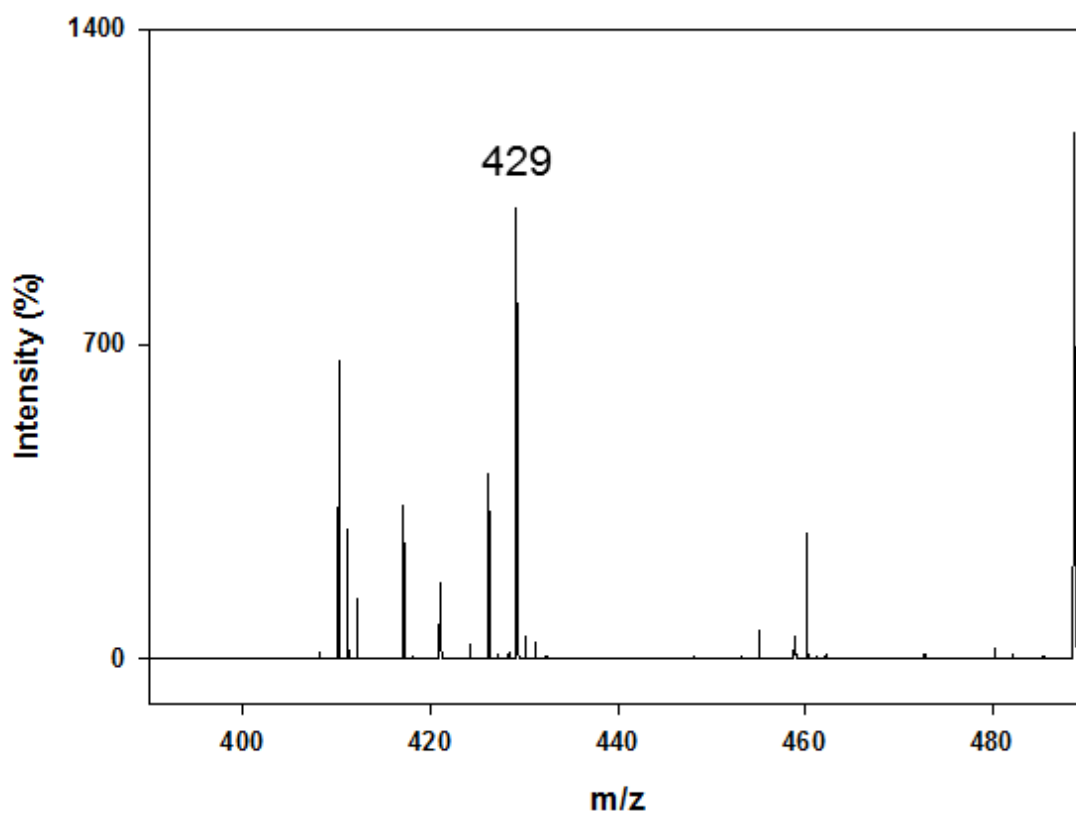


Figure S8-19 Mass spectrum for the analysis of flufenamic acid spiked in human plasma, $[M+H]^+$ signal appears at m/z 429.