Microwave-Assisted Preparation of Molecularly Imprinted Monolith Combining Imidazolium Ionic Liquid and POSS for Enhanced Extraction of Baicalin-Like Compounds in *Scutellaria Baicalensis* by means of In-Capillary SPME Followed by on-line LC and off-line LC-MS/MS

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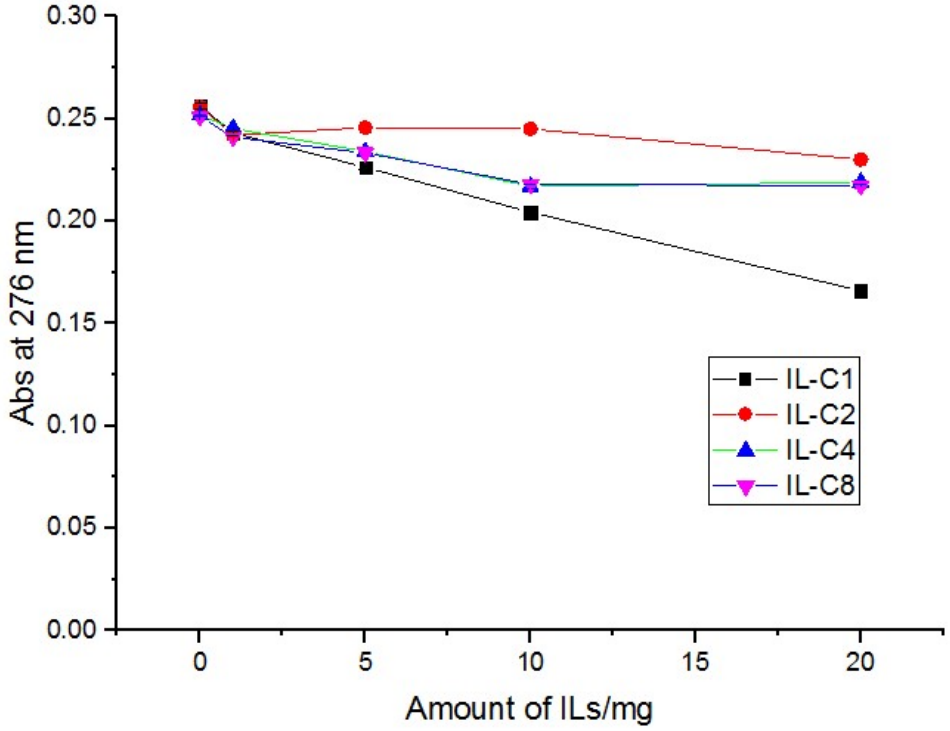


Figure S1 UV spectrum for the interaction between IL monomers and baicalin.

In these experiments, 276 nm was the highest signal of baicalin. The signals at 276 nm could be attributed to flavone structure. When the amount of ILs grew, the signals at 276 nm decreased. When carbon chain length grew, the decreasing trend increased. The IL-1C gave the highest decreasing trend. It could only be speculated that the changes of signals at 276 nm showed the interaction between flavone structure and the imidazolium group, and the longer carbon chain could interfere with this interaction.

Experiment for UV absorption spectra of baicalin-IL interaction

5 mg baicalin and one type of IL were dissolved in 100 μL DMSO. Then the solutions were diluted 10,000 times by acetonitrile. The UV spectra in the range of 200-500 nm were collected. 4 types of ILs with different lengths of carbon chain (named as IL-1C, IL-2C, IL-4C and IL-8C by number of carbon atom) were used. For each IL, a series of amount (0 mg, 1 mg, 5 mg, 10 mg and 20 mg) were used.

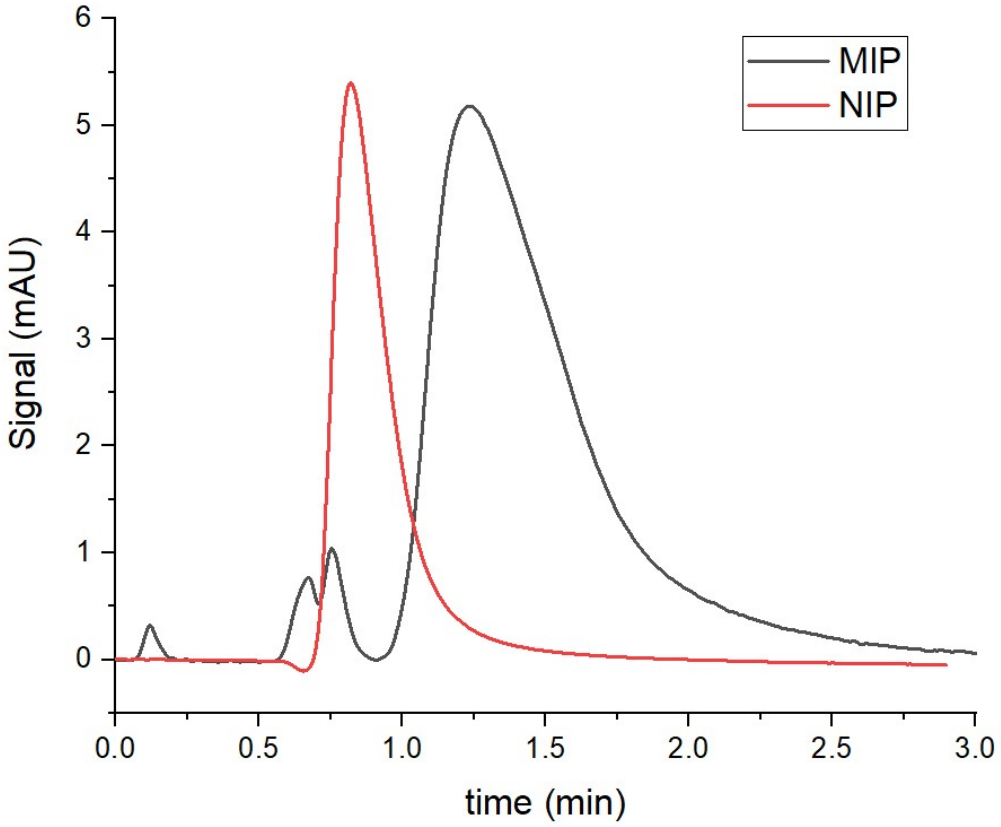


Figure S2 CLC results at the optimal conditions.

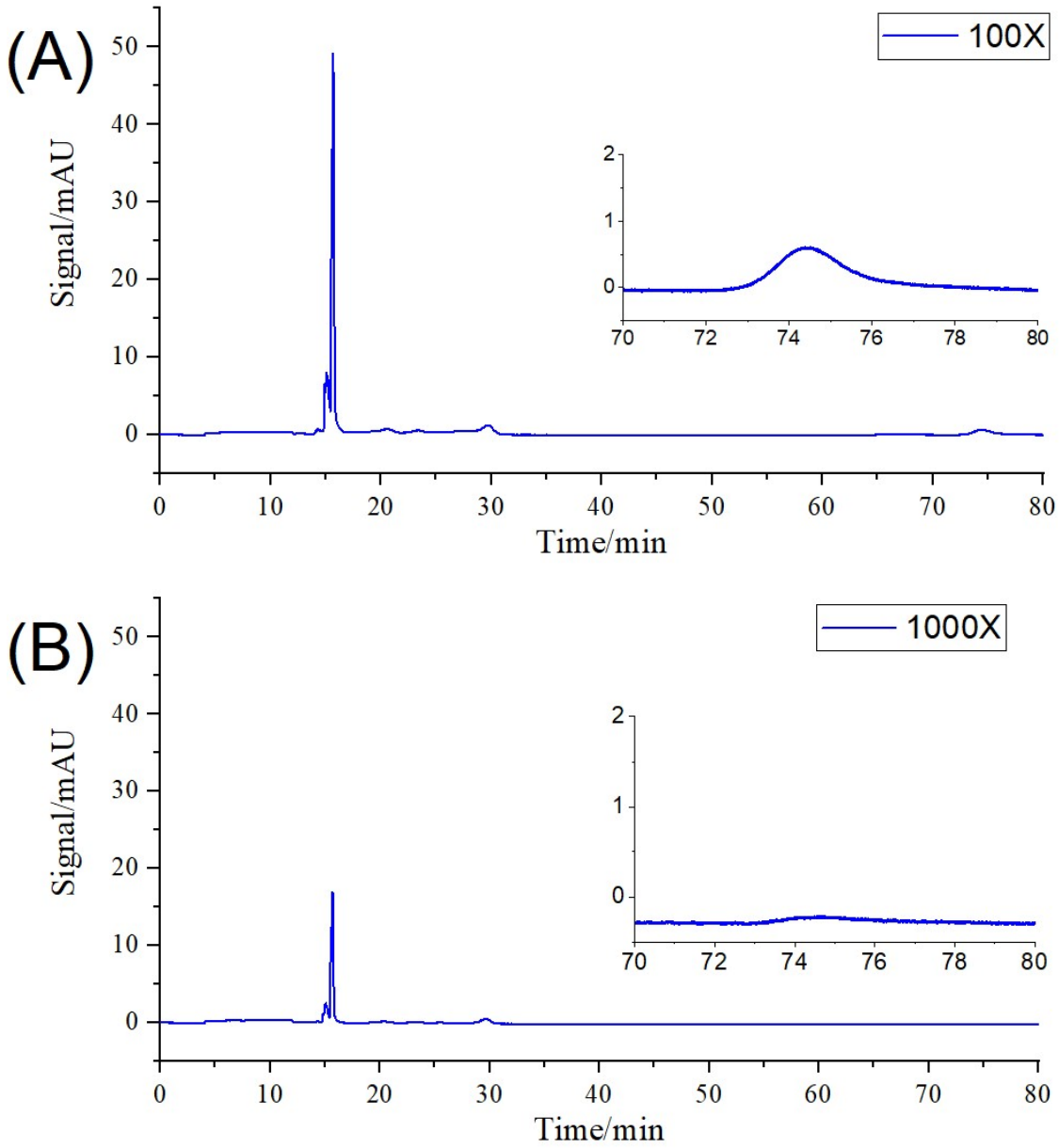


Figure S3 Chromatograms in range of 0-80 min for MIP-based SPME-HPLC analysis of microwave-assisted extraction of *Scutellaria baicalensis* (A) 100-fold diluted extraction. (B) 1000-fold diluted extraction.

There was one peak at 74.7 min. At 100-fold diluted sample, this peak was detectable. However, at 1000-fold diluted sample, this peak became smaller and was almost undetectable. So the peak at 74.7 min was from the extracted sample. Due to the isocratic elution and LC column used in the 2nd LC, the retention time was so long. Because there was no on-line LC-MS system in our lab, the off-line LC-MS was used to analyze the extracted peaks. And the off-line LC-MS used gradient elution and UPLC column to decrease analysis time. In addition, on-line 2nd SPME-LC system, due to the large sample volume eluted from SPME and directly loaded onto the 2nd

analysis, without any special instrumentation, UPLC column is not proper to handle such large sample volume and only LC column can be used. That is why the off-line LC-MS showed more resolution and less analysis time than the on-line LC result. So it is reasonable to stop LC-TOF-MS when no signals were detected above the baseline, and the results can the group-capture ability of the imprinted monolith. Because different LC columns and LC methods were used, it was difficult to directly attribute the peak at 74.7 min to any peak in the result of the off-line LC-MS. However, the results were showed that this peak was eluted within one run so that it would not interfere with the next analysis.

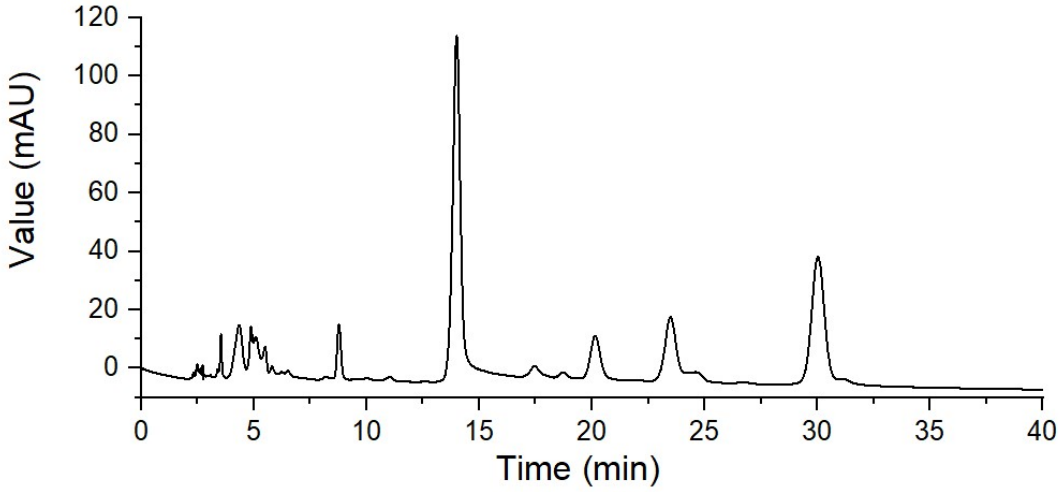


Figure S4 LC chromatograms of *Scutellaria baicalensis* extraction solution without any pretreatment or dilution.

Column = WondaSil C18 column (4.6 mm × 250 mm, 5 μm). The mobile phase = acetonitrile:water (containing 0.1% acetic acid) = 25:75, v/v) , the flow rate was set at 1.0 mL/min, the injection volume was 5 μL, the detected wavelength was 280 nm.

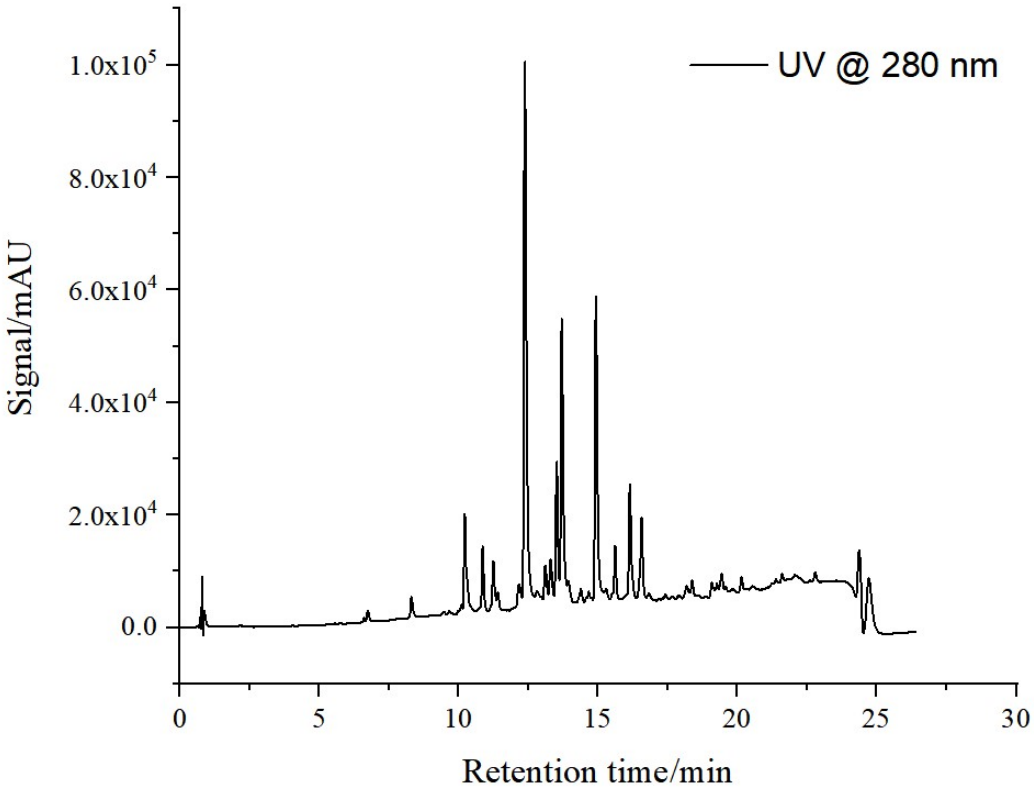
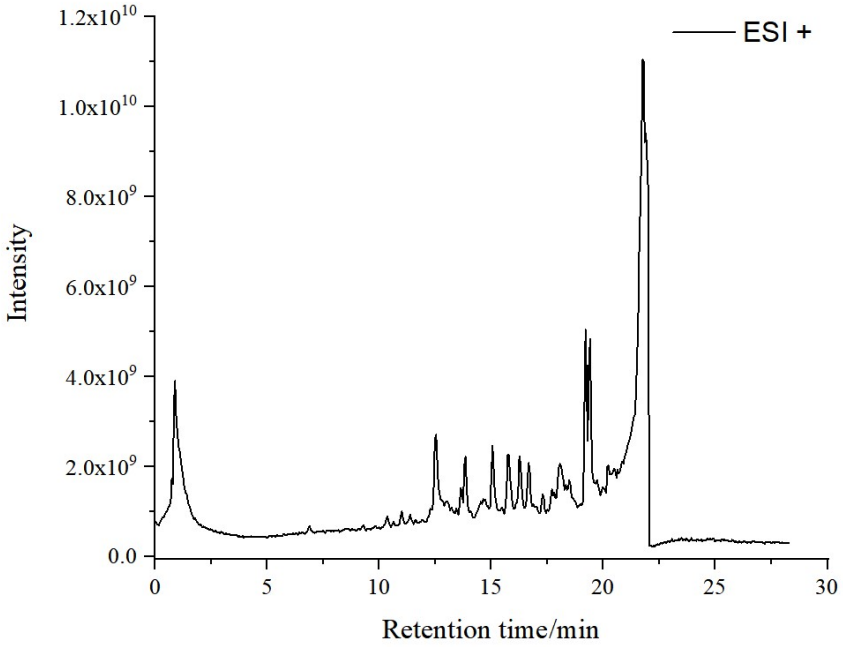


Figure S5 LC chromatogram at 280 nm

Column = ZORBAX Eclipse XDB-C18 (2.1×50 mm, 1.8 μm), the mobile phase was (A) methanol containing 0.1% formic acid and (B) water containing 0.1% formic acid. The gradient (shown as A%, v/v) was 5%-95%@0-20 min, 95%-95%@20-22 min, 95%-5%@22-22.1 min, 5%-5%@22.1-30 min. The injection volume was 2 μL. The flow rate was 0.2 mL/min. The detection wavelength was 280 nm.

(A)



(B)

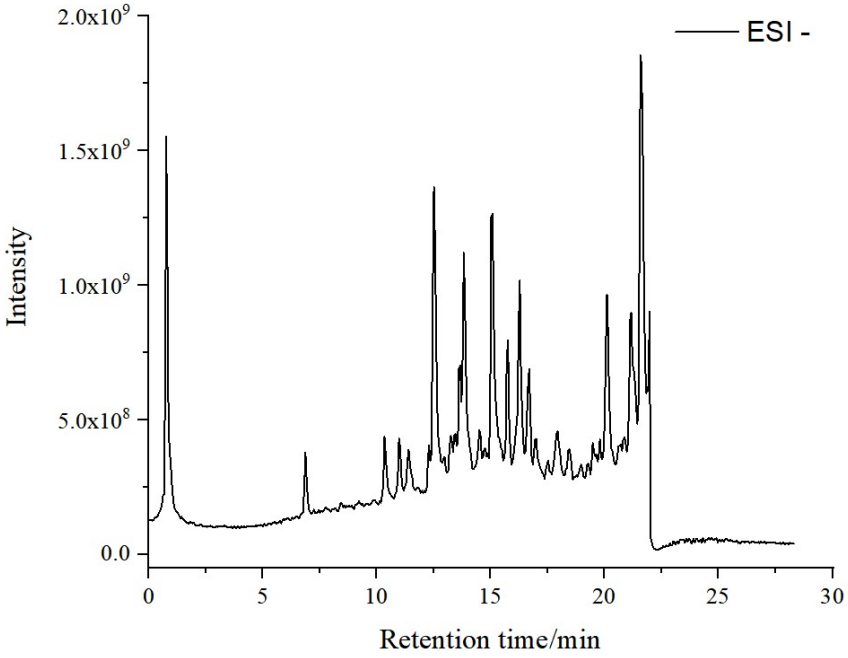


Figure S6 TIC (A) ESI+ (B) ESI-

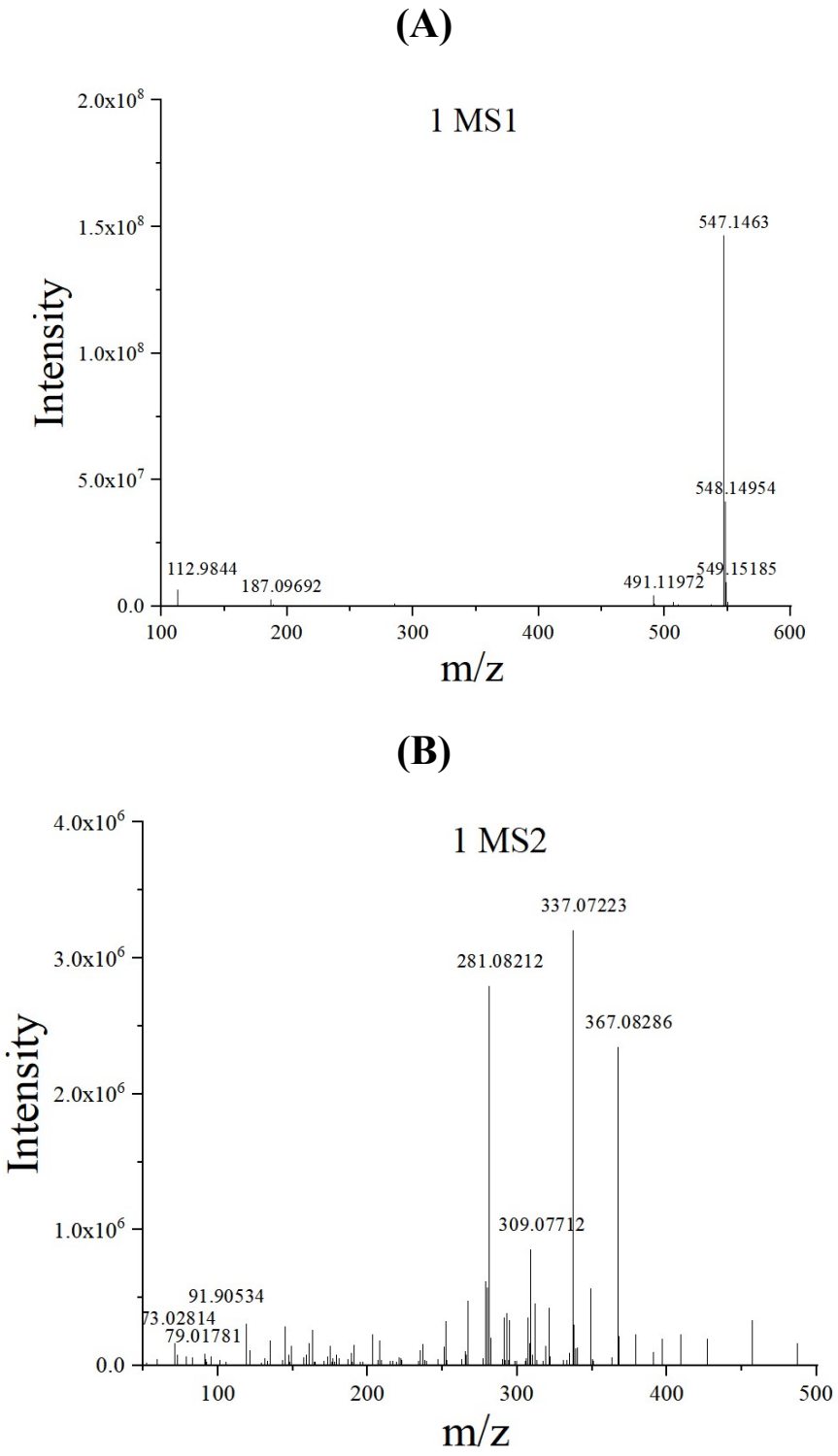


Figure S7 MS/MS for compound 1 (A) primary MS and (B) secondary MS

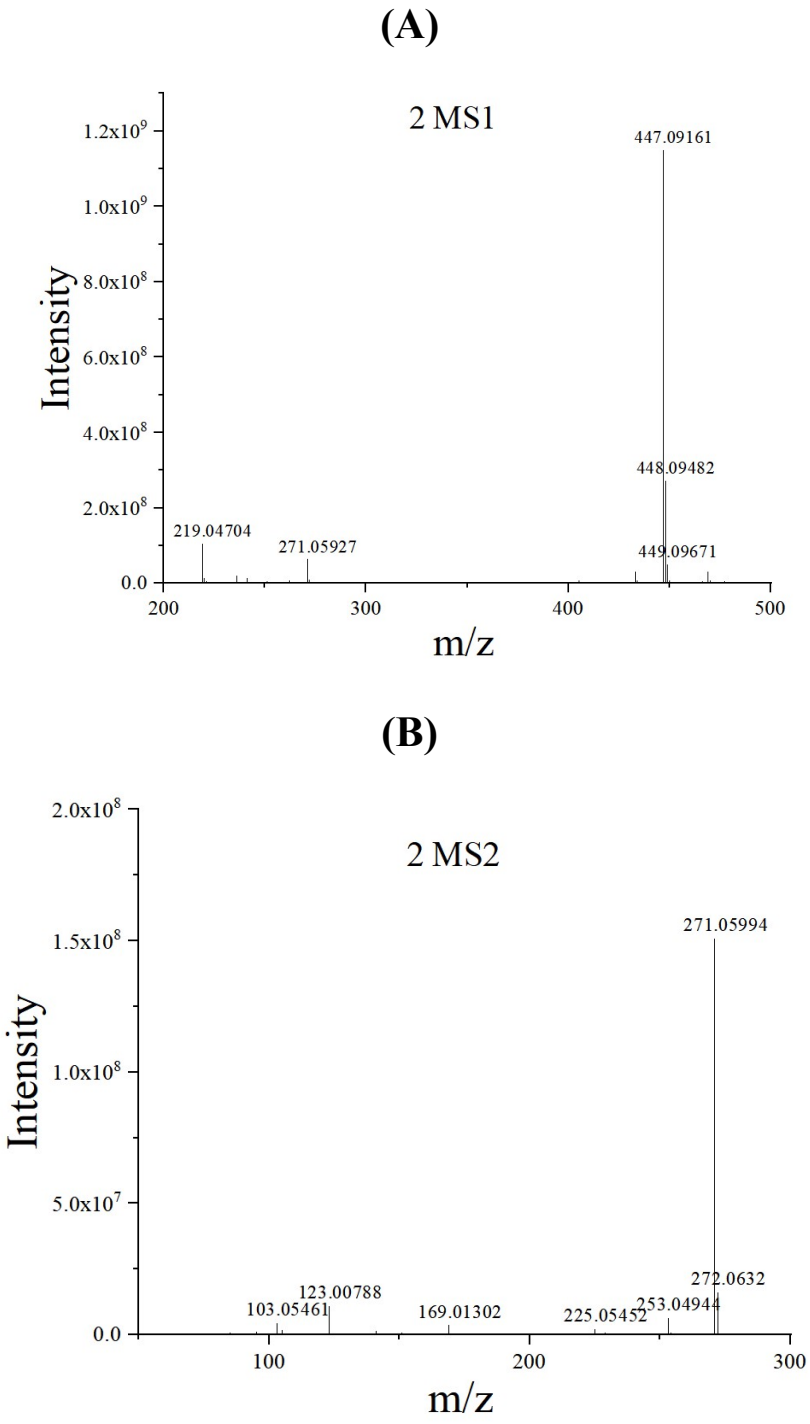


Figure S8 MS/MS for compound 2 (A) primary MS and (B) secondary MS

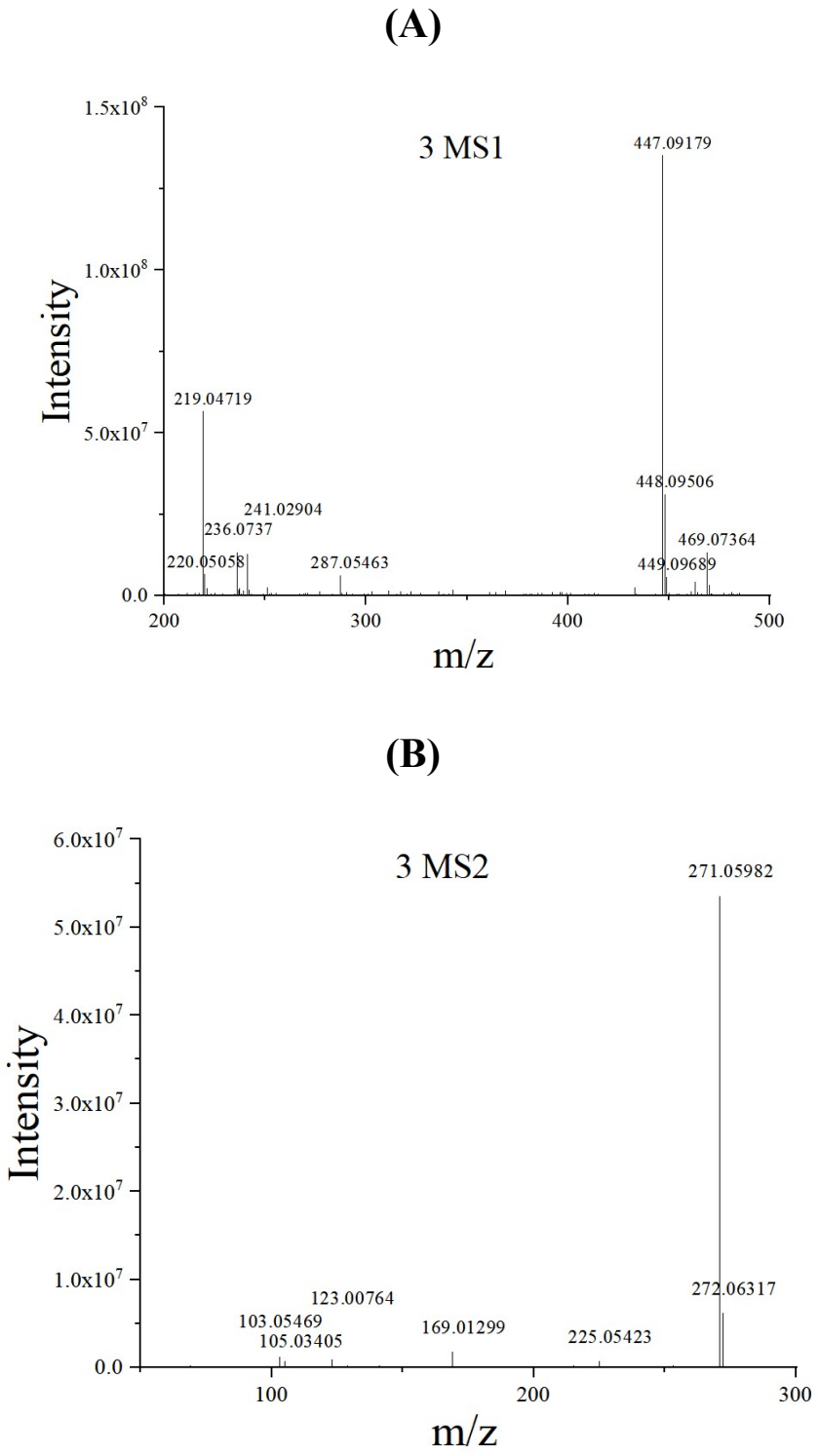


Figure S9 MS/MS for compound 3 (A) primary MS and (B) secondary MS

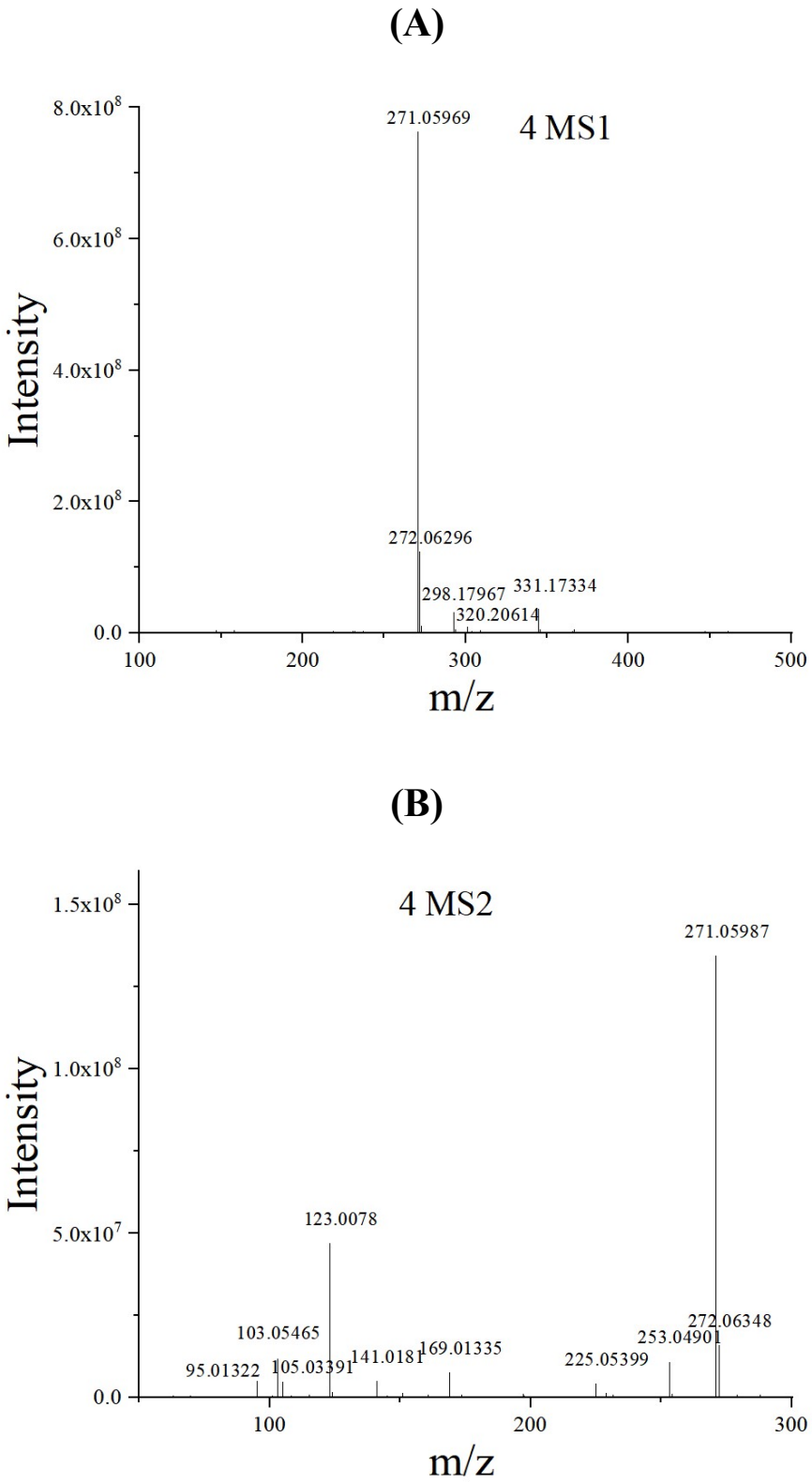


Figure S10 MS/MS for compound 4 (A) primary MS and (B) secondary MS

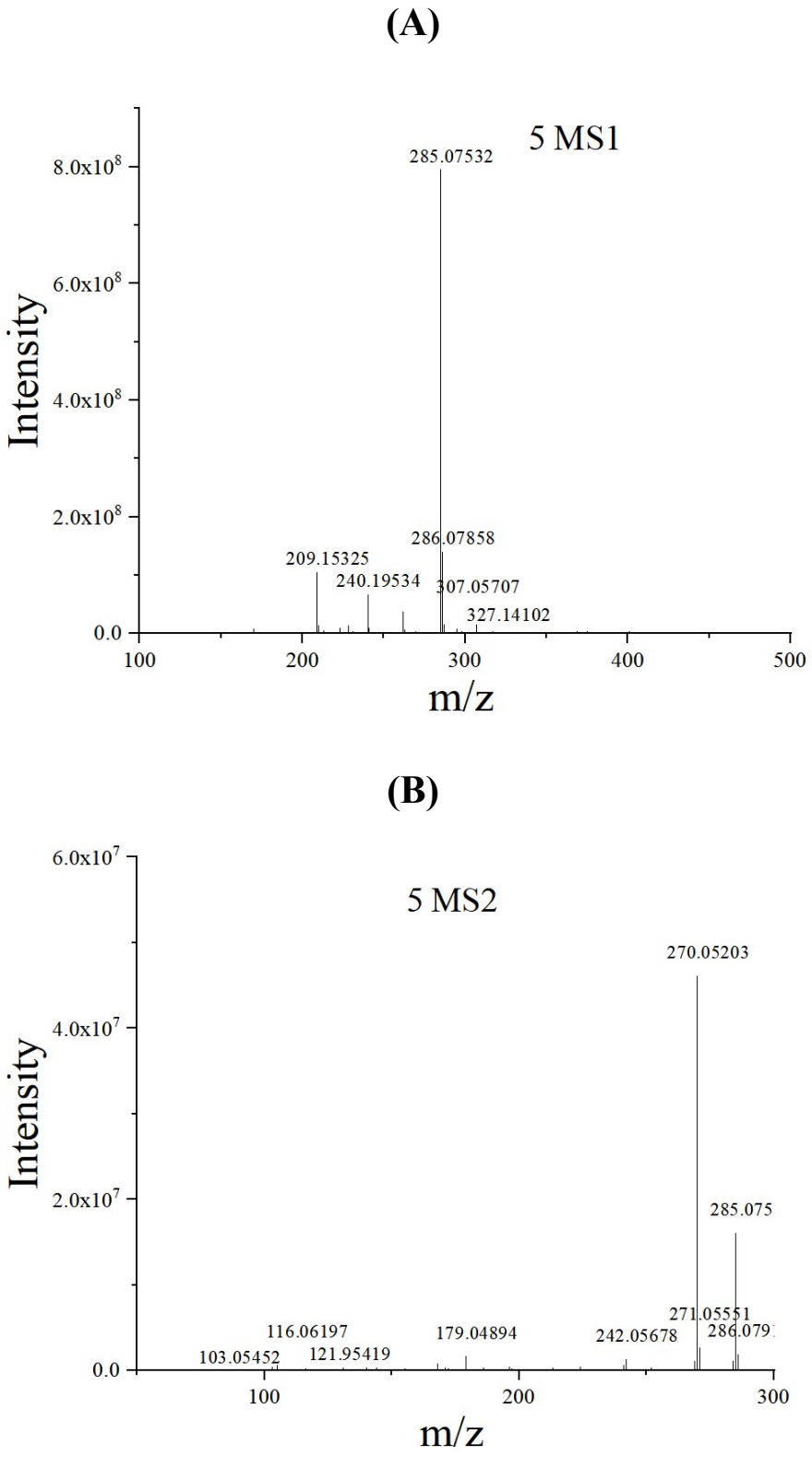


Figure S11 MS/MS for compound 5 (A) primary MS and (B) secondary MS

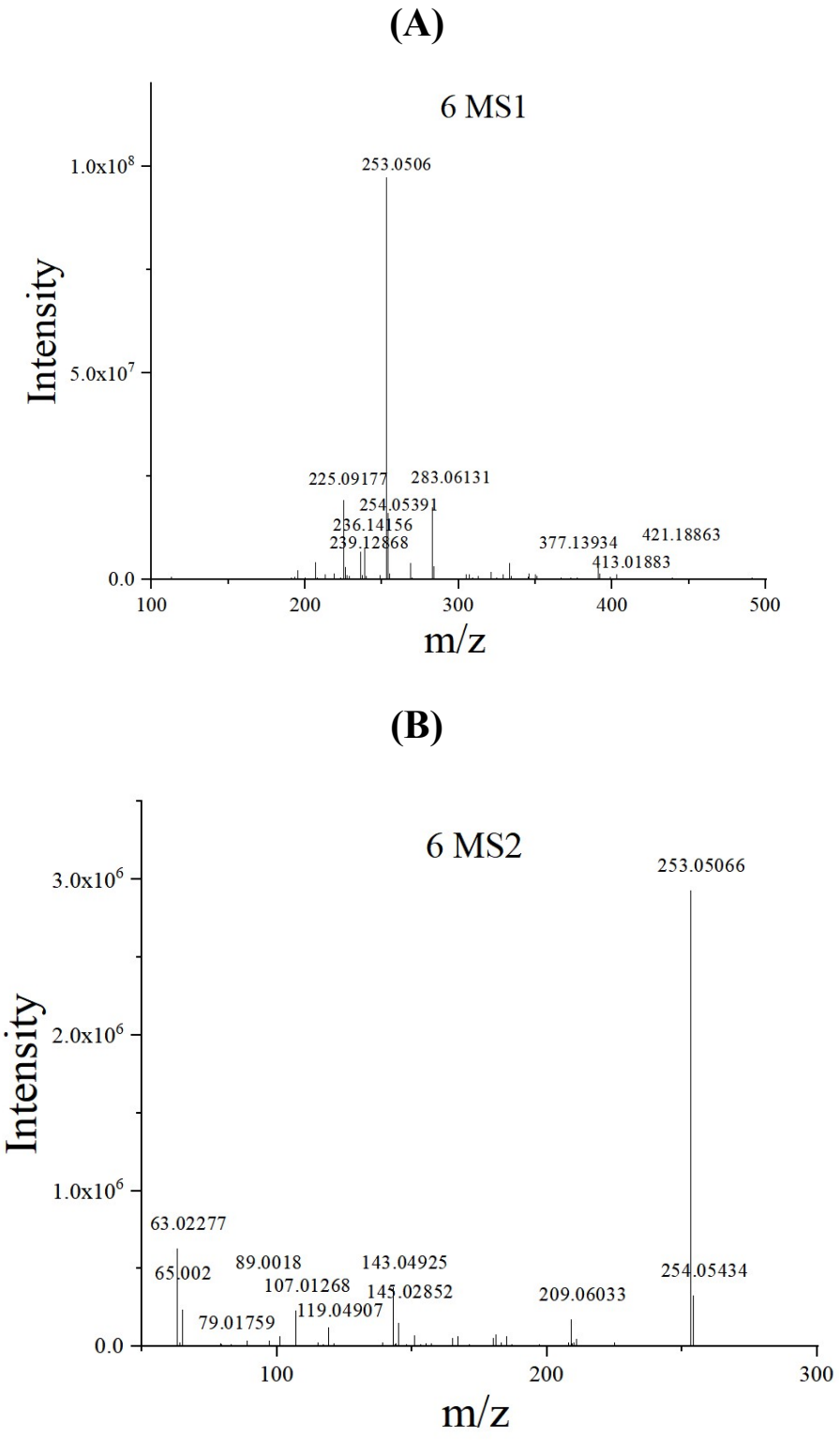


Figure S12 MS/MS for compound 6 (A) primary MS and (B) secondary MS

Table S1 Comparison of MIPs performance for analysis o baicalin

Reference	Imprinting Matertials	Sample	Applications	Performance
(1)	polymer particles	natural herb Plantago asiatica L, traditional Chinese medicine Longdanxiegan bolus	SPE Off-line HPLC	IF = 2.17 LOD/liner range, not provided
(2)	polymer particles (surface imprinted)	Biological samples (liver/spleen)	SPE Off-line HPLC	IF = 2.3 LOD = 0.6/0.7μg/mL Liner range: 1.0-7.0/15.0μg/mL
(3)	polymer particles	herb of *S. baicalensis Georgi*	SPE Off-line HPLC	IF = 4 LOD/liner range, not provided
(4)	polymer particles	*Scutellaria baicalensis Georgi*	SPE Off-line HPLC	IF = 1.77 LOD = 0.3 ng/mL Liner range: 1.0 to 20 μg/mL
(5)	Magnetic particles (surface imprinted)	*S. baicalensis*	SPE Off-line HPLC	IF = 5.43 LOD = 0.0387 μg/mL Liner range: 0.500–179 μg/mL
(6) Previous work	Monolith in capillary	*Scutellaria baicalensis Georgi*	On-line SPME-HPLC Off-line SPME-LC-MS	IF = 2.2 LOD = 0.001μg/mL Liner range: 0.001 mg/mL to 1 mg/mL, 1μg/mL to 100μg/mL
This work	Monolith in capillary	*Scutellaria baicalensis Georgi*	On-line SPME-HPLC Off-line SPME-LC-TOF-MS/MS	IF = 5.4 LOD = 0.001 μg/mL Liner range: 0.001 μg/mL to 0.1 μg/mL, 0.1 μg/mL to 100 μg/mL

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