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Table S1: The gradient elution program of two mobile phases in LC-MS/MS

Time (min)	Mobile phase A (%)	Mobile phase B (%)
0	95%	5%
1	95%	5%
2	65%	35%
3	65%	35%
4	20%	80%
6	20%	80%
6.5	95%	5%
8	95%	5%

Table S2: Q1/Q3 ion pairs, De-clustering Potential (DP), Collision Energy (CE) of MRM, and retention time for the optimized LC–MS/MS method

Drug	Retention time (min)	Precursor ions (Q1, m/z)	Product ions (Q3, m/z)	DP (V)	CE (eV)
Paracetamol	3.03	152	110*, 93	63	23,29
Propyphenazone	5.03	231	201, 189*	84	28,30
Aspirin	4.01	179	137*	-25	-7
Caffeine	3.36	195	138*, 110	68	28,34

Note: *Quantitative ions

Table S3: Comparison of two sample pretreatment methods for four drugs in LC-MS/MS

Drug	Spiked level (μg/L)	Recovery (%)		RSD (%)	
		Method 1*	Method 2**	Method 1*	Method 2**
Paracetamol	4	95.9	92.5	6.2	6.3
	20	94	93.7	5.5	5.8
	40	96.6	91.3	3.9	6.8
Propyphenazone	0.5	101.5	90.8	1.4	2.9
	4	98.5	93.2	3.2	5.2
	8	96.3	87.4	3.3	4.9
Aspirin	10	102.2	91.6	4.2	4.3
	100	102	93.2	2.6	5.4
	180	100.2	94.3	1.6	4.1
Caffeine	5	93	85.7	2.2	4.7
	60	93.4	90.9	1.8	6
	90	98.4	93.2	2.1	5.7

Note: Method 1*: low pressure distillation; Method 2**: boiling evaporation

Correspondence to: Anping Deng, Department of Chemical Engineering and Materials Science, Soochow University, Suzhou, China, E-mail: denganping@suda.edu.cn

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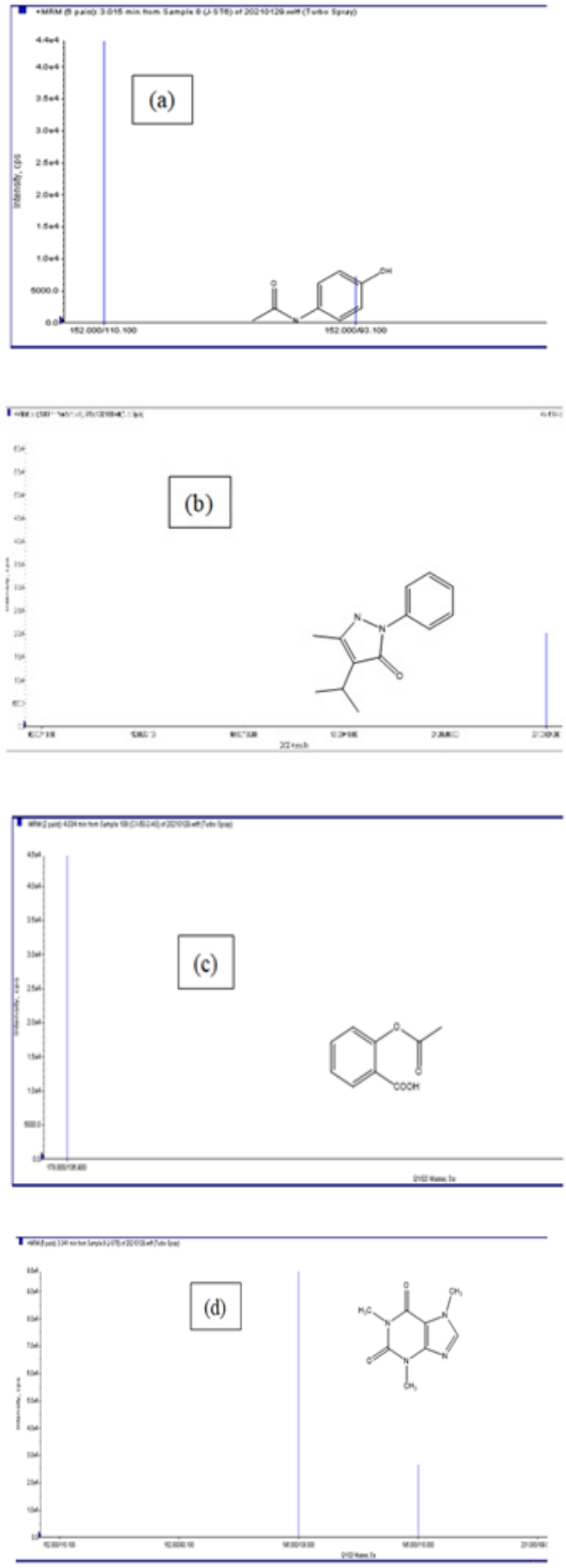

Figure S1: Mass spectra. (a) Paracetamol, (b) Propyphenazone, (c) Aspirin, (d) Caffeine.