Supplementary Material

Exploring the changes of anticoagulant active ingredients before and after bovine bile fermentation of Traditional Chinese Medicine Yaomu via an aggregation-induced emission fluorescence sensor

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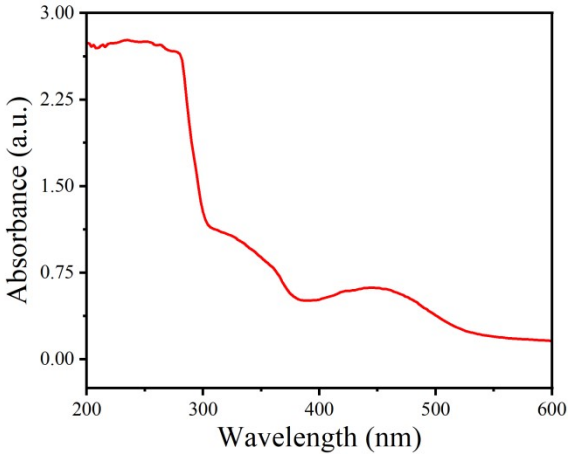

Fig. S1. The UV-vis absorption spectra of NITPA.

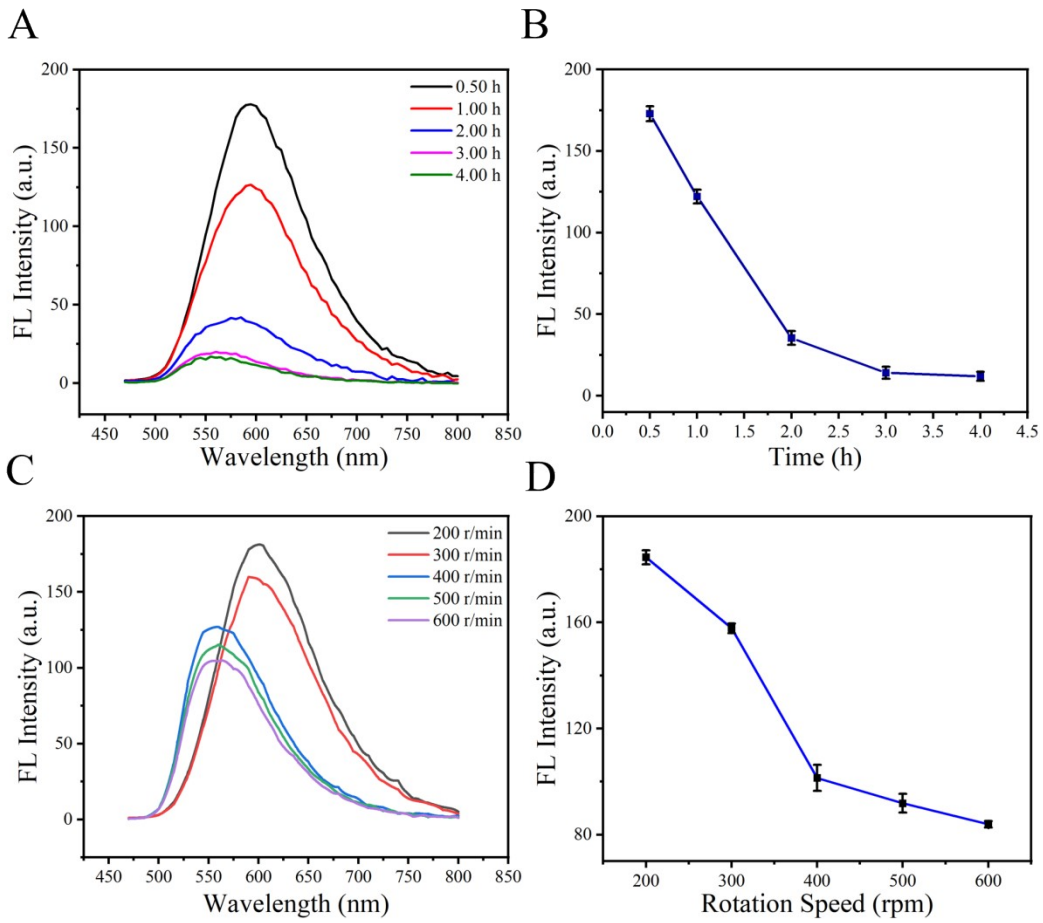

Fig. S2. Synthesis conditions of NITPA-S sensor (λex=448 nm, λem=595 nm). The fluorescence emission spectra and intensity of NITPA-S sensor with different of (**A** and **B**) magnetic stirring time and (**C** and **D**) revolutions (λex=448 nm, λem=595 nm, n=3).

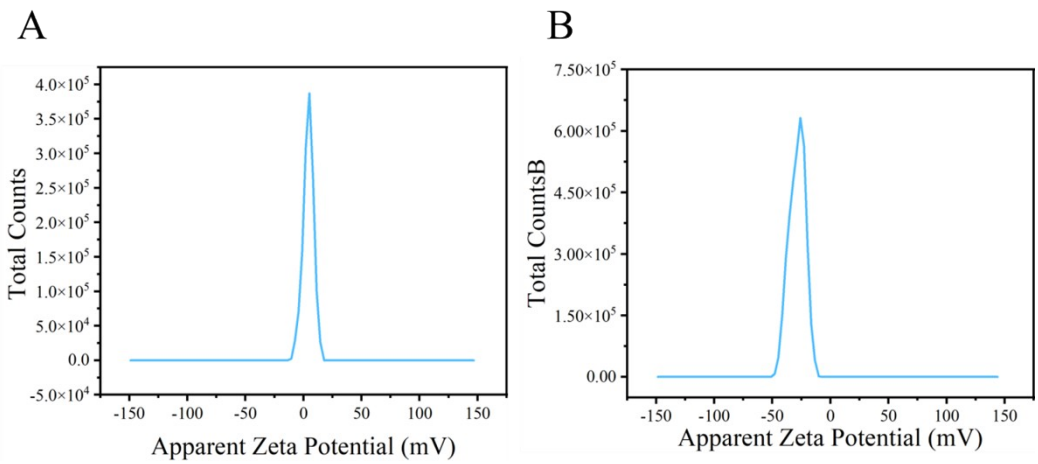

Fig. S3. Zeta potential. The approximately Zeta potential of (**A**) S-2238 and (**B**) NITPA (n=3).

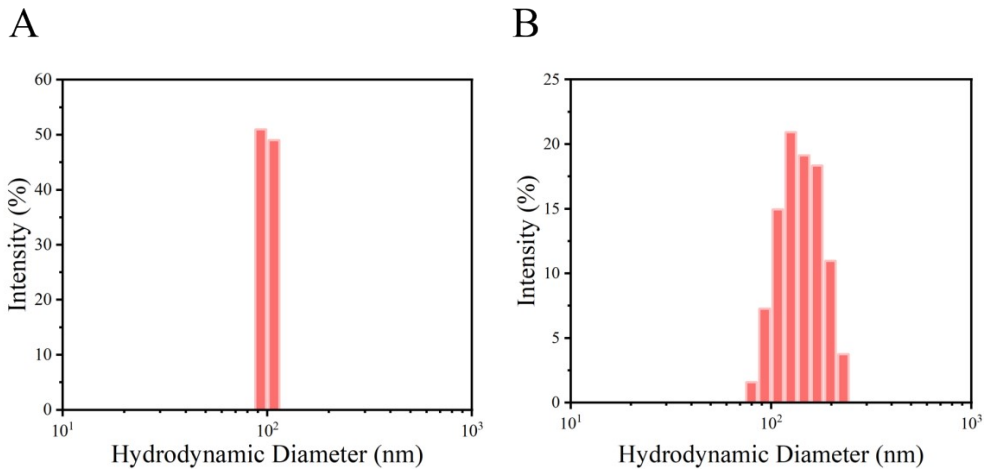

Fig. S4. The Dynamic light scattering. The average hydrodynamic diameter of (**A**) S-2238 and (**B**) NITPA (n=3).

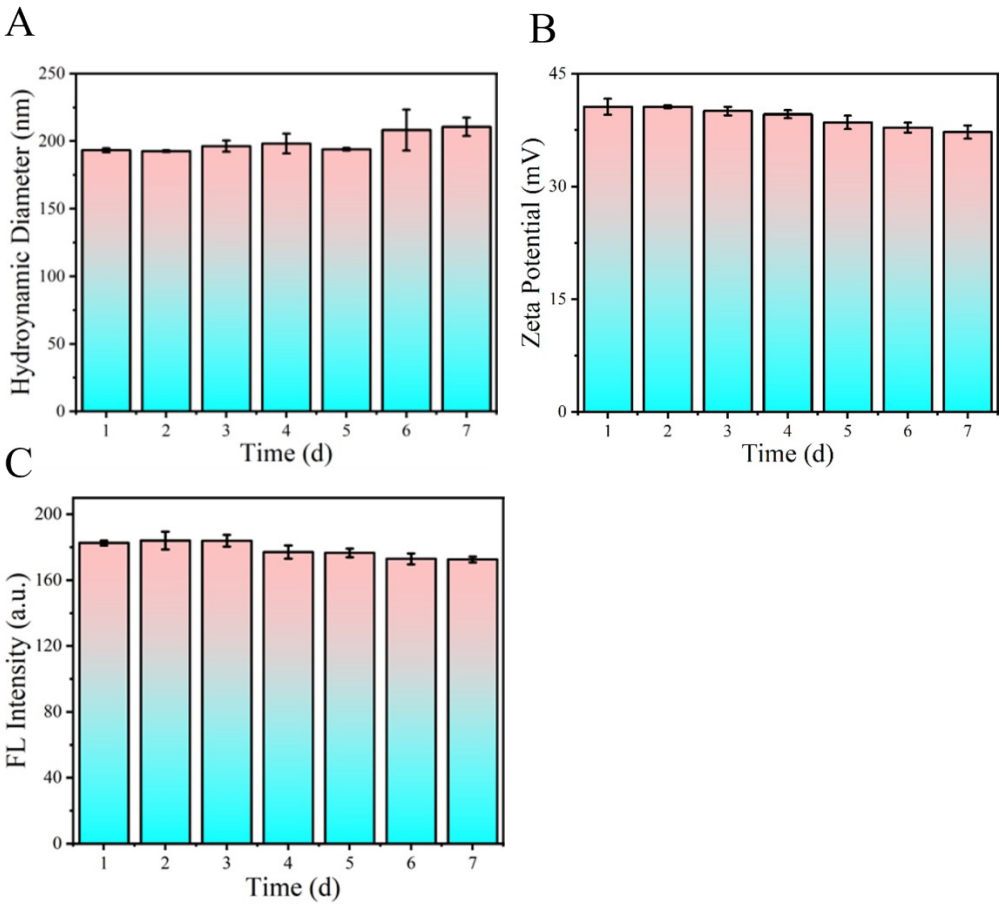

Fig. S5. Stability analysis of NITPA-S sensor stability. (**A**) Hydrodynamic diameter, (**B**) Zeta potential and (**C**) fluorescence intensity of NITPA-S during seven days (λex=448 nm, λem=595 nm, n=3).

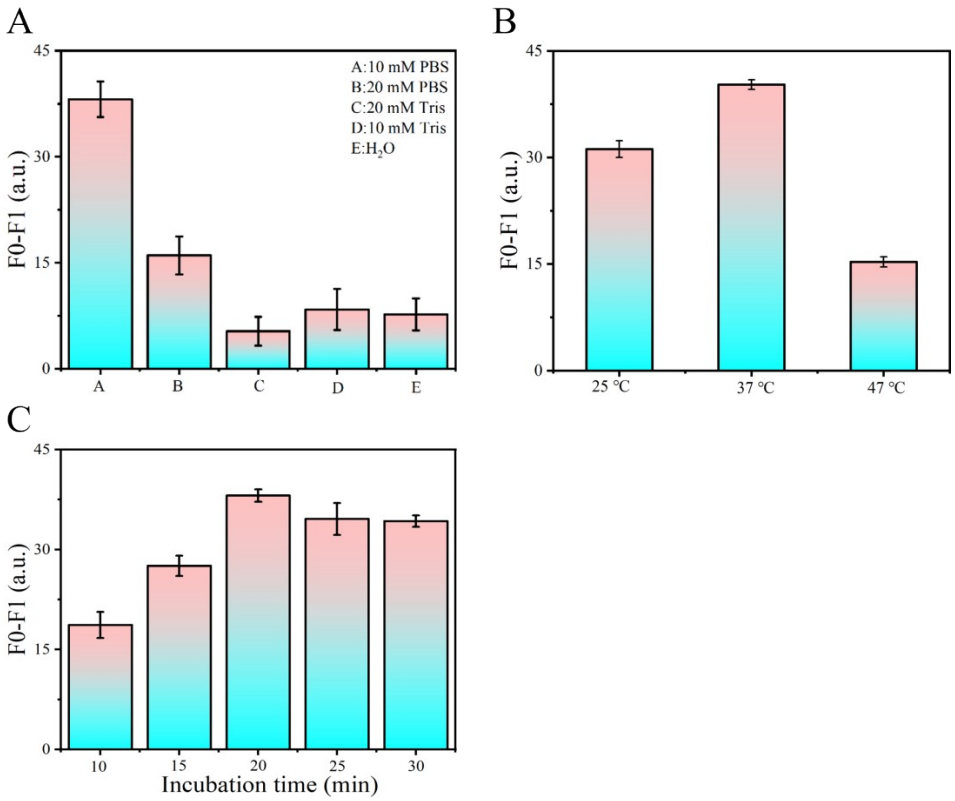

Fig. S6. Conditions of thrombin-substrate reaction (λex=448 nm, λem=595 nm). The impact of (**A**) buffer type and concentration, (**B**) incubation time temperature, (**C**) incubation temperature on the detection of thrombin. (F0 represents fluorescence intensity before the sensor reaction. F1 was fluorescence intensity after thrombin reaction, λex=448 nm, λem=595 nm, n=3).

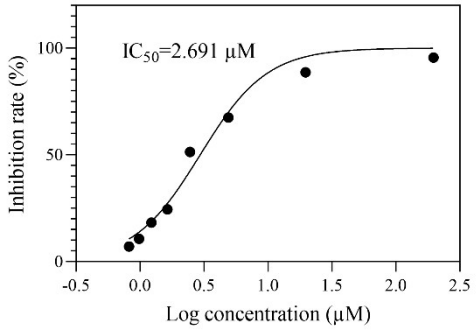

Fig. S7. The inhibitory activity of argatroban on the NITPA-S sensor (n=3).

Table S1. Time program of the gradient elution in HPLC.

Time	A%	B%
0	95	5
8	95	5
35	85	15
45	65	35
50	55	40
55	30	70
60	5	95

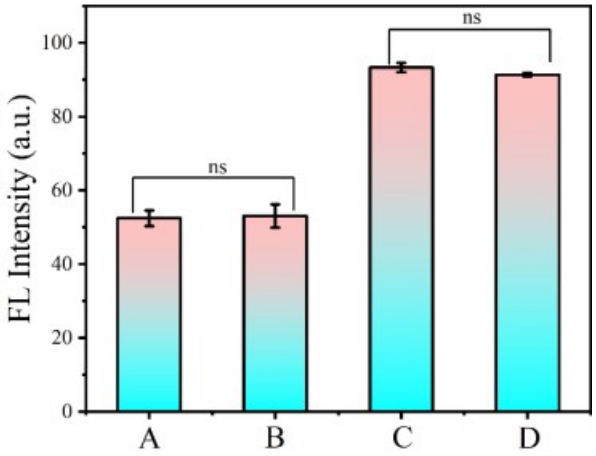

Fig. S8. The impact of 70% methanol solvent on the sensor reaction system (λex=448 nm, λem=595 nm). (**A**) H_2O+thrombin+sensor. (**B**) 70% methanol+thrombin+sensor. (**C**) senor. (**D**) 70% methanol+sensor. (λex=448 nm, λem=595 nm, n=3, $^{*}P > 0.05$)

Table S2. Time program of the gradient elution in UHPLC.

Time	A%	B%
0	95	5
8	95	5
35	85	15
45	65	35

50	55	40
55	30	70
60	5	95
65	5	95

Table S3. Mass spectrometry information of 211 compounds from YM.

Peak No.	RT (min)	Formula	ion	Mass (*m/z*)	Fragment Ions (*m/z*)	Identification	ppm
1	1.28	$C_5H_{11}NO_2$	$[M+H]^+$	118.0864	118.0860,58.0645	valine	2.1
2	1.3	$C_7H_7NO_2$	$[M+H]^+$	138.0533	138.054, 92.0491,94.0647, 78.0336	trigonelline	-1.8
3	2.78	$C_5H_5N_5O$	$[M+H]^+$	152.0566	135.0296,110.0344	guanine	1.9
4	2.89	$C_6H_{13}NO_2$	$[M+H]^+$	132.1135	132.1121,116.0576,86 .0962	isoleucine	3.7
5	3.55	$C_5H_5N_5$	$[M+H]^+$	136.0618	136.0614,119.0349,92 .0240	adenine	1.7
6	4.63	$C_5H_4N_4O$	$[M+H]^+$	137.0647	137.0641,119.0348,11 0.0351	6-hydroxypurine	3.7
7	5.02	$C_9H_{12}N_2O_6$	$[M-H]^-$	243.0627	130.9660,110.0253	uridine	1.8
8	5.03	C_8H_9N	$[M+H]^+$	120.0810	120.0804,103. 0540,77.0382	N-Benzylidenemethy lamine	1.9
9	5.4	$C_5H_9NO_4$	$[M+H]^+$	148.0616	148.0779,130.0485,84 .0440	L-glutamic acid	3.8
10	6.11	$C_{10}H_{13}N_5O_5$	$[M+H]^+$	284.1440	152.0562,135.0305	guanosine	2.2
11	6.31	$C_{10}H_{13}N_5O_4$	$[M+H]^+$	268.1037	136. 0612,119.0351	adenosine	-1.2
12	6.59	$C_9H_{10}O_2$	$[M+H]^+$	151.0448	91.0534,77.0363	3-phenylpropionic acid	1.1
13	6.38	$C_5H_4N_4O_2$	$[M+H]^+$	153.1247	153.1245,136.0135,11 0.0354	2,6-dihydroxypurine	0.1
14	7.96	$C_{22}H_{35}NO_5$	$[M+H]^+$	394.2548	394.2257,362.2173,33 0.2089,58.0647	Karacolidine	1.1
15	8.03	$C_{23}H_{37}O_7$	$[M+H]^+$	440.2651	440.2643,422.2549,39 0.2273,58.0647	9-hydroxysenbusine A isomer	1.5
16	8.95	$C_{23}H_{37}NO_6$	$[M+H]^+$	424.2699	424.2698,406.2581,37 4.2336,58.0642	senbusine A isomer	2.9
17	9.02	$C_{23}H_{37}NO_5$	$[M+H]^+$	408.2747	408.2754,390.2292,35 8.2407,105.0698,58.0 647,105.0698	isotalatizidine isomer	0.9
18	9.51	$C_{24}H_{39}NO_9$	$[M+H]^+$	486.2706	486.2703,454.2648,43 6.2327,404.2075,58.0	mesaconine isomer	-1.8

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19	9.91	$C_{11}H_{12}N_2O_2$	$[M+H]^+$	205.0974	188.0712,146.0600	tryptophan	1.2
20	11.33	$C_{23}H_{35}NO_6$	$[M+H]^+$	422.2554	422.2542,404.2094,372.2342,58.0651	gadesine isomer	0.7
21	11.98	$C_{11}H_9NO_2$	$[M+H]^+$	188.0711	188.0401,170.0606,142.0652,115.0549	3-amino-2-naphthoic acid	2.6
22	13.08	$C_{22}H_{35}NO_6$	$[M+H]^+$	410.2544	410.2550,378.2559,328.1939,58.0646	N-deeth-ylaconine isomer	1.7
23	13.54	$C_{21}H_{33}NO_4$	$[M+H]^+$	364.2481	364.2480,346.2381,328.2282,58.0649	16-hydroxy-cardiopetaline	-0.4
24	13.76	$C_{24}H_{39}NO_9$	$[M+H]^+$	486.2689	486.2673,454.2435 436.2318,404.2068,155.0852	mesaconine	2.2
25	13.91	$C_{15}H_{29}NO_4$	$[M+H]^+$	288.2161	288.2162,270.2058,210. 1853	N-Lauroyl-L-Serine	4.4
26	14.47	$C_{16}H_{17}NO_3$	$[M+H]^+$	272.1287	255.1021,161.0599,237.0914,107.0489	higenamine	2.1
27	14.52	$C_{22}H_{33}NO_4$	$[M+H]^+$	376.2486	376.2491,358.2385,326.2127,58.0650	beiwusine A	1
28	15.04	$C_{24}H_{39}NO_7$	$[M+H]^+$	454.2804	454.2805,436.2708,404.2431,58.0657	fuziline isomer	-0.3
29	15.15	$C_{22}H_{35}NO_4$	$[M+H]^+$	378.2628	378.2616,360.2516,342.2430,58.0646	karakoline	3.1
30	15.32	$C_{23}H_{37}NO_5$	$[M+H]^+$	408.2398	408.2391,390.2290,58.0646	isotalatizidine	0.9
31	15.46	$C_{23}H_{37}NO_5$	$[M+H]^+$	408.2729	408.2719,390.2610,358.2367,58.0644	talatisidine	-1.3
32	15.43	$C_{23}H_{37}NO_7$	$[M+H]^+$	440.2654	440.26503,422.2574, 408.2402,390.2308,58.0646	9-hydroxysenbusine A	1.5
33	16.82	$C_{23}H_{37}NO_6$	$[M+H]^+$	424.2701	424.2703,392.2438,374.2333,58.0646	senbusine A	2.9
34	16.85	$C_{25}H_{41}NO_9$	$[M+H]^+$	500.2844	500.2830,468.2598,450.2480,418.2230,58.0646	aconine	-0.8
35	17.03	$C_{24}H_{39}NO_6$	$[M+H]^+$	438.2846	438.2844,406.2591,388.2491,58.0652	6-epiforsticine isomer	0.4
36	17.12	$C_{25}H_{39}NO_7$	$[M+H]^+$	466.2810	448.2686,416.2452,58.0644	delbruine isomer	0.4
37	17.12	$C_{25}H_{41}NO_8$	$[M+H]^+$	448.2916	448.2897,466.2773,434.2557,58.0637	deoxyaconine	1.5
38	17.14	$C_{11}H_{19}NO_6$	$[M+H]^+$	262.1297	262.0881,244.1189,216,0881	N-(4-methyl-2-pentanoicacid)-glutamic acid	1.5
39	17.19	$C_{25}H_{39}NO_7$	$[M+H]^+$	466.2806	466.2816, 448.2687,416.2443,58	delbruine isomer	0.4

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40	17.37	$C_{22}H_{35}NO_6$	$[M+H]^+$	410.2814	410.2512,378.2559,360.2185,105.0760,58.0643	N-deethylaconine	0.3
41	18.27	$C_{24}H_{39}NO_7$	$[M+H]^+$	454.2792	454.2784,422.2534,404.2445,58.0647	foresticine isomer	-1.4
42	18.52	$C_{23}H_{35}NO_6$	$[M+H]^+$	422.2536	422.2544,404.2444,372.2199,58.0654	gadesine	0.7
43	18.81	$C_{15}H_{16}O_2$	$[M+H]^+$	229.0620	229.1232,201.1252,187.0770,185.0711	cucumin A	2.2
44	19.08	$C_{24}H_{37}NO_6$	$[M+H]^+$	436.2324	436.2318,418.2222,386.1962,58.0647	guiwuline	0.3
45	19.48	$C_{24}H_{39}NO_8$	$[M+H]^+$	470.2744	470.2725,438.2472,406.2224	hypaconine	-2.4
46	19.57	$C_{11}H_9NO_2$	$[M+H]^+$	188.0719	170.0951,146.0597,118.0659	6-amino-2-naphthoic acid	4.2
47	19.83	$C_{24}H_{39}NO_7$	$[M+H]^+$	454.2783	454.2777,436.2677,404.2434,372.2172,58.0649	foresticine	-3.4
48	20.59	$C_{25}H_{39}NO_6$	$[M+H]^+$	450.2859	450.2835,418.2607,400.2433,58.0645	condelphine isomer	1.5
49	20.73	$C_{24}H_{33}NO_5$	$[M+H]^+$	416.2444	416.2440,330.2075,312.1972,103.0387	guan-fu base Z	0.9
50	20.77	$C_{24}H_{37}NO_6$	$[M+H]^+$	436.2694	436.2708,418.1618,404.2449, 58.0657	guiwuline isomer	0.1
51	20.80	$C_{24}H_{39}NO_7$	$[M+H]^+$	454.2794	454.2775 436.2691,404.2433,58.0647	fuziline isomer	-3.4
52	21.09	$C_{23}H_{37}NO_5$	$[M+H]^+$	408.2744	408.2748,390.2647,376.2502,58.0650	isotalatizidine isomer	0.1
53	21.16	$C_{24}H_{39}NO_6$	$[M+H]^+$	438.2826	438.2841,420.2728,388.2471,58.0647	neoline isomer	0.6
54	21.21	$C_{24}H_{39}NO_6$	$[M+H]^+$	438.2833	438.2849,420.2723,388.2466,58.0647	6-epiforsticine	0.6
55	21.58	$C_{15}H_{20}O_4$	$[M+H]^+$	265.1445	247.1332,229.1219,201.1272	zedoarofuran	4.4
56	21.60	$C_{15}H_{16}O_2$	$[M+H]^+$	229.0630	229.2342,211.0512,201.0641	gweicurculactone	1.3
57	22.34	$C_{24}H_{37}NO_8$	$[M+H]^+$	468.2949	468.2945,436.2326,418.2596,386.2326,58.0646	1,7,8-trihydroxy-16-methoxy-4-(methoxymethyl)aconitan-14-ylacetate	1.3
58	22.44	$C_{24}H_{37}NO_5$	$[M+H]^+$	420.2742	420.2731,402.2638,384.2545,370.2380,58.0646	N-ethylhokbusine B	-0.6

59	22.55	$C_{27}H_{31}NO_5$	$[M+H]^+$	450.2861	450.2849,432.2748,400.2487,58.0646	ignavine	1.4
60	22.60	$C_{25}H_{39}NO_7$	$[M+H]^+$	466.2826	466.2814,448.2659,434.2562	delbruine	0.4
61	22.76	$C_{24}H_{39}NO_7$	$[M+H]^+$	454.2791	422.2520,404.2433,58.0647	fuziline isomer	-3.4
62	23.08	$C_{25}H_{41}NO_7$	$[M+H]^+$	468.2969	468.2976,436.2697,404.2454,58.0640	lycoctonin isomer	0.9
63	23.17	$C_{26}H_{41}NO_7$	$[M+H]^+$	480.2961	480.2969,448.2692,430.2618,58.0663	bullatine C	0.3
64	23.32	$C_{22}H_{33}NO_3$	$[M+H]^+$	360.2542	360.2538,342.2432,298.2155,58.0642	spiramine H	1.9
65	23.54	$C_{23}H_{33}NO_6$	$[M+H]^+$	420.2746	420.2748,388.2489,356.2229,58.0645	giraldine F isomer	-0.6
66	23.64	$C_{25}H_{41}NO_6$	$[M+H]^+$	452.3006	452.3009,420.2750,388.2490,58.0650	chasmanine	-0.6
67	23.81	$C_{23}H_{37}NO_4$	$[M+H]^+$	392.2881	392.2785,360.2528,342.2428,58.0646	sachaconitine	-0.9
68	23.88	$C_{26}H_{28}O_{14}$	$[M-H]^-$	563.2849	563.1402,353.0659	apigenin-6-C-β-D-Galactose-8-C-α-L-arabinopyranoside	3.7
69	23.9	$C_{15}H_{22}O_4$	$[M+H]^+$	267.1598	249.1476,231.1379,203.1425	zedoalactone A	0.1
70	23.92	$C_{22}H_{35}NO_5$	$[M+H]^+$	394.2588	394.2586,362.2327,330.2070,58.0642	chuanfumine	1
71	23.94	$C_{22}H_{33}NO_5$	$[M+H]^+$	392.2788	392.2783,360.2530,342.2436,58.0648	hokbusine B	1.7
72	23.99	$C_{25}H_{39}NO_6$	$[M+H]^+$	450.2853	450.2534,418.2597,400.2501,58.0647	condelphine	1.5
73	23.99	$C_{23}H_{33}NO_6$	$[M+H]^+$	420.2750	420.2751,388.2497,356.2219,58.0647	giraldine F	4.1
74	24.11	$C_{26}H_{28}O_{14}$	$[M+H]^+$	565.1556	529.1357,511.1250	schafftoside	-0.9
75	24.16	$C_{24}H_{39}NO_6$	$[M+H]^+$	438.2841	438.282,406.2572,388.2479,58.0645	neoline	1.8
76	24.28	$C_{15}H_{29}NO_3$	$[M+H]^+$	272.2225	254.2117,81.0693	thirteen acyl glycine	1
77	24.82	$C_{27}H_{31}NO_5$	$[M+H]^+$	450.2855	418.2600,400.2467,58.0652	talatizamine	1.4
78	26.99	$C_{25}H_{41}NO_7$	$[M+H]^+$	468.2952	468.2954,436.2697,404.2454,58.0646	lycoctonine	0.9
79	27.95	$C_{26}H_{41}NO_7$	$[M+H]^+$	480.2958	480.2964,448.2701,430.2595,58.0646	bullatine C isomer	0.3
80	28.37	$C_{27}H_{43}NO_8$	$[M+H]^+$	510.3074	510.3079,492.2967,460.2708,58.0658	14-O-Acetylbrowniine	1.3
81	28.57	$C_{15}H_{24}O_3$	$[M+H]^+$	253.1800	253.1807,235.1696,17	zedoarondiol	1.1

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82	28.84	$C_{31}H_{43}NO_9$	$[M+H]^+$	574.2645	574.2655,542.2393,510.2133,105.0334	benzoylhypacoitine isomer	1.1
83	28.89	$C_{15}H_{18}O_2$	$[M+H]^+$	231.1383	231.1114,203.0815	epicurzerenone	1.1
84	29.87	$C_{26}H_{41}NO_7$	$[M+H]^+$	480.2949	480.2952,448.2704,430.2591,58.0648	8-deoxy-14-dehydro-aconosine	1.9
85	30.21	$C_{26}H_{41}NO_6$	$[M+H]^+$	464.2999	464.2967,432.2730,414.2651,58.0646	Monoacetyltaliza mine	-0.1
86	30.82	$C_{31}H_{43}NO_{11}$	$[M+H]^+$	606.2916	556.2565,524.2301,105.0326	(-)-(A-b) -14α-benzoyloxy-3α,10β,13β,15α-pentahydroxy-1α,6α,16β,18-tetramethoxy-N-methylaconitane	0.7
87	31.94	$C_{15}H_{20}O_4$	$[M+H]^+$	265.0975	265.0971,247.0868,219.0919	curcumenolactone C	0.6
88	32.02	$C_{19}H_{20}O$	$[M+H]^+$	265.0973	265.0975,247.0874,219.1251	trans-17-diphenyl-1,3-heptadien-5-o	-0.9
89	32.06	$C_{15}H_{18}O$	$[M+H]^+$	215.1436	215.1429,197.1335,187.1481,167.0851	agassizin	2.1
90	33.60	$C_9H_{16}O_4$	$[M-H]^-$	187.0956	125.0977,123.0816	azelaic acid	1.2
91	34.77	$C_{15}H_{20}O_3$	$[M+H]^+$	249.1489	249.1541,231.1382,161.0949	curdionolide B	1.5
92	34.82	$C_{22}H_{37}NO_3$	$[M+H]^+$	364.2847	364.2868,346.2746,328.2615,310.2540	N-(2-Hydroxyethyl)-Eicosapentaenoic acid-amide	0.2
93	34.84	$C_{15}H_{18}O_3$	$[M+H]^+$	247.1334	247.1346,229.1277,201.1262	curcolone	0.9
94	34.93	$C_{31}H_{41}NO_8$	$[M+H]^+$	556.2545	556.2554,524.2267,492.2075,105.0340	dehydrated benzoylhypaconine	0.9
95	34.98	$C_{31}H_{43}NO_{10}$	$[M+H]^+$	590.2963	590.2977,540.2570,508.2334,105.0323	benzoylmesaconine isomer	-1.3
96	35.17	$C_{18}H_{35}NO_4$	$[M+H]^+$	330.2643	330.2633,312.2555,57.0337	N-[(dodecyloxy)carbonyl]-valine	1.3
97	35.21	$C_8H_4O_3$	$[M+H]^+$	149.0236	121.0278,93.0327$_2$	phthalic anhydride	2.5
98	35.22	$C_{21}H_{37}NO$	$[M+H]^+$	320.2222	302.2582,287.8937	(2S)-2-(dodecylamino) -3-phenyl-1-propanol	4.1
99	35.69	$C_{22}H_{37}NO_2$	$[M+H]^+$	348.9902	348.2748,330.2423,312.2335	arachidonylethanolamide	0.8

100	36.06	$C_{31}H_{43}NO_{10}$	$[M+H]^+$	590.2922	590.2937,540.2570,508.2330,105.0326	benzoylmesaconine	1.2
101	36.29	$C_{31}H_{43}NO_9$	$[M+H]^+$	574.3027	574.3020,542.2758,524.2592,105.0339,58.0648	benzoylhypaconine isomer	2.0
102	38.19	$C_{32}H_{45}NO_{10}$	$[M+H]^+$	604.3104	604.3090,572.2861,554.2745,522.2495,105.0330	benzoylaconine	-0.9
103	38.51	$C_{30}H_{41}NO_7$	$[M+H]^+$	528.2964	528.2956,510.2857,496.2714,105.0336	6-demethoxy benzoylneoline	1.4
104	38.90	$C_{15}H_{18}O_3$	$[M+H]^+$	247.1336	247.355,229.1243,201.1263,189.0910	zederone	1.3
105	38.68	$C_{15}H_{10}O_4$	$[M+H]^+$	255.0658	255.0660,227.0683,199. 0765,181.0647	daidzein	2.0
106	38.99	$C_{26}H_{45}NO_6S$	$[M-H]^-$	498.8339	498.2845,454.2968,408.2911,79.9591	taurochenodeoxycholic acid	1.4
107	39.69	$C_{31}H_{43}NO_9$	$[M+H]^+$	574.2998	574.2991,542.2740,510.2494,105.0332	benzoylhypacoitine	-0.8
108	39.74	$C_{33}H_{45}NO_9$	$[M+H]^+$	600.2812	600.2822,540.2615,480.2749,105.0327	13-deoxyhypaconitine isomer	1.4
109	39.88	$C_{21}H_{33}NO_4$	$[M+H]^+$	364.2844	364.2854,346.2779,328.2626,276.2319	16-hydroxy-cardiopetaline isomer	-0.6
110	40.07	$C_{32}H_{43}NO_9$	$[M+H]^+$	586.3005	586.3022,554.2763,536.2724	1,15-dimethoxy-3-hydroxy-14-benzoyl-16-ketoneoline	0.4
111	40.12	$C_{15}H_{20}O_2$	$[M+H]^+$	233.1549	233.1532,215.1440,175.1123	furanogermenone	-0.5
112	40.85	$C_{34}H_{47}NO_{11}$	$[M+H]^+$	646.3225	646.3233,586.3121,554.2711,105.0335	aconitine	1.6
113	41.12	$C_{15}H_{22}O_3$	$[M+H]^+$	251.1646	251.1627,233.1531,215.1442	aerugidiol	0.1
114	41.21	$C_{15}H_{22}O_3$	$[M+H]^+$	251.1642	251.1651,233.1531,215.1422	procurcumadiol	0.1
115	41.30	$C_{33}H_{45}NO_{12}$	$[M+H]^+$	648.3025	648.3013,588.2806,556.2553,105.0338	beiwutine	-0.1
116	41.36	$C_{31}H_{41}NO_8$	$[M+H]^+$	556.2912	556.2924,524.2660,506.2617,105.0327	dehydrated benzoylhypaconine isomer	1.3
117	41.51	$C_{30}H_{41}NO_7$	$[M+H]^+$	528.2961	528.2969,496.2714,478.2590,105.0344	(-) -(A-b)-14α-benzoyloxy-N-ethyl-1α,8β,15α-trihydroxy-	1.6

118	41.63	$C_{31}H_{43}NO_8$	$[M+H]^+$	558.3045	558.3041,526.2795,508.2707,105.0332	16β,18-dimethoxy aconitane (-)-(A-b)-14α-benzoyloxy-N-ethyl-1α,8β，15α-trihydroxy-	0.5
119	41.77	$C_{32}H_{45}NO_9$	$[M+H]^+$	588.3050	588.3145,556.2897,524.2657,105.0336	6α,16β,18-trimethoxyaconitane 14-benzoyldeoxyaconine isomer	0.5
120	42.08	$C_{15}H_{20}O$	$[M+H]^+$	217.1593	217.1599,199.1512,161.0945,105.0700	comosone II	0.1
121	42.21	$C_{31}H_{43}NO_7$	$[M+H]^+$	542.3122	542.3115,510.2864,492.2797,105.0344	14-benzoylneoline	1.1
122	42.47	$C_{33}H_{45}NO_{11}$	$[M+H]^+$	632.3070	632.3066,572.2866,540.2593,508.2358,105.0327	10-hydroxy-hypaconitine	1.1
123	42.56	$C_{26}H_{48}NO_7P$	$[M+H]^+$	518.3215	518.3229,500.3025,459.1897,114.0658	LPC (18:3)	-2.0
124	43.02	$C_{15}H_{16}O_3$	$[M+H]^+$	245.1179	245.1172,229.0857,181.1007	cucumin C	0.7
125	43.11	$C_{34}H_{47}NO_{10}$	$[M+H]^+$	630.2015	630.2002,570.1844,510.1603,105.0330	3-deoxyaconine isomer	-0.6
126	43.18	$C_{32}H_{43}NO_9$	$[M+H]^+$	586.3021	586.3020,554.2783,536.2647,526.2810	1,15-dimethoxy-3-hydroxy-14-benzoyl-16-ketoneoline isomer	0.8
127	43.25	$C_{26}H_{43}NO_6$	$[M-H]^-$	464.3024	464.3022,428.2297,74.0248	glycocholic acid	1.2
128	43.47	$C_{22}H_{37}NO_2$	$[M+H]^+$	348.2903	348.2900,330.2788,312.2691	N-(1-Hydroxy-2-propyl)-5,8,11,14-eicosatetraenamide	1.7
129	43.55	$C_{33}H_{45}NO_{11}$	$[M+H]^+$	632.3058	632.3050,572.2858,540.2614,105.0331	mesaconitine	0.1
130	43.67	$C_{33}H_{45}NO_{10}$	$[M+H]^+$	616.3149	616.3136,556.2924,524.2646,105.0316	hypaconitine	-1.0
131	43.72	$C_{31}H_{43}NO_7$	$[M+H]^+$	542.3125	542.3097,510.2853,492.2758,105.0332	14-benzoylneoline isomer	1.1
132	43.88	$C_{34}H_{47}NO_{12}$	$[M+H]^+$	662.3169	662.3161,602.2973,570.2117,105.0330	10-hydroxyaconitine	1.3
133	44.48	$C_{32}H_{45}NO_9$	$[M+H]^+$	588.3180	588.3021,556.2911,524.2670,105.0306	14-benzoyldeoxyaconine	-1.4
134	44.55	$C_{33}H_{45}NO_8$	$[M+H]^+$	584.3229	584.3222,522.2976,534.2886,58.0655	patentine	1.9

135	44.57	$C_{15}H_{10}O_5$	$[M-H]^-$	269.0466	269.0457,241.0524,225.0547	apigenin	3.9
136	44.88	$C_{26}H_{43}NO_6$	$[M-H]^-$	464.3030	464.3032,420.3124,402.3019,74.0245	glycocholic acid isomer	0.3
137	45.38	$C_{32}H_{45}NO_8$	$[M+H]^+$	572.3217	572.3200,540.2960,508.2707,105.0332	14-O-anisoylneoline	0.7
138	45.50	$C_{34}H_{47}NO_{11}$	$[M+H]^+$	646.3239	646.3219,586.3020,554.2758,105.0339	(-)-(A-b) -8β-acetoxy-14α-benzoyloxy-N-ethyl-3α,10β,13β-trihydroxy-1α,6α,16β，18-tetra-methoxyaconitane	1.1
139	45.65	$C_{20}H_{37}NO_2$	$[M+H]^+$	324.2902	306.2797,288.2686,256.1093	linoleoyl ethanolamide	1.5
140	45.87	$C_{33}H_{45}NO_7$	$[M+H]^+$	568.3284	568.3284,550.3178,518.2933,58.0637	8-O-cinnamoylneoline	0.9
141	45.99	$C_{33}H_{45}NO_9$	$[M+H]^+$	600.3165	600.3165,540.2953,508.2699,480.2749,105.0328	13-deoxyhypaconitine	-0.3
142	46.97	$C_{34}H_{47}NO_9$	$[M+H]^+$	614.3332	614.3331,554.3103,522.2861,490.2592,105.0331	chasmaconitine	1.4
143	47.32	$C_{34}H_{47}NO_{10}$	$[M+H]^+$	630.3267	630.3261,570.3055,538.2805,510.2855	3-deoxyaconine	0.5
144	47.56	$C_{15}H_{18}O_2$	$[M+H]^+$	231.1137	231.1383,213.1256,203.1444,	curzerenone	0.6
145	47.79	$C_{26}H_{43}NO_6$	$[M-H]^-$	464.3017	464.3012, 420.3126,402.3016,400.2861,74.0247	glycohyocholic acid	0.9
146	47.96	$C_{15}H_{22}O_2$	$[M+H]^+$	235.1699	235.1679,217.1625, 189.1632,	curcumenol	-1.1
147	48.13	$C_{26}H_{43}NO_5$	$[M-H]^-$	448.3069	448.3077,386.3069,74.0248	glycohyodeoxycholic acid	0.1
148	48.62	$C_{27}H_{43}NO_5$	$[M+H]^+$	462.3216	444.3101,426.3013,337.2535,90.0548	6-ketone-glycohyodeoxycholic acid methyl ester	0.4
149	49.01	$C_{27}H_{43}NO_5$	$[M+H]^+$	462.3218	444.3133,426.3012,337.2534,90.0548	7-ketone-glycochenodeoxycholic acid methyl	0.2

						ester	
150	49.02	$C_{27}H_{45}NO_6$	$[M+H]^+$	480.3320	462.2317,444.3109,426.2990,337.2520,90.0546	glycohyocholic acid methyl ester	-0.3
151	49.09	$C_{34}H_{47}NO_9$	$[M+H]^+$	614.3331	614.3327,554.3126,522.2848,105.0333	chasmaconitine isomer	1.4
152	49.22	$C_{15}H_{22}O$	$[M+H]^+$	219.1745	219.1755,201.1649,191.1778	bisacumol	3.0
153	49.81	$C_{26}H_{41}NO_5$	$[M-H]^-$	446.2927	446.2919,402.3037,348.2914, 74.0245	6-keto-glycohyodeoxycholic acid	2.2
154	50.52	$C_{23}H_{39}NO_2$	$[M+H]^+$	362.3058	362.3039,344.2947,326.2846,299.2365	N-(3-hydroxy-propyl)arachidonoylamide	-0.4
155	50.67	$C_{26}H_{43}NO_5$	$[M-H]^-$	448.3079	448.3064,386.3052,74.0252	glycodeoxycholtc acid	1.3
156	50.67	$C_{27}H_{45}NO_5$	$[M+H]^+$	464.3386	464.3573,428.3159,339.2678,90.0538	glycochenodeoxycholic acid methyl ester	1.4
157	51.07	$C_{24}H_{40}O_5$	$[M-H]^-$	407.2806	407.2815,345.2806,289.2182	hyocholic acid	0.5
158	51.10	$C_{24}H_{38}O_4$	$[M+H]^+$	391.2846	373.2750,255.2619,337.2534,319.2425	7-ketolithocholic acid	0.8
159	51.14	$C_{24}H_{40}O_5$	$[M-H]^-$	407.2800	407.2808,389.2701,371.2601,345.2795,343.2639	cholic acid	-0.7
160	51.52	$C_{26}H_{43}NO_5$	$[M-H]^-$	448.3080	448.3065,386.3069,74.0246	glycochenodeoxycholic acid	0.5
161	52.18	$C_{26}H_{41}NO_5$	$[M-H]^-$	446.2923	446.2919,402.3028,348.2910,74.0249	7-keto-glycochenodeoxycholic Acid	2.5
162	52.49	$C_{20}H_{41}NO_2$	$[M+H]^+$	328.3210	328.3203,310.3105,292.1033,98.0967	N-(2-hydroxyethyl)stearamide	0.6
163	52.90	$C_{18}H_{33}NO$	$[M+H]^+$	280.2632	280.2634,262.2530,250.2524,233.2276	crucigasterin E	-1
164	52.91	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.2742	280.2632,262.2535,250. 2536	Palmitoleoyl-ethanolamide	3.5
165	52.92	$C_{18}H_{39}NO_3$	$[M+H]^+$	318.2991	318.2985,300.2882,282.2776,270.2785	phytosphingosine	1.7
166	53.34	$C_{15}H_{18}O_3$	$[M+H]^+$	247.1330	229.1221,159.0806,139.0385	zedoarol	0.5

167	53.39	$C_{27}H_{45}NO_5$	$[M+H]^+$	464.3375	464.3573,428.3149,339.2680,90.0542	glycohyodeoxycholic acid methyl ester	-0.6
168	53.41	$C_{27}H_{45}NO_5$	$[M+H]^+$	464.3375	464.3270,428.3148,339.2680,90.0545	glycoursodeoxycholic acid methyl ester.	-0.3
169	53.42	$C_{24}H_{40}O_4$	$[M-H]^-$	391.2854	391.2914,355.2648,345.2798,327.2695	chenodeoxycholic acid	1.1
170	53.59	$C_{15}H_{20}O$	$[M+H]^+$	217.1583	217.1581,189.1629,105.0694	furanodiene	1.0
171	53.61	$C_{15}H_{22}O_2$	$[M+H]^+$	235.1695	235.1678,217.1593,177.1271,105.0694	curcumenone	-1.1
172	53.68	$C_{18}H_{39}NO_2$	$[M+H]^+$	302.3050	302.3048 284.2948,266.2843,256.2135	dihydrosphingosine	1.2
173	54.85	$C_{15}H_{24}O_2$	$[M+H]^+$	237.1848	219.1747, 191.1789,135.1166	curcumol	1.7
174	54.90	$C_{15}H_{24}O_2$	$[M+H]^+$	237.1851	237.1847,219.1747,135.1164,107.0854	neocurdione	0.8
175	55.34	$C_{24}H_{40}O_4$	$[M-H]^-$	391.2846	391.2847,355.2644,345.2796,327.2693	hyodeoxycholic acid	1.2
176	55.37	$C_{24}H_{40}O_4$	$[M-H]^-$	391.5852	391.2845,355.2645,345.2798,327.2693	deoxycholic acid	1.6
177	55.49	$C_{20}H_{43}NO_2$	$[M+H]^+$	330.3378	330.3358,312.3264,88.0754	eicosasphinganine	-0.8
178	55.71	$C_{18}H_{39}NO$	$[M+H]^+$	286.3102	268.2996,226.2499,180.9724,97.1005	N-hexadecyl amino ethanol	-0.8
179	56.12	$C_{20}H_{37}NO_3$	$[M+H]^+$	340.2708	340.2823,294.1332,109.1007	oleoylglycine	3.8
180	56.36	$C_{15}H_{18}O_2$	$[M+H]^+$	231.1379	231.1381,213.1274,173.0955,149.0595	furanodienone	1.9
181	56.46	$C_{26}H_{50}NO_7P$	$[M+H]^+$	520.3398	520.3394,502.3309,184.0730,104.1066	LPC (18:2)	-0.3
182	56.47	$C_{28}H_{48}NO_7P$	$[M+H]^+$	542.3228	542.3230,483.2493,337.2733,146.9815,104.1065	LPC (20:5)	3.7
183	57.2	$C_{16}H_{30}O_2$	$[M+H]^+$	255.2316	255.2138,237.2204,219.2114,163.1478,69.0692	2(Z)-hexadecenoic acid	-1.8
184	57.28	$C_{19}H_{38}O_4$	$[M+H]^+$	331.2633	331.2625,313.2524,295.2419,257.2261	glycerol monopalmitate	4.2
185	57.54	$C_{24}H_{50}NO_7P$	$[M+H]^+$	496.3401	496.3391,478.3278,184.0729,104.1067	LPC (16：0)	-1.3
186	57.59	$C_{15}H_{22}O$	$[M+H]^+$	219.1748	219.1477,210.1638,	germacrone	0.3

187	57.95	$C_{15}H_{22}O$	$[M+H]^+$	219.1750	159.1140 219.1736,201.1633,159.1163,105.0696	(+)-Nootkatone	0.3
188	58.16	$C_{15}H_{22}$	$[M+H]^+$	203.1798	203.1805,147.1165,105.0692,119.0852	α-curcumene	-0.6
189	58.36	$C_{23}H_{46}NO_7P$	$[M+H]^+$	480.3089	462. 2982,339.2894,308. 2941,184.0733 104.1074	LPC (15:1)	0.9
190	58.50	$C_{28}H_{50}NO_7P$	$[M+H]^+$	544.3379	544.3390,485.26246,339. 2901,104.1069	LPC (20:4)	0.4
191	58.53	$C_{26}H_{52}NO_7P$	$[M+H]^+$	522.3553	522.3556,504.3556,184.0731,104.1067	LPC (18:1)	-1.1
192	58.89	$C_{15}H_{20}O$	$[M+H]^+$	217.1591	217.1581,189.1648,175.1095,91.0522	ar-tumerone	1.0
193	60.21	$C_{15}H_{22}O$	$[M+H]^+$	219.1740	219.1736,201.1633,163.1116	(s)-turmerone	-0.6
194	60.98	$C_{18}H_{30}O_2$	$[M+H]^+$	279.2322	279.0936,149.0229,57.0693	linolenic acid	1.2
195	61.22	$C_{26}H_{54}NO_7P$	$[M+H]^+$	524.3720	524.3742,506.4509,184.0728,104.1070	LPC(18:0)	1.8
196	61.27	$C_{15}H_{24}$	$[M+H]^+$	205.1958	205.1929,149.0232,135.1184,109.1004	beta-elemene	0.6
197	61.49	$C_{15}H_{24}$	$[M+H]^+$	205.0866	149.0226,121.0285	α-zingiberene	-0.4
198	61.62	$C_{18}H_{34}O_2$	$[M+H]^+$	283.2622	265.2518,247.2416,191.1795,209.1889	8-trans-11-octadecenoic acid	3.4
199	61.77	$C_{25}H_{42}O_4$	$[M+H]^+$	407.3147	407.3216,389.2937,371.2903	chenodeoxycholic acid methyl ester	2.2
200	61.82	$C_{30}H_{62}O_{10}$	$[M+H]^+$	583.4416	415.2556,133.0853	nonaethylene glycol monododecyl ether	-0.1
201	61.91	$C_{28}H_{58}O_9$	$[M+H]^+$	539.4158	371.2284,133.0860	dodecyloctaethyleneglycol ether	1.9
202	61.98	$C_{26}H_{54}O_8$	$[M+H]^+$	495.3908	327.2002,133.0857	heptaethylene glycol monododecyl ether	0.3
203	62.09	$C_{24}H_{50}O_7$	$[M+H]^+$	451.3633	283.1749,133.0869	Hexaethylene glycol monododecyl ether	0.8
204	62.84	$C_{25}H_{42}O_4$	$[M+H]^+$	407.3364	407.3003,389.3069,37	hyodeoxycholic	2.1

					1.2959	acid methyl ester	
205	63.86	$C_{21}H_{38}O_4$	$[M+H]^+$	355.2632	355.2645,337.2538,263.2365, 245.2278	linoleic acid glyceride	3.2
206	64.49	$C_{16}H_{33}NO$	$[M+H]^+$	256.2629	256.2620,116.1062,88.0751	hexadecanamide	2.3
207	65.27	$C_{21}H_{36}O_4$	$[M+H]^+$	353.2680	353.2679,335.2575,291.2321	2,3-dihydroxy-methyl linolenat	-1.8
208	65.36	$C_{19}H_{38}O_4$	$[M+H]^+$	331.2845	331.2181,313.2726,257.2477	glycerol monopalmitate isomer	-1.4
209	65.54	$C_{28}H_{58}O_8$	$[M+H]^+$	523.4201	327.1978,133.0859	3,6,9,12,15,18,21-heptaoxapentatriacontan-1-ol	3.1
210	65.61	$C_{26}H_{54}O_7$	$[M+H]^+$	479.3933	283.1749,133.0869	hexaethylene glycol monotetradecyl ether	3.2
211	65.68	$C_{24}H_{50}O_6$	$[M+H]^+$	435.3677	239.1494,133.0855	pentaethylene glycol monotetradecyl ether	-0.7

Table S4. MRM parameters of five compounds and two ISs.

Compounds	Q1	Q3	DP	EP	CE	CXP
Karakoline	378.5	360.3	121.0	11.0	41.0	11.0
Neoline	438.4	388.3	115.0	10.0	44.0	12.0
Talatisamine	422.2	390.1	116.0	9.0	41.0	13.0
Chasmanine	452.0	420.4	90.0	12.0	43.0	13.0
Lannaconitine(IS)	585.2	356.3	124.0	10.0	46.0	11.0
Schaftoside	565.1	547.2	120.0	8.0	20.0	10.0
Rutin(IS)	611.1	303.0	81.0	10.0	30.0	11

Table S5. Time program of the gradient elution in UHPLC.

Time	A%	B%
0	86	14
5	73	27
7	73	27

8	60	40
9	10	40

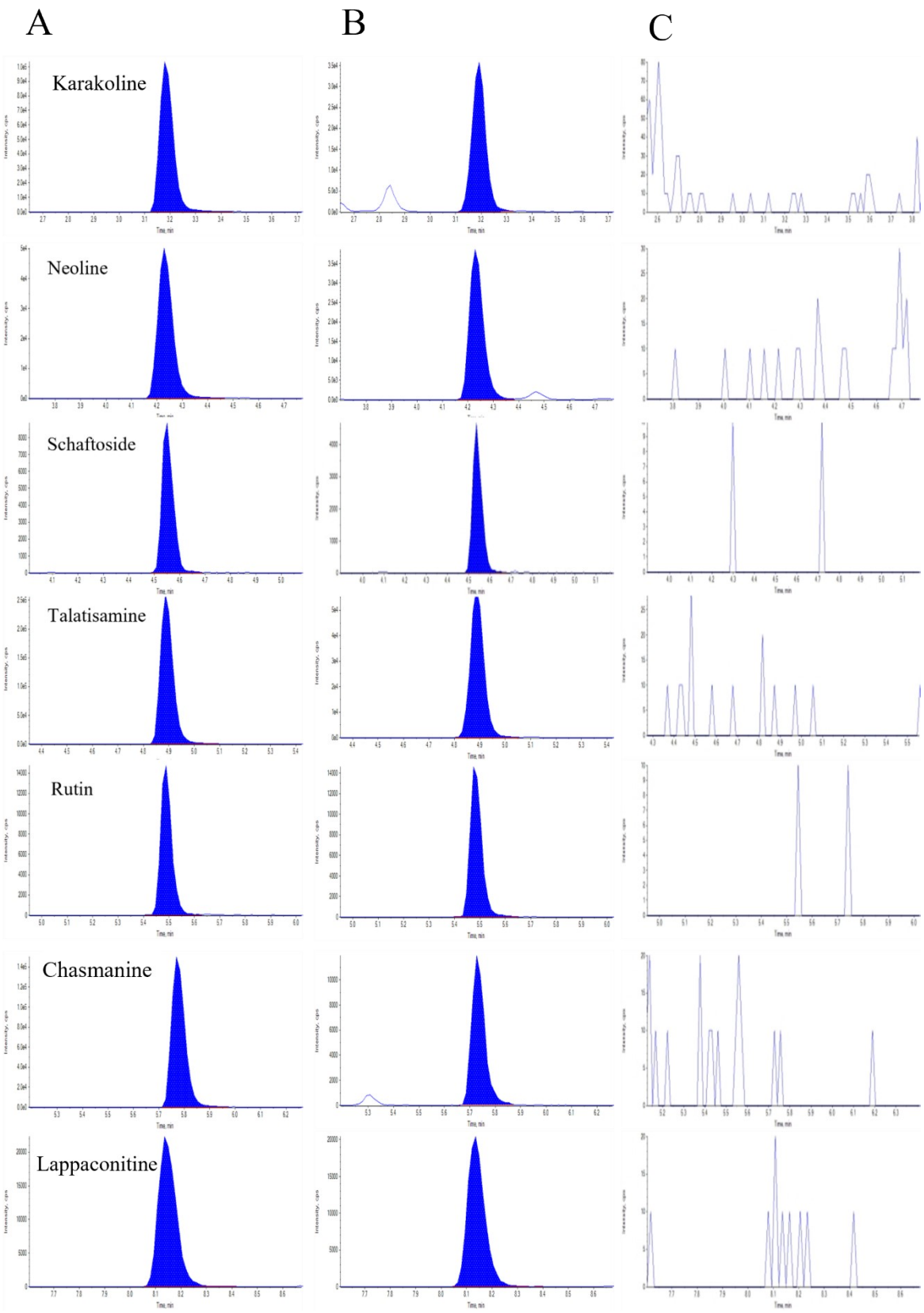
A
B
C
Karakoline
Neoline
Schaftoside
Talatisamine
Rutin
Chasmanine
Lappaconitine

Fig. S9. The mass spectrometry of five compounds and two ISs. (**A**) Typical mass spectrometry of (**A**) standards, (**B**) YM extrac, and (**C**) blank of five compounds and two ISs.

Table S6. The linear regression equation, linear range, LLOQ of the five compounds.

compounds	Regressive equation	Linear range (ng/mL)	R	LLOQ (ng/mL)
Karakoline	Y=0.00389X+0.133	50-1000	0.9973	0.05
Talatisamine	Y=0.0087X+0.013	50-1000	0.9974	0.05
Neoline	Y=0.00197X+0.0554	50-1000	0.9946	0.05
Chasmanine	Y=0.00584X+0.00301	50-1000	0.9938	0.05
Schaftoside	Y=0.000594X+0.0109	50-1000	0.9991	5

Table S7. The intraday, interday, stability of the five compounds (n=6).

Compounds	Concentration	Intraday		Interday		Stability	
	(ng/mL)	Accracy (%)	RSD (%)	Accracy (%)	RSD (%)	Accuracy (%)	RSD (%)
Karakoline	1000	89.55	1.63	88.10	2.90	87.15	2.86
	600	98.50	1.77	96.53	2.54	103.0	4.44
	50	88.63	4.28	88.27	4.48	89.34	2.23
Talatiamine	1000	92.22	1.40	92.93	1.72	103.5	4.83
	600	100.8	1.23	100.5	1.17	105.1	7.35
	50	106.2	2.45	108.0	2.52	105.7	4.85
Neoline	1000	86.22	2.31	86.56	2.59	87.23	4.25
	600	96.25	1.26	95.93	1.54	97.12	3.66
	50	98.67	3.06	97.66	5.73	93.17	5.85
Chasmanine	1000	91.08	1.79	92.42	1.74	93.11	5.51
	600	100.1	1.40	100.6	1.27	103.9	2.78
	50	95.83	4.89	100.7	8.84	110.7	2.31
Schaftoside	1000	90.82	3.02	91.82	3.46	91.45	4.24
	600	94.94	5.05	95.16	4.82	97.62	4.54
	50	108.9	3.18	109.8	4.02	108.	6.30

Table S8. The repeatability of the five compounds of YM extract (n=6).

compounds	Concentration (ng/mL)	RSD
Karakoline	230.00	1.72
Talatisamine	867.00	1.35
Neoline	831.00	0.44
Chasmanine	58.95	1.91
Schaftoside	457.67	1.80

Table S9. The recovery of five compounds of YM extract (n=6).

Conmpounds	Original (ng/mL)	Spiked (ng/mL)	Found (ng/mL)	Average (%)	Recovery (%)	RSD (%)
		92.00	214.17	96.65	107.79	6.50
		115.00	234.83	97.94	104.20	6.50
Karakoline	115.00	138.00	243.71	103.81	92.75	8.29
		344.74	805.00	96.35	108.51	2.38
		430.92	921.67	93.58	113.88	6.38
Talatisamine	430.92	517.10	963.33	98.41	102.96	7.63
		355.06	814.50	98.08	104.40	1.41
		443.83	897.17	98.94	102.14	6.76
Neoline	443.83	532.60	946.33	103.18	94.35	7.51
		25.45	56.06	102.14	95.28	5.46
		31.81	61.08	104.16	92.02	9.44
Chasmanine	31.81	38.17	66.46	105.29	90.77	5.93
		179.74	426.50	94.82	112.29	3.33
		224.67	470.33	95.54	109.34	4.72
Schaftoside	224.67	269.60	510.67	96.79	106.08	1.34

Table S10. The concentration five compounds of YM and unfermented YM extract (n=6).

Type	Sample	Karakoline（μg/g）	Talatisamine（μg/g）	Neoline（μg/g）	Chasmanine（μg/g）	Schaftside（μg/g）
	S1	27.98	35.62	77.42	6.85	47.40
	S2	30.13	36.02	99.17	6.06	50.52
	S3	29.07	46.97	94.72	7.65	53.03
	S4	31.53	51.33	70.43	4.50	45.43
YM	S5	30.75	53.52	81.20	6.96	47.97

	S6	24.53	54.72	84.55	6.41	59.22
	S7	26.58	33.68	73.51	5.38	41.30
	S8	26.10	35.48	76.12	5.70	45.68
UNYM	S9	28.58	35.40	75.97	5.64	43.43
	S10	25.73	35.33	74.47	5.82	45.48
	S11	24.20	34.88	73.08	5.28	42.53
	S12	19.98	28.03	68.52	3.05	46.13

(Samples S1 to S6 represented fermented YM and samples S7 to S12 represented unfermented YM)