Supplementary Materials

Materials and methods

Chemical analysis of YXS Intestinal Absorption Liquid

YXS intestinal absorption liquid and cold acetonitrile were mixed at a ratio of 1:3 and then vortexed for 30 s prior to analysis. The mixture was de-proteinized by centrifugation at 4°C (21,130 g for 30 min) and the supernatant was put into a new centrifugal tube and dried using N2 at room temperature (25°C). The residue was then dissolved in 5 ml of methanol and injected into the UPLC. The blank intestinal absorption liquid was also manufactured as stated above. Analysis was performed by UPLC (1290 Infinity Binary LC System, Agilent Technologies, USA) and coupled with ESI-Q/Tof-MS. The LC system was comprised of an Agilent ZORBAX RRHD Eclipse Plus C18 column (100 x 3 mm, 1.8 µm). The mobile phase was composed of solvent A (0.1% formic acid-water) and solvent B (0.1% formic acid-acetonitrile) with a gradient elution (0–7 min, 10–40% B; 7–9.5 min, 40–55% B; 9.5–12 min, 55–55% B; 12–17 min, 55–88% B.). The flow rate of the mobile phase was 0.5 mL•min-1. The column temperature was maintained at 45°C, and the sample manager temperature was set at 4°C. The injection volume was 1 µl-1.

Mass spectrometry was performed on a Quadrupole/Time-Of-Flight Mass Spectrometer (QTOF-MS; model G6540B Agilent Technologies, USA) using a Dual Agilent Jet Stream (AJS) ESI source. The instrument was operated in positive and negative-ion modes, respectively. The scanning mass-to-charge (m/z) range was from 50 to 1500 with a scan rate of 1.00 spectra•sec-1. The capillary voltage was set to 4000 V and 3500 V (positive and negative mode, respectively) and the fragmentor was set to 175 V. The pressure of the nebulizer was set at 35 psi, the gas temperature to 325°C, and the continuous gas flow to 5 L•min-1. The software used for data acquisition and analysis was Agilent MassHunter Workstation. According our previous study, the use of molecular feature orientated precursor ion selection, tandem mass spectrometry structure elucidation and the reference standards identified 276 chemical components of the Chinese medicine YXS capsules (Wang HP 2015). The database of chemical compounds within the Yixin-Shu capsule in the UPLC-Q/TOF-MS was then constructed. In this study, the chemical structures of YXS capsule intestinal absorption liquid were identified according to exact mass and retention time data. When necessary, further confirmation was acquired through comparisons with authentic standards and MS/MS fragmentation patterns.

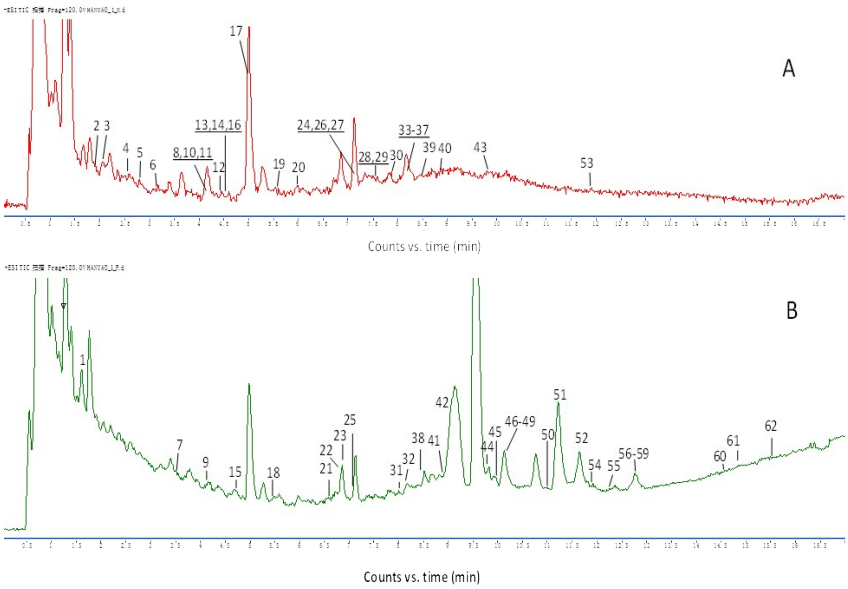

Figure S1. Typical total ion chromatography (TIC) profiles of YXS intestinal absorption liquid in the negative (A) and positive (B) signal modes. Names, molecular formulas and structures of the compounds (No. 1-62) are in the Supplementary Materials section.

Table S1. Summary of chemical constituents identified in YXS Capsules intestinal absorption liquid by UPLC-ESI-Q/TOF-MS

NO.	Rt(min)	Compound names	Molecular formula	Expected neutral mass (Da)	Observed neutral mass (Da)	Mass accuracy (ppm)	measured mass m/z(Da)
1	1.66	Chlorogenic acid*	C16H18O9	354.0951	354.0958	2.0	355.1031 $[M+H]^+$
2	1.91	Protocatechuic acid*	C7H6O4	154.0266	154.0265	-0.6	153.0192 $[M-H]^-$
3	2.10	Vanillin*	C8H8O3	152.0473	152.0466	-4.6	151.0393 $[M-H]^-$ 197.0448 $[M+HCOO]^-$
4	2.60	Vanillic acid*	C8H8O4	168.0423	168.042	-1.8	167.0347 $[M-H]^-$
5	2.72	Danshensu*	C9H10O5	198.0528	198.0521	-3.5	197.0448 $[M-H]^-$
6	3.15	Caffeic acid*	C9H8O4	180.0423	180.042	-1.7	179.0347 $[M-H]^-$
7	3.52	Calycosin-7-O-β-D-glucoside*	C22H22O10	446.1213	446.1197	-3.6	447.1270 $[M+H]^+$
8	4.13	Rosmarinic acid*	C18H16O8	360.0845	360.0839	-1.7	359.0766 $[M-H]^-$
9	4.21	Lithospermic acid*	C27H22O12	538.1111	538.1124	2.4	539.1197 $[M-H]^-$
10	4.23	Salvianolic acid A*	C26H22O10	494.1213	494.121	-0.6	493.1137 $[M-H]^-$
11	4.31	Protocatechuic aldehyde*	C7H6O3	138.0317	138.0329	-8.7	137.0256 $[M-H]^-$
12	4.46	Re 4	C47H80O18	932.5345	932.5304	-4.4	931.5231 $[M-H]^-$
13	4.59	Salvianolic acid B*	C36H30O16	718.1534	718.1507	-3.8	717.1434 $[M-H]^-$
14	4.69	Notoginsenoside R1	C47H80O18	932.5345	932.5311	-3.6	931.5238 $[M-H]^-$
15	4.75	Formononetin-7-O-β-D-glycoside	C22H22O9	430.1264	430.1269	1.2	431.1342 $[M+H]^+$
16	4.83	Isoferulic acid	C10H10O4	194.0579	194.0579	0.0	193.0506 $[M-H]^-$
17	4.99	Re*	C48H82O18	946.5501	946.5476	-2.6	945.5403 $[M-H]^-$
18	5.50	Rg1/Ia,	C42H72O14	800.4922	800.493	1.0	801.5003

							$[M+H]^+$
19	5.53	Calycosin	C16H12O5	284.0685	284.068	-1.8	283.0607 $[M-H]^-$ 285.0753 $[M+H]^-$
20	5.98	Acetyl-Re	C50H84O19	988.5607	988.5569	-3.8	987.5496
21	6.73	Cyclocanthoside E	C41H70O14	786.4766	786.4779	1.7	787.4852 $[M+H]^+$
22	6.86	Ursolic acid/Oleanlic acid	C30H48O3	456.3603	456.3611	1.8	457.3684 $[M+H]^+$
23	6.87	Rf	C42H72O14	800.4922	800.4932	1.2	801.5005 $[M+H]^+$
24	7.13	Rb1*	C54H92O23	1108.6029	1108.5985	-4.0	1107.5912 $[M-H]^-$
25	7.13	Rg2/Rg3/Ginsenoside F2	C42H72O13	784.4973	784.4981	1.0	785.5054 $[M+H]^+$
26	7.23	Malonyl-ginsenoside Rb1	C57H94O26	1194.6033	1194.5981	-4.4	1193.5908 $[M-H]^-$
27	7.38	Rc	C53H90O22	1078.5924	1078.5875	-4.5	1077.5802 $[M-H]^-$
28	7.61	Acetyl-Rb1	C56H94O24	1150.6135	1150.6108	-2.3	1149.6035 $[M-H]^-$
29	7.63	Rb2/Rb3	C53H90O22	1078.5924	1078.5863	-5.7	1077.5790 $[M-H]^-$
30	7.84	Quinquenoside R1	C56H94O24	1150.6135	1150.6079	-4.9	1149.6006 $[M-H]^-$
31	8.02	Acetyl-Rf/Acetyl-Rg1/Yesanchinoside D	C44H74O15	842.5028	842.5041	1.5	843.5114 $[M+H]^+$
32	8.03	Agroastragaloside II	C43H72O15	828.4871	828.4882	1.3	829.4955 $[M+H]^+$
33	8.11	Acetyl-Rc/Rs1/RS2	C55H92O23	1120.6029	1120.5962	-6.0	1119.5889 $[M-H]^-$
34	8.14	Rd	C48H82O18	946.5501	946.5453	-5.1	945.5380 $[M-H]^-$
35	8.18	Tanshindiol B/Tanshindiol C	C18H16O5	312.0998	312.0996	-0.6	311.0923 $[M-H]^-$
36	8.34	Acetyl-Rb2/Acetyl-Rb3	C55H92O23	1120.6029	1120.5962	-6.0	1119.5889 $[M-H]^-$
37	8.49	Gypenoside XVII	C48H82O18	946.5501	946.5454	-5.0	945.5381 $[M-H]^-$
38	8.52	Tanshinol B*	C18H16O4	296.1049	296.104	-3.0	297.1113 $[M+H]^+$
39	8.63	Kadsuranin	C23H28O6	400.1886	400.1863	-5.7	399.1790 $[M-H]^-$

40	8.86	Pseudo-ginsenoside RC1/Acetyl-gypenoside XVII/Acetyl-Rd	C50H84O19	988.5607	988.5556	-5.2	987.5483 $[M-H]^-$
41	9.06	1,2,6,7,8,9-Hexahydro-1,6,6-trimethyl-3,11-dioxanaphth[2,1-e]azulene-10,12-dione	C19H20O4	312.1362	312.1364	0.6	313.1437 $[M+H]^+$
42	9.28	Tanshinone IIB	C19H18O4	310.1205	310.1206	0.3	311.1279 $[M+H]^+$
43	9.78	Tanshinone VI	C18H16O4	296.1049	296.1043	-2.0	295.0970 $[M-H]^-$
44	9.82	Gomisin D	C28H34O10	530.2152	530.2154	0.4	531.2227 $[M+H]^+$
45	9.91	Gomisin J	C22H28O6	388.1886	388.1873	-3.3	389.1946 $[M+H]^+$
46	10.13	Gomisin O/Epi-gomisin O	C23H28O7	416.1835	416.1845	2.4	417.1918 $[M+H]^+$
47	10.19	1-Oxomiltirone	C19H20O3	296.1412	296.1415	1.0	297.1488 $[M+H]^+$
48	10.66	Tanshinone I	C18H12O3	276.0786	276.0804	6.5	277.0877 $[M+H]^+$
49	10.73	Schisandrol B*	C23H28O7	416.1835	416.1792	-10.3	417.1865 $[M+H]^+$
50	11.11	Danshenxinkun B	C18H16O3	280.1099	280.1102	1.1	281.1175 $[M+H]^+$
51	11.23	Schisandrin B*	C23H28O6	400.1886	400.1889	0.7	401.1962 $[M+H]^+$
52	11.67	Tanshinone IIA*	C19H18O3	294.1256	294.126	1.4	295.1333 $[M+H]^+$
53	11.70	Schisandrin C	C22H24O6	384.1573	384.1619	12.0	383.1546 $[M-H]^-$
54	11.93	Gomisin G	C30H32O9	536.2046	536.2025	-3.9	537.2098 $[M+H]^+$
55	12.25	(-)Gomisin K1/(+) Gomisin K2	C23H30O6	402.2042	402.2047	1.2	403.2120 $[M+H]^+$
56	12.62	1,2-Didehydromiltirone	C19H20O2	280.1463	280.1433	-10.7	281.1506 $[M+H]^+$
57	12.77	Schisantherin A*	C30H32O9	536.2046	536.2024	-4.1	537.2097 $[M+H]^+$
58	12.85	Cryptotanshinone	C19H20O3	296.1412	296.1415	1.0	297.1488 $[M+H]^+$
59	13.20	Schisanhenol	C23H30O6	402.2042	402.2049	1.7	403.2122 $[M+H]^+$
60	14.70	Senkyunolide B/C/E	C12H12O3	204.0786	204.0788	1.0	205.0861 $[M+H]^+$
61	14.90	Schisandrin A*	C24H32O6	416.2199	416.2208	2.2	417.2281

							$[M+H]^+$
62	15.59	Gomisin N	C23H28O6	400.1886	400.1887	0.2	401.1960 $[M+H]^+$

* Compound identified by comparision with the reference standards

Reference

Wang HP, Chen C., Liu Y, Yang HJ, Wu HW, Xiao HB. 2015. Identificationof the chemical constituentsof Chinese medicine Yi-Xin-Shucapsuleby molecular feature orientated precursor ion selection and tandem mass spectrometry structure elucidation. J Sep Sci. 38: 3687-3695.