Electronic Supplementary Material (ESI) for RSC Advances.

Table S1. The identified results of the constituents in rat plasma after oral administration of KXS by UPLC/Q-TOF-MS/MS and multivariate data processing approach.

No	Rt/ min	Compound	Positive (m/z)		Negative (m/z)		Formula	MW(Da)	Fragment ions (m/z)	Origin
1	0.83	Bergapten	—	—	215.0344	0	$C_{12}H_8O_4$	216.0423	215[M-H]$^-$,179[M-H-3C]$^-$, 161[M-H-C_3H_2O]$^-$,89[M-H-$C_7H_{10}O_2$]$^-$	d
2	0.90	Mannose	—	—	179.0556	1.1	$C_6H_{12}O_6$	180.0634	179[M-H]$^-$,161[M-H-H_4O]$^-$,96[M-H-CH_8O_4]$^-$	a
3	0.93	Valine	118.0863	2.9	—	—	$C_5H_{11}NO_2$	117.0790	103[M+H-NH]$^+$,100[M+H-H_2O]$^+$	d
4	0.93	Dimethyl(R)-(+)-malate	—	—	161.0398	5	$C_6H_{10}O_5$	162.0528	148[M+H-CH_3]$^+$,119[M+H-C_2H_4O]$^+$, 161[M-H]$^-$,142[M-H-H_2O]$^-$, 99[M-H-2CH_2OH]$^-$,57[M-H-2CH_2OH-CO-CH_2]$^-$	b
5	1.12	Sucrose	—	—	341.1084	-9.1	$C_{12}H_{22}O_{11}$	342.1162	341[M-H]$^-$,179[M-H-(Glc-H_2O)]$^-$, 161[M-H-Glc]$^-$,119[M-H-(Glc-H_2O)-CO_3]$^-$, 113[M-H-Glc-CH_4O_2]$^-$	a, c
6	1.54	Nicotinic acid	124.0399	-9.7	—	—	$C_6H_5NO_2$	123.0320	124[M+H]$^+$,108[M+H-O]$^+$, 106[M+H-H_2O]$^+$,80[M+H-C_2H_6N]$^+$	a
7	1.62	Benzoic acid	123.0446	1.8	—	—	$C_7H_6O_2$	122.0368	123[M+H]$^+$,108[M+H-O]$^+$	d
8	1.62	Adenine	136.0623	1.2	—	—	$C_5H_5N_5$	135.0545	136[M+H]$^+$,119[M+H-H_3N]$^+$,109[M+H-CHN]$^+$	b

9	1.62	Adenosine	268.1046	1.8	—	—	$C_{10}H_{13}N_5O_4$	267.0968	268[M+H]$^+$,136[M+H-$C_4H_{10}N_3O_2$]$^+$,119[M+H-$C_5H_{13}N_2O_3$]$^+$	a
10	2.41	Sibiricose A1	—	—	547.1663	-1.5	$C_{23}H_{32}O_{16}$	548.1741	547[M-H]$^-$,385[M-H-(Fru-H_2O)]$^-$,367[M-H-Fru]$^-$,325[M-H-$C_{11}H_{10}O_5$]$^-$,223[M-H-Fru-(Glc-2H_2O)]$^-$,205[M-H-Fru-(Glc-H_2O)]$^-$	c
11	2.61	Ethyl benzoylacetate*	193.0821	-2.6	—	—	$C_{11}H_{12}O_3$	192.0786	193[M+H]$^+$,165[M+H-CO]$^+$,150[M+H-CO-CH_3]$^+$,135[M+HCO-2CH_3]$^+$	c
12	2.63	Salicylic acid	—	—	137.0239	-1.9	$C_7H_6O_3$	138.0317	137[M-H]$^-$,108[M-H-2O]$^-$	a
13	2.95	PolygalaxanthoneIII	—	—	567.1332	-5.3	$C_{25}H_{28}O_{15}$	568.1428	569[M+H]$^+$,551[M+H-H_2O]$^+$,317[M+H-Api-$C_4H_6O_3$]$^+$,287[M+H-(Api-H2O)-$C_6H_{14}O_4$]$^+$,567[M-H]$^-$,447[M-H-$C_7H_4O_2$]$^-$,417[M-H-Api]$^-$,345[M-H-Api-$C_3H_4O_2$]$^-$,315[M-H-Api-$C_4H_6O_3$]$^-$,272[M-H-(Api-H_2O)-$C_8H_3O_4$]$^-$,259[M-H-Api-$C_6H_6O_5$]-	c
14	3.62	1-(3,4-Dimethoxyphenyl)ethan-1-one	181.0865	-2.2	—	—	$C_{10}H_{12}O_3$	180.0786	181[M+H]$^+$,166[M+H-CH_3]$^+$,151[M+H-2CH_3]$^+$,121[M+H-CH_3-C_2H_5O]$^+$	c

15	4.42	2-O-Methyl-α-D-glucopyranose*	195.0601	-1.2	—	—	$C_7H_{14}O_6$	194.0790	195[M+H]$^+$,165[M+H-C_2H_3NO-CHN]$^+$, 137[M+H-C_2H_3NO-CH_2O-CHN]$^+$	c
16	4.44	M1*	—	—	257.0838	-3.5	$C_8H_{18}O_9$	258.0784	257[M-H]$^-$,221[M-H-2H_2O]$^-$,179[M-H-2H_2O-$C_2H_6O_3$]$^-$	a
17	4.45	M2*	410.1240	3.4	—	—	$C_{18}H_{19}NO_{10}$	409.1009	410[M+H]$^+$,193[M+H-C_2H_3NO-$C_5H_4O_6$]$^+$, 165[M+H-C_2H_3NO-$C_5H_4O_6$-2CH_2]$^+$	a
18	4.47	M3*	181.0830	-1.1	—	—	$C_{10}H_{12}O_3$	180.0786	181[M+H]$^+$,151[M+H-2CH_3]$^+$,136[M+H-3CH_3]$^+$	d
19	4.48	M4*	298.1275	-5.2	—	—	$C_{14}H_{19}NO_6$	297.1212	298[M+H]$^+$,136[M+H-CHN-$C_{10}H_9N_2O_2$]$^+$, 91[M+H-CHN-$C_{12}H_{14}N_2O_3$]$^+$	d
20	6.31	2-Hydroxybenzonic acid	—	—	137.0239	-4.4	$C_7H_6O_3$	138.0317	137[M-H]$^-$,93[M-H-CO_2]$^-$	c
21	7.59	[(2S)-5-Oxotetrahydro-2-furanyl]methyl benzoate*	221.0785	-1.3	—	—	$C_{12}H_{12}O_4$	220.0736	221[M+H]$^+$,206[M+H-CH_3]$^+$,191[M+H-2CH_3]$^+$, 135[M+H-2CH_3-2CO]$^+$	c
22	7.78	Dibutyl oxalate	—	—	201.1129	-1	$C_{10}H_{18}O_4$	202.1205	201[M-H]$^-$,183[M-H-H_2O]$^-$,139[M-H-C_2H_5-CH_4-OH]$^-$	a
23	7.84	3,4,5-Trimethoxy cinnamic acid	—	—	237.076	7.2	$C_{12}H_{14}O_5$	238.0841	237[M-H]$^-$,197[M-H-C_3H_4]$^-$,193[M-H-CO_2]$^-$	c

					3					
24	12.80	M5*	221.0795	0.9	—	—	$C_8H_{12}O_7$	220.0583	221$[M+H]^+$,206$[M+H-CH_3]^+$,191$[M+H-2CH_3]^+$, 135$[M+H-2CH_3-C_3H_5O]^+$	c
25	13.76	Acoronene	235.1698	1.1	—	—	$C_{15}H_{22}O_2$	234.1620	235$[M+H]^+$,217$[M+H-CH_6]^+$, 189$[M+H-C_3H_{10}]^+$,119$[M+H-C_7H_{16}O]^+$	d
26	13.81	M6*	373.1637	3.3	—	—	$C_{17}H_{24}O_9$	372.1420	373$[M+H]^+$,355$[M+H-H_2O]^+$,151$[M+H-C_5H_8O_6-2CH_3-CH]^+$	d
27	14.97	Poricoic acid H	—	—	499.3424	-0.8	$C_{31}H_{48}O_5$	500.3502	499$[M-H]^-$,481$[M-H-H_2O]^-$, 419$[M-H-C_6H_8]^-$,389$[M-H-C_7H_{10}-O]^-$	b
28	15.76	Poricoic acid G	—	—	485.3267	-3.5	$C_{30}H_{46}O_5$	486.3345	487$[M+H]^+$,407$[M+H-H_2O-CH_2O_2-CH_4]^+$, 201$[M+H-C_{19}H_{26}O_2]^+$,159$[M+H-C_8H_{12}O_2-C_{11}H_{24}O_2]^+$, 485$[M-H]^-$,425$[M-H-CH_4-CO_2]^-$, 387$[M-H-C_6H_9-OH]^-$,369$[M-H-C_6H_{12}-CO_2]^-$	b
29	17.59	Gomisin A	417.1875	1.2	—	—	$C_{23}H_{28}O_7$	416.1835	417$[M+H]^+$,224$[M+H-C_{11}H_{13}O_3]^+$, 193$[M+H-C_{12}H_{16}O_4]^+$,165$[M+H-C_{14}H_{20}O_4]^+$	a
30	17.62	3β,16α-Dihydroxylanosta-7,9(11),24-trien-21-oic acid	471.3474	-5.9	—	—	$C_{30}H_{46}O_4$	470.3396	471$[M+H]^+$,453$[M+H-H_2O]^+$, 407$[M+H-CH_2O_2-H_2O]^+$,313$[M+H-C_8H_{12}O_2-H_2O]^+$, 469[M-H]-,407$[M-H-CO_2-H_2O]^-$,	b

									367[M-H-C_6H_{12}-H_2O]$^-$	
31	17.66	Poricoic acid B	—	—	483.3111	-1.9	$C_{30}H_{44}O_5$	484.3189	483[M-H]$^-$,439[M-H-CO_2]$^-$, 409[M-H-CO_2-2CH_2]$^-$,367[M-H-2CO_2-2CH_2]$^-$	b
32	17.90	6,7-Dehydroporicoic acid H	—	—	497.3267	-2.6	$C_{31}H_{46}O_5$	498.3345	497[M-H]$^-$,479[M-H-H_2O]$^-$, 453[M-H-2CH_3-CH_2]$^-$,423[M-H-C_2H_6-CO_2]$^-$	b
33	17.97	16-Deoxyporicoic acid B	—	—	467.3161	4.7	$C_{30}H_{44}O_4$	468.3240	469[M+H]$^+$,451[M+H-H_2O]$^+$, 311[M+H-$C_8H_{12}O_2$-H_2O]$^+$,293[M+H-$C_8H_{12}O_2$-CH_8O]$^+$	b
34	18.04	Tumulosic acid	—	—	485.3631	2.3	$C_{31}H_{50}O_4$	486.3709	467[M-H]$^-$,423[M-H-CO_2]$^-$, 407[M-H-CO_2-CH_4]$^-$,374[M-H-C_7H_9]$^-$ 485[M-H]$^-$,441[M-H-CO_2]$^-$,423[M-H-CO_2-H_2O]$^-$	b
35	18.09	cis/trans-Methylisoeugenol	179.0726	6.7	—	—	$C_{11}H_{14}O_2$	178.0994	179[M+H]$^+$,165[M+H-CH_2]$^+$, 151[M+H-2CH_2]$^+$,121[M+H-2CH_3-2CH-2H]$^+$	d
36	18.19	3β-Hydroxy-16α-acetoxy-lanosta-7,9(11),24-trien-21-oic acid	513.3580	-1.9	—	—	$C_{32}H_{48}O_5$	512.3502	513[M+H]$^+$,495[M+H-H_2O]$^+$, 453[M+H-$COCH_3$-OH]$^+$, 355[M+H-$C_8H_{12}O_2$-H_2O]$^+$, 295[M+H-$C_8H_{12}O_2$-CH_4O_2-H_2O]$^+$,	b

37	18.31	Daedaleanic acid A	—	—	481.3318	-3.7	$C_{31}H_{46}O_4$	482.3396	483[M+H]$^+$,465[M+H-H_2O]$^+$, 419[M+H-C_3H_{10}-H_2O]$^+$,309[M+H-$C_9H_{16}O_2$-H_2O]$^+$, 481[M-H]$^-$,437[M-H-CO_2]$^-$, 421[M-H-C_3H_8-O]$^-$,403[M-H-C_3H_8-2HO]$^-$	b
38	18.48	(5ξ,20S)-24-Methylene-3-oxolanosta-7,9(11)-dien-21-oic acid*	—	—	465.3127	-1.9	$C_{31}H_{46}O_3$	466.3447	465[M-H]$^-$,421[M-H-CO_2-2H_2O]$^-$, 403[M-H--2CH_3-CH_2-2H_2O]$^-$	b
39	18.49	Dehydroeburiconic acid	467.3525	0.2	—	—	$C_{31}H_{46}O_3$	466.3447	467[M+H]$^+$,449[M+H-H_2O]$^+$, 311[M+H-$C_9H_{16}O_2$]$^+$,293[M+H-$C_{10}H_{22}O_2$]$^+$	b
40	18.50	Dehydrotu-mulosic acid	—	—	483.3474	-2.3	$C_{31}H_{48}O_4$	484.3553	483[M-H]$^-$,437[M-H-CH_2O_2]$^-$, 421[M-H-CO_2-H_2O]$^-$,337[M-H-C_6H_{12}-CO_2-H_2O]$^-$	b
41	18.71	2,6-Di-sec-butyl-4-methylphenol	221.1905	-7.2	—	—	$C_{15}H_{24}O$	220.1827	221[M+H]$^+$,203[M+H-CH_6]$^+$, 193[M+H-CH_3-CH]$^+$,133[M+H-CH_3-CH-4CH_3]$^+$	a
42	19.99	Pachymic acid	—	—	527.3737	-0.8	$C_{33}H_{52}O_5$	528.3815	527[M-H]$^-$,483[M-H-C_2H_4O]$^-$, 465[M-H-C_2H_4O-H_2O]$^-$,221[M-H-$C_{18}H_{26}O_4$]$^-$	b

Note: a: Ginseng Radix; b: Poria; c: Polygalae Radix; d: Acori Tatarinowii Rhizoma; * means the metabolites;
42 components were identified by pattern recognition methods, 21 of them were detected in positive ion mode and others were detected in negative mode.

Table S2. The identified results of the constituents in rat plasma after oral administration of KXS by Metabolynx software.

No	Rt/ min	Compound	Positive (m/z)		Negative (m/z)		Formula	MW(Da)	Fragment ions (m/z)	Origin
Ⅰ	2.07	3-(2-furyl)-3-oxopropanenitrile	136.0544	0.9	—	—	$C_7H_5NO_2$	135.0320	136$[M+H]^+$,119$[M+H-OH]^+$,109$[M+H-CHN]^+$	d
Ⅱ	2.27	M7	—	—	307.0481	3.7	$C_{14}H_{12}O_8$	308.0532	307$[M-H]^-$,247$[M-H-C_2H_4O_2]^-$,227$[M-H-C_2H_8O_3]^-$	c
Ⅲ	2.61	N-(2,5-Dimethoxyphenyl)-2-methoxyacetamide	226.1137	2.7	—	—	$C_{11}H_{15}NO_4$	225.1001	226$[M+H]^+$,210$[M+H-CH_3]^+$,167$[M+H-CH_3N-2CH_3]^+$, 152$[M+H-CH_3N-3CH_3]^+$	d
Ⅳ	2.91	M8	—	—	289.0375	2.1	$C_{14}H_{10}O_7$	290.0427	289$[M-H]^-$,274$[M-H-CH_3]^-$,263$[M-H-CH_3-2CH]^-$	c
Ⅴ	9.25	M9	—	—	273.0432	4.6	$C_{10}H_{10}O_9$	274.0324	273$[M-H]^-$,193$[M-H-Glc]^-$,163$[M-H-Glc-CH_2O]^-$, 135$[M-H-Glc-CH_2O-C_2H_4]^-$	a
Ⅵ	18.33	M10	—	—	507.3721	4.5	$C_{33}H_{48}O_4$	508.3553	507$[M-H]^-$,461$[M-H-2CH_2-H_2O]^-$	b
Ⅶ	20.60	M11	299.1357	4.6	—	—	$C_{14}H_{18}O_7$	298.1053	299$[M+H]^+$,284$[M+H-CH_3]^+$, 271$[M+H-CO]^+$,134$[M+H-C_5H_{10}O_5-CH_3]^+$	c

Note: a: Ginseng Radix; b: Poria; c: Polygalae Radix; d: Acori Tatarinowii Rhizoma; three metabolites were identified in positive ion mode and four metabolites were identified in negative ion mode. Glc: β-D-glucose; Xyl: β-D-xylose; Fru: β-D-fructose; Api:β-D-Apiose.