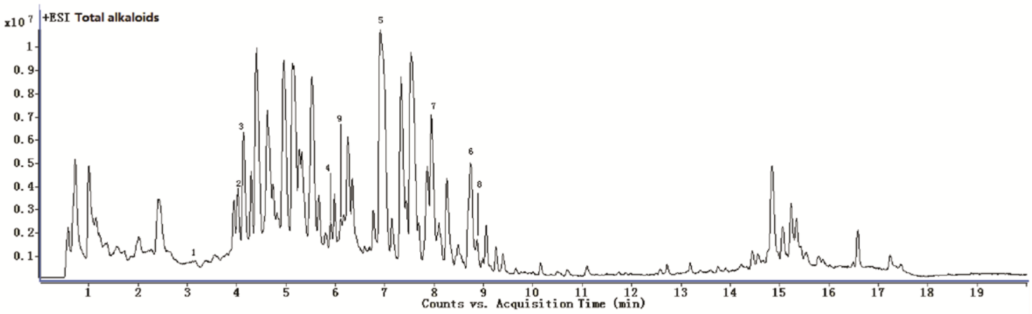
A



B

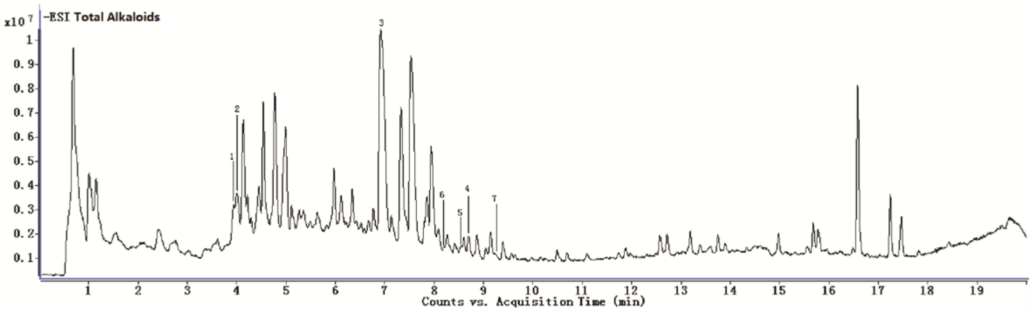


Fig. S1 Total ion chromatograms (TICs) for total alkaloids in positive mode (A) and negative mode (B). The peak numbers represent the same meanings as in Supplementary Information Table S2

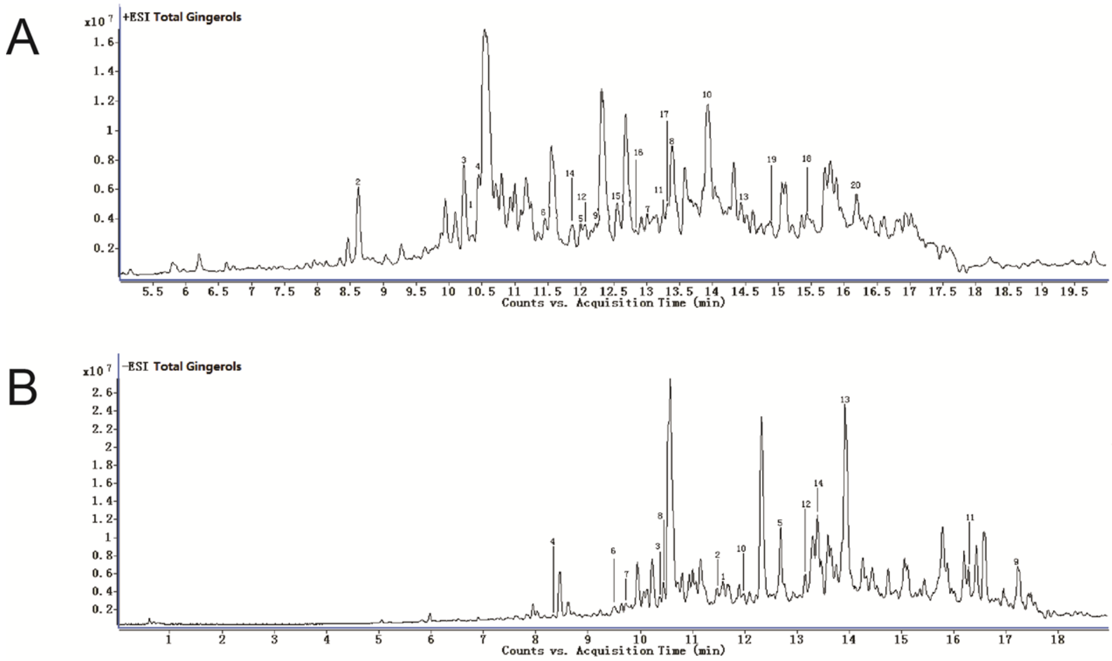


Fig. S2 Total ion chromatograms (TICs) for total gingerols in positive mode (A) and negative mode (B). The peak numbers represent the same meanings as in Supplementary Information Table S3

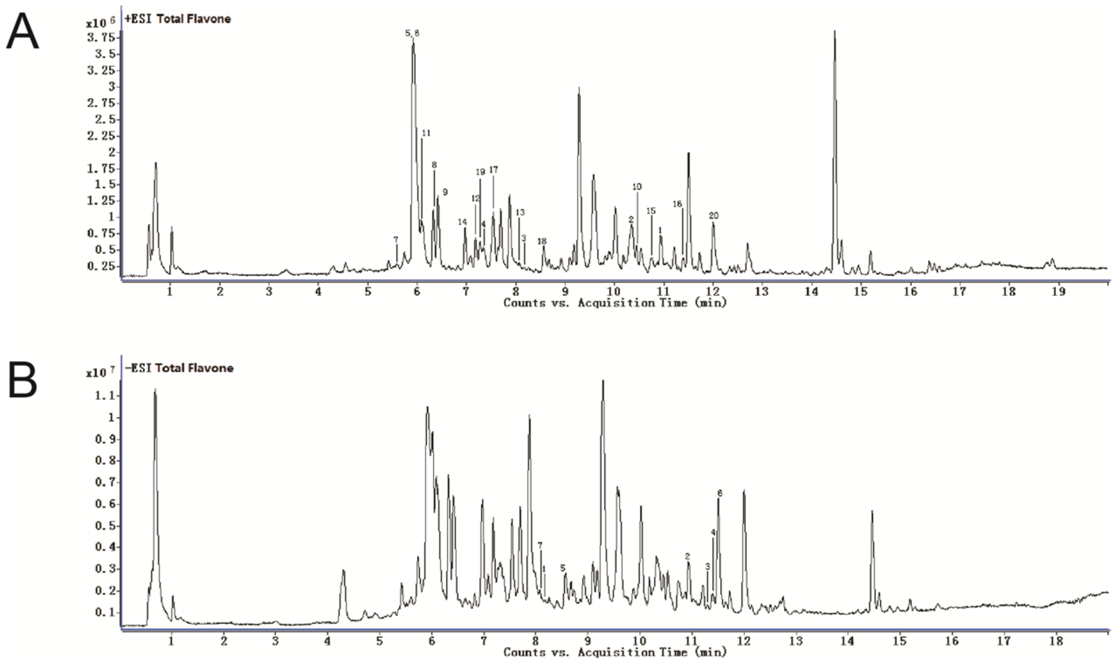


Fig. S3 Total ion chromatograms (TICs) for total flavones in positive mode (A) and negative mode (B). The peak numbers represent the same meanings as in Supplementary Information Table S4

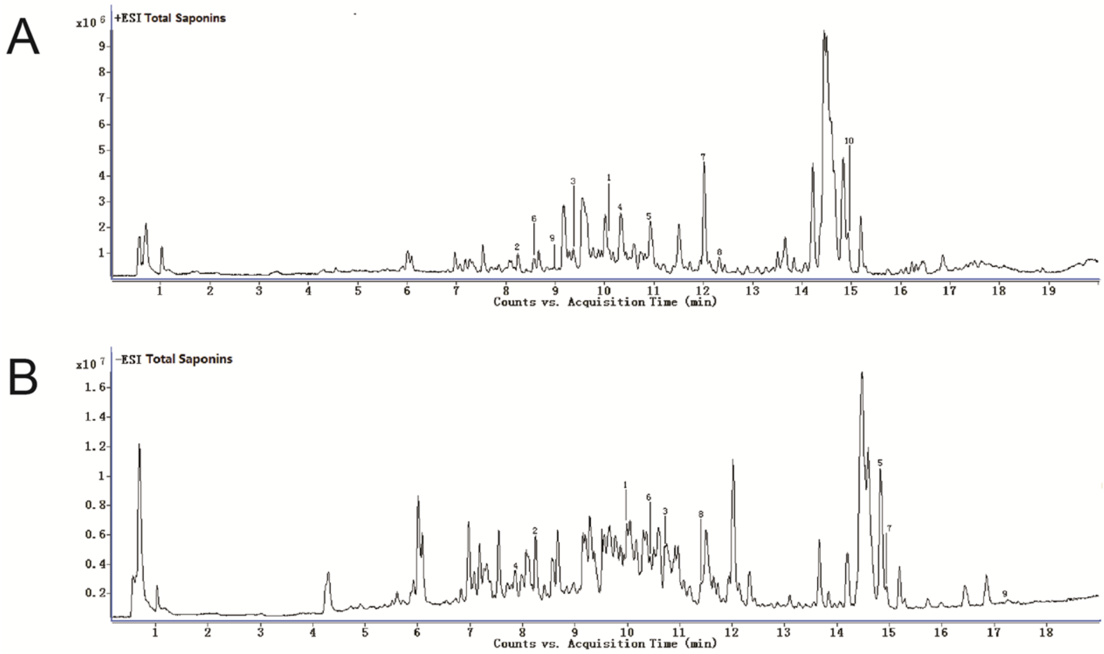


Fig. S4 Total ion chromatograms (TICs) for total saponins in positive mode (A) and negative mode (B). The peak numbers represent the same meanings as in Supplementary Information Table S5

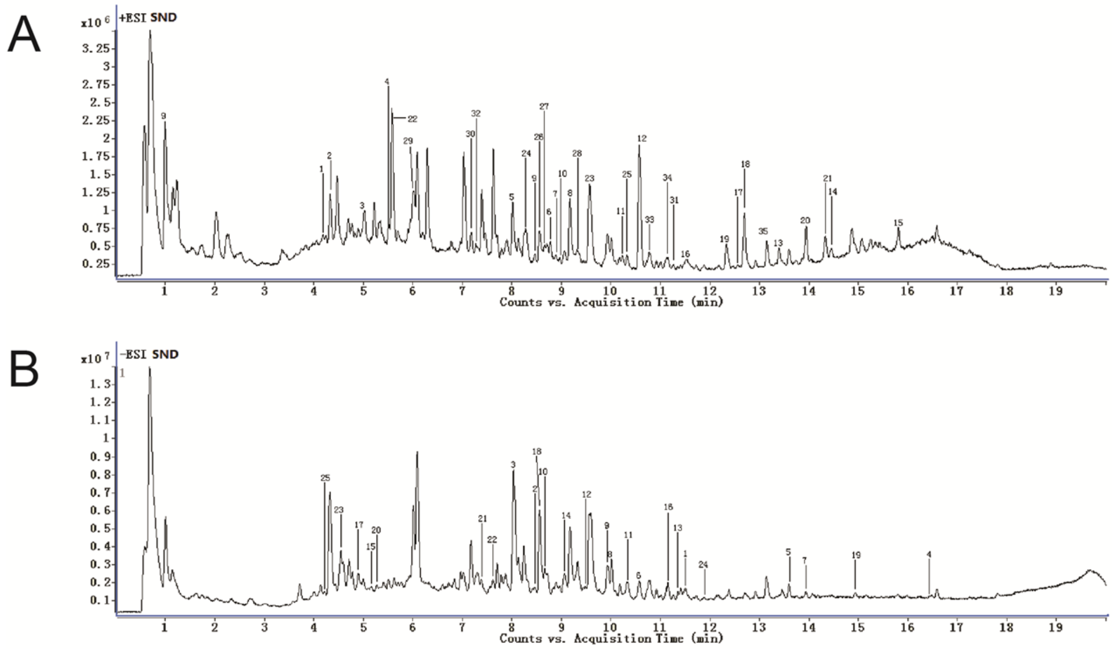


Fig. S5 Total ion chromatograms (TICs) for *SND* in positive mode (A) and negative mode (B). The peak numbers represent the same meanings as in Supplementary Information Table S6

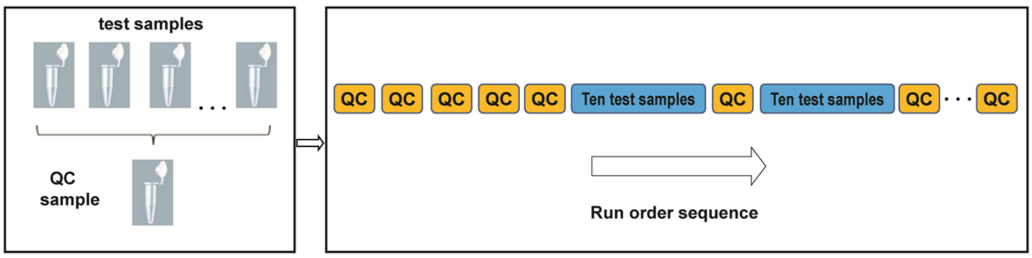


Fig. S6 Flow chart of the processing of QC samples.

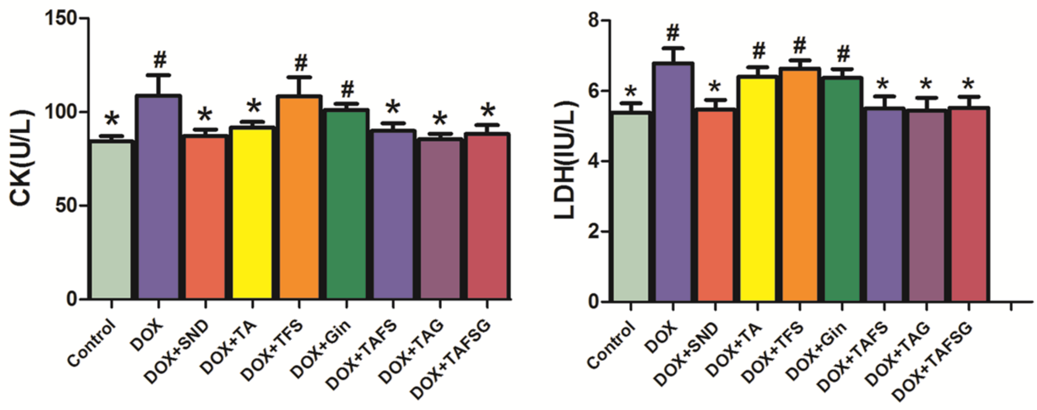


Fig. S7 LDH and CK levels in nine groups,* p<0.05 vs. DOX group, # p<0.05 vs. Control group.

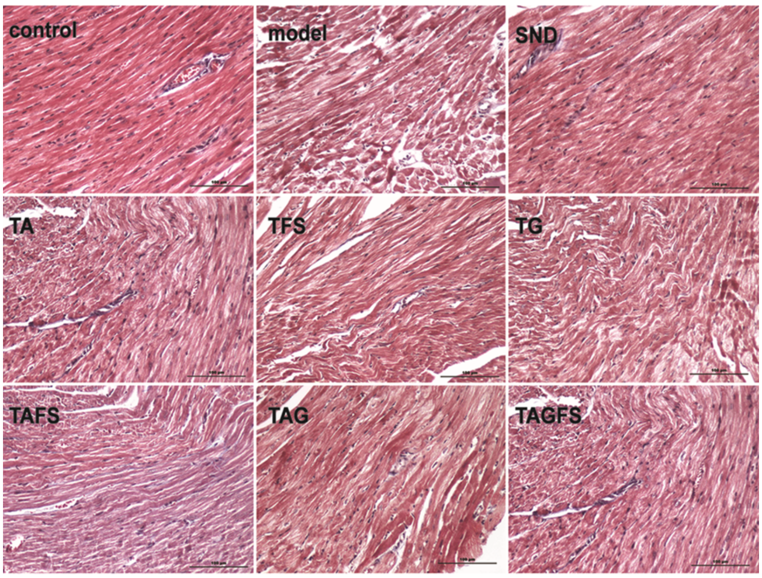


Fig. S8 Cardiac muscle tissue of mice in microscope(magnification×200).

Table S1. Detailed information of Compounds in alkaloids (S), gingerols (J), flavones (H), saponins (Z)

NO.	Composition	Compounds
S1	C22H33NO5	Hokbusine B
S2	C22H35NO4	Karakoline
S3	C24H39NO9	Mesaconine
S4	C23H37NO6	Senbusine A
S5	C23H37NO6	Senbusine B
S6	C23H37NO5	Talatizidine
S7	C25H41NO9	Aconine
S8	C24H39NO8	Hypaconine
S9	C24H39NO7	Fuziline
S10	C24H39NO6	Neoline
S11	C25H41NO7	Bikhaconine
S12	C24H39NO5	Talatisamine
S13	C26H41NO7	14-O-acetylneoline
S14	C26H41NO6	14-O-acetyltalatizamine
S15	C31H43NO10	Benzoylmesaconine
S16	C32H45NO10	Benzoylaconine
S17	C31H43NO9	Benzoylhypaconine
S18	C35H49NO12	Jesaconitine
S19	C33H45NO12	Beiwutine

S20	C32H45NO9	Benzoyldeoxyaconitine
S21	C33H45NO11	Mesaconitine
S22	C34H47NO12	Aconifine
S23	C33H45NO7	14-O-cinnamoylneoline
S24	C32H45NO8	14-O-anisoylneoline
S25	C34H47NO11	Aconitine
S26	C33H45NO10	Hypaconitine
S27	C33H45NO9	Isodelphinine
S28	C34H47NO10	Deoxyaconitine
S29	C35H49NO9	Foresaconitne
S30	C35H49NO10	Crassicauline A
S31	C10H13NO2	Salsolinol
S32	C11H18NO2	Coryneine
S33	C22H35NO5	Chuanfumine
S34	C22H33NO4	Karakanine
S35	C22H31NO3	Songorine
S36	C20H24NO4	Fuzitine
S37	C27H31NO5	Ignavine
S38	C22H29NO3	Songoramine
S39	C16H17NO3	Higenamine
J1	C15H24O4	[4]-Gingerdiol
J2	C17H28O4	[6]-Gingerdiol

J3	$C_{19}H_{32}O_4$	[8]-Gingerdiol
J4	$C_{21}H_{36}O_4$	[10]-Gingerdiol
J5	$C_{16}H_{24}O_4$	Methoxy-[4]-gingerol
J6	$C_{18}H_{28}O_4$	Methoxy-[6]-gingerol
J7	$C_{20}H_{32}O_4$	Methoxy-[8]-gingerol
J8	$C_{22}H_{36}O_4$	Methoxy-[10]-gingerol
J9	$C_{17}H_{24}O_4$	[6]-Gingerdione
J10	$C_{19}H_{28}O_4$	[8]-Gingerdione
J11	$C_{21}H_{32}O_4$	[10]-Gingerdione
J12	$C_{23}H_{36}O_4$	[12]-Gingerdione
J13	$C_{18}H_{26}O_3$	1-Dehydro-[6]-gingerdione
J14	$C_{19}H_{26}O_4$	1-Dehydro-[8]-gingerdione
J15	$C_{21}H_{30}O_4$	1-Dehydro-[10]-gingerdione
J16	$C_{23}H_{34}O_4$	1-Dehydro-[12]-gingerdione
J17	$C_{17}H_{24}O_5$	Acetoxy-[4]-gingerol
J18	$C_{19}H_{28}O_5$	Acetoxy-[6]-gingerol
J19	$C_{20}H_{30}O_5$	Methyl acetoxy-[6]-gingerol
J20	$C_{21}H_{32}O_5$	Acetoxy-[8]-gingerol
J21	$C_{23}H_{36}O_5$	Acetoxy-[10]-gingerol
J22	$C_{17}H_{26}O_3$	[6]-Paradol
J23	$C_{18}H_{28}O_3$	Methyl-[6]-paradol
J24	$C_{19}H_{30}O_3$	[8]-Paradol

J25	$C_{21}H_{34}O_3$	[10]-Paradol
J26	$C_{17}H_{26}O_5$	3-Acetoxy-[4]-gingerdiol
J27	$C_{19}H_{30}O_5$	3-Acetoxy-[6]-gingerdiol
J28	$C_{20}H_{32}O_5$	Methyl-3-acetoxy-[6]-gingerdiol
J29	$C_{17}H_{24}O_4$	6-Hydroxy-[6]-shogaol
J30	$C_{19}H_{28}O_4$	6-Hydroxy-[8]-shogaol
J31	$C_{21}H_{32}O_4$	6-Hydroxy-[10]-shogaol
J32	$C_{15}H_{20}O_3$	[4]-Shogaol
J33	$C_{16}H_{22}O_3$	Methyl-[4]-shogaol
J34	$C_{16}H_{22}O_2$	Demethoxy-[6]-shogaol
J35	$C_{17}H_{24}O_3$	[6]-Shogaol
J36	$C_{17}H_{22}O_4$	Methyl-[6]-shogaol
J37	$C_{19}H_{28}O_3$	[8]-Shogaol
J38	$C_{20}H_{30}O_3$	Methyl-[8]-shogaol
J39	$C_{21}H_{32}O_3$	[10]-Shogaol
J40	$C_{23}H_{36}O_3$	[12]-Shogaol
J41	$C_{19}H_{28}O_6$	Diacetoxy-[4]-gingerdiol
J42	$C_{20}H_{30}O_6$	Methyl diacetoxy-[4]-gingerdiol
J43	$C_{21}H_{32}O_6$	Diacetoxy-[6]-gingerdiol
J44	$C_{22}H_{34}O_6$	Methyl diacetoxy-[6]-gingerdiol
J45	$C_{23}H_{36}O_6$	Diacetoxy-[8]-gingerdiol
J46	$C_{24}H_{38}O_6$	Methyl diacetoxy-[8]-gingerdiol

J47	C25H40O6	Diacetoxy-[10]-gingerdiol
J48	C26H42O6	Methyl diacetoxy-[10]-gingerdiol
J49	C17H24O4	1-Dehydro-[6]-gingerol
J50	C17H26O4	1-Hydroxy-[6]-paradol
J51	C15H22O4	[4]-Gingerol
J52	C16H24O4	Methyl-[4]-gingerol
J53	C16H24O3	Demethoxy-[6]-gingerol
J54	C17H26O4	[6]-Gingerol
J55	C18H28O4	Methyl-[6]-gingerol
J56	C19H30O4	[8]-Gingerol
J57	C20H32O4	Methyl-[8]-gingerol
J58	C21H34O4	[10]-Gingerol
J59	C22H36O4	Methyl-[10]-gingerol
J60	C23H38O4	[12]-Gingerol
J61	C17H24O4	6-Dehydro-[6]-gingerol
J62	C17H28O3	Dihydro-[6]-paradol
J63	C16H24O2	3-Dihydro-[6]-demethoxyshogaol
J64	C21H32O4	1-Dehydro-3-dihydro-[10]-gingerdione
Z1	C42H62O16	Glycyrrhizic acid
Z2	C48H72O21	Licoricesaponin A3
Z3	C50H76O21	Licoricesaponin D3
Z4	C42H64O15	Licoricesaponin B2

Z5	$C_{42}H_{62}O_{17}$	Licoricesaponin G2
Z6	$C_{42}H_{64}O_{16}$	Licoricesaponin J2
Z7	$C_{30}H_{46}O_4$	18b-Glycyrrhetinic acid
Z8	$C_{32}H_{48}O_6$	22b-Acetyoxy glybric acid
Z9	$C_{30}H_{44}O_4$	3-Oxo-glycyrrhizic acid
Z10	$C_{32}H_{48}O_5$	3-Acetyl glycyrrhetinic acid
Z11	$C_{31}H_{48}O_5$	Methyl-18-hydroxy glycyrrhetate
Z12	$C_{31}H_{48}O_4$	Methyl glycyrrhetate
Z13	$C_{31}H_{48}O_5$	Methyl 24-hydroxy glycyrrhetate
Z14	$C_{30}H_{46}O_5$	24-Hydroxy glycyrrhetic acid
Z15	$C_{42}H_{62}O_{16}$	Uralsaponin B
Z16	$C_{42}H_{62}O_{16}$	Glycyrrhizin
Z17	$C_{31}H_{44}O_6$	Glyuranolide
Z18	$C_{42}H_{60}O_{16}$	Licoricesaponin E2
Z19	$C_{48}H_{72}O_{19}$	Licoricesaponin F3
Z20	$C_{31}H_{44}O_5$	3b-Formyl glabrolide
Z21	$C_{30}H_{44}O_5$	24-Hydroxy glabrolide
Z22	$C_{30}H_{44}O_4$	Glabrolide
Z23	$C_{42}H_{62}O_{15}$	Licoricesaponin C2
Z24	$C_{42}H_{62}O_{16}$	Licoricesaponin K2
Z25	$C_{31}H_{48}O_4$	Methyl 3b, 24-dihygroxy olean-11,13(18)-diene 30-O ate

Z26	$C_{30}H_{46}O_3$	3b-Hydroxy-olean-9(11), 12-dien-30-oic acid
Z27	$C_{30}H_{46}O_3$	Betulic acid
Z28	$C_{30}H_{44}O_4$	Uralenolide
H1	$C_{17}H_{14}O_6$	Kumatakenin A
H2	$C_{20}H_{18}O_4$	Licoflavone
H3	$C_{21}H_{20}O_7$	Uralenol-3-methylether
H4	$C_{21}H_{20}O_7$	Uralene
H5	$C_{17}H_{14}O_7$	Quercitin-3,3'-dimethyleter
H6	$C_{20}H_{18}O_6$	Gancaonin O
H7	$C_{15}H_{10}O_4$	Kumatakenin B
H8	$C_{20}H_{18}O_7$	Uralenol
H9	$C_{20}H_{18}O_7$	Neouralenol
H10	$C_{27}H_{30}O_{16}$	Rutin
H11	$C_{15}H_{10}O_7$	Quercetin
H12	$C_{21}H_{20}O_{12}$	Isoquercetin
H13	$C_{27}H_{30}O_{15}$	Kaempferin -3-O-rutinoside
H14	$C_{21}H_{20}O_{11}$	Quercitrin
H15	$C_{28}H_{32}O_{16}$	Isorhamnetin-3-O- rutinoside
H16	$C_{21}H_{22}O_5$	Licobenzofuran
H17	$C_{20}H_{18}O_7$	Gancaonin P
H18	$C_{20}H_{20}O_6$	Uralenin

H19	C15H12O4	Pinocembrin
H20	C15H12O4	Liquiritigenin
H21	C21H22O9	Liquiritin
H22	C20H20O5	Cyclolicoflavanone
H23	C27H32O14	Liquiritigenin-7,4'-diglucosid
H24	C26H30O13	Lliquiritigenin-4'-apiosyl (1-2)-glucoside
H25	C25H28O6	Gancaonin E
H26	C21H22O4	Licochalcone A
H27	C16H14O5	Licochalcone B
H28	C16H14O4	Echinatin
H29	C15H12O4	Isoliquiritigenin
H30	C21H22O8	Neochalcoside
H31	C20H22O3	Glepidotin C I
H32	C20H22O4	Glepidotin C II
H33	C26H30O13	Neolicuroside
H34	C16H12O4	Formononetin
H35	C22H22O6	Licoricone
H36	C22H22O9	Ononin
H37	C21H20O5	Gancaonin A
H38	C21H20O6	Gancaonin B
H39	C20H18O5	Gancaonin C

H40	C21H20O7	Gancaonin D
H41	C20H18O6	Gancaonin L
H42	C21H20O5	Gancaonn M
H43	C21H20O6	Gancaonin N
H44	C26H32O5	Licoricidin
H45	C27H34O5	Licorisoflavan A
H46	C26H32O5	Licorisoflavan B
H47	C20H20O4	Glabridin
H48	C21H18O6	Glycyrol
H49	C21H18O6	Neoglycyrol
H50	C21H18O6	Noglycyrolisomer
H51	C22H20O6	5-O-Methylglycyrol
H52	C21H16O6	Isoglycyrol
H53	C15H8O5	Coumestrol
H54	C21H20O6	Glycycoumarin
H55	C22H22O6	Glycyrin

Table S2. Compounds identified from total alkaloids in *Aconitum carmichaili*

Labels	**Compounds**	**Retention time(min)**	**M±X**	**m/z(expected)**	**m/z(experimental)**
ESI(+)					
1	Karakoline	3.153	+H	378.2639	378.2648
2	Talatizidine	4.02	+H	408.2744	408.2747
3	Hypaconine	4.142	+H	470.2748	470.2755
4	14-O-acetylneoline	5.908	+H	480.2956	480.2937
5	Benzoylhypaconine	6.922	+H	574.3011	574.3016
6	14-O-anisoylneoline	8.705	+H	572.3218	572.3242
7	Aconitine	7.912	+H	646.3222	646.3249
8	Isodelphinine	8.877	+H	600.3167	600.315
9	Songoramine	6.105	+H	356.222	356.2234
10	Mesaconitine	7.47	+H	632.3065	632.3072
11	Aconifine	7.454	+H	662.3171	662.3191
12	Deoxyaconitine	7.822	+H	630.3273	630.328
13	Salsolinol	2.474	+NH4	197.1285	197.1285
14	Chuanfumine	2.471	+Na	416.2407	416.2405
15	Karakanine	5.393	+H	376.2482	376.2495
16	Ignavine	5.9	+Na	472.2094	472.2092
17	Bikhaconine	5.9	+H	468.2956	468.2946
18	Neoline	5.328	+Na	460.267	460.2663

19	Jesaconitine	7.797	+H	676.3328	676.3343
ESI(-)					
1	Karakoline	3.938	+HCOO	422.2548	422.2564
1	Senbusine A	3.938	-H	422.2548	422.2564
1	Senbusine B	3.938	-H	422.2548	422.2564
2	Hypaconine	4.028	-H	468.2603	468.2615
3	Benzoylmesaconine	6.922	-H	588.2814	588.2843
4	14-O-anisoylneoline	8.696	+HCOO	616.3127	616.3147
5	Deoxyaconitine	8.541	-H	628.3127	628.3144
6	Aconitine	8.206	-H	644.3076	644.3091
7	Crassicauline A	9.277	-H	642.3284	642.3288
8	Mesaconine	3.962	-H	484.2552	484.2558
9	Aconine	5.32	-H	498.2709	498.2729
10	Fuziline	5.32	+HCOO	498.2709	498.2726
11	Neoline	5.148	+HCOO	482.2759	482.2772
12	Benzoylaconine	7.437	-H	602.2971	602.299
13	Aconifine	8.32	+Cl	696.2792	696.2809
14	Songorine	5.859	-H	356.2231	356.2243
15	Hokbusine B	4.077	-H	390.2286	390.2288
16	Benzoylhypaconine	7.437	-H	572.2865	572.2876
17	Jesaconitine	8.001	-H	674.3182	674.3201
18	Benzoyldeoxyaconitine	6.17	-H	586.3022	586.3031

19	Isodelphinine	8.018	-H	598.3022	598.3012

Table S3. Compounds identified from total gingerols in *rhizoma zingiberis*

Labels	Compounds	Retention time(min)	M±X	m/z (expected)	m/z (experimental)
ESI(+)					
1	Demethoxy-[6]-shogaol	10.37	+H	247.1693	247.1686
2	[4]-Gingerol	8.62	+Na	289.1410	289.1421
3	[6]-Paradol	10.223	+H	279.1955	279.1966
4	1-Hydroxy-[6]-paradol	10.443	+H	295.1904	295.1908
4	[6]-Gingerol	10.443	+H	295.1904	295.1908
5	[8]-Paradol	11.989	+H	307.2268	307.2269
6	Methyl-[6]-gingerol	11.441	+Na	331.1880	331.1895
6	Methoxy-[6]-gingerol	11.441	+Na	331.1880	331.1895
7	Methyl-[8]-shogaol	13.011	+NH4	336.2533	336.2545
8	6-Hydroxy-[8]-shogaol	13.387	+H	321.206	321.2069
8	[8]-Gingerdione	13.387	+H	321.206	321.2069
9	[8]-Gingerol	12.226	+H	323.2217	323.2226
10	[10]-Shogaol	13.935	+H	333.2424	333.2438
11	Methoxy-[8]-gingerol	13.264	+Na	359.2193	359.2195
11	Methyl-[8]-gingerol	13.264	+Na	359.2193	359.2195
12	3-Acetoxy-[6]-gingerdiol	12.054	+Na	361.1985	361.1992
13	[10]-Gingerdione	14.434	+NH4	366.2639	366.2651
13	6-Hydroxy-[10]-shogaol	14.434	+NH4	366.2639	366.2651

13	1- Dehydro-3-dihydro-[10]-gingerdione	14.434	+NH4	366.2639	366.2651
14	Diacetoxy-[4]-gingerdiol	11.858	+Na	375.1778	375.1794
15	Methyl-3-acetoxy-[6]-gingerdiol	12.553	+NH4	370.2588	370.2591
16	Methyl diacetoxy-[4]-gingerdiol	12.831	+Na	389.1935	389.1931
17	1-Dehydro-[12]-gingerdione	13.322	+H	375.2530	375.2515
18	[12]-Gingerol	15.431	+Na	401.2662	401.2674
19	Acetoxy-[10]-gingerol	14.891	+NH4	410.2901	410.2902
20	Diacetoxy-[10]-gingerdiol	16.175	+Na	459.273	459.2727
27	Methyl-[4]-shogaol	9.683	+H	263.1642	263.1646
28	Demethoxy-[6]-gingerol	10.37	+H	265.1798	265.1795
29	Dihydro-[6]-paradol	13.33	+NH4	298.2377	298.2378
30	1-Dehydro-[6]-gingerdione	13.698	+H	291.1955	291.1954
31	Methyl-[6]-shogaol	11.147	+Na	313.1410	313.1411
32	6-Hydroxy-[6]-shogaol	13.305	+H	293.1747	293.1754
33	1-Dehydro-[6]-gingerol	13.305	+H	293.1747	293.1754
34	[6]-Gingerdione	13.305	+H	293.1747	293.1754
35	6-Dehydro-[6]-gingerol	13.305	+H	293.1747	293.1754

36	Methyl-[6]-paradol	10.901	+H	293.2111	293.2113
37	[6]-Gingerdiol	10.223	+Na	319.1880	319.1895
38	[8]-Shogaol	14.344	+Na	327.1931	327.1945
39	Acetoxy-[4]-gingerol	10.672	+Na	331.1516	331.1515
40	3-Acetoxy-[4]-gingerdiol	7.157	+H	311.1853	311.1857
41	1-Dehydro-[8]-gingerdione	10.231	+H	319.1904	319.1894
42	[10]-Paradol	13.33	+H	335.2581	335.2584
43	Acetoxy-[6]-gingerol	12.373	+Na	359.1829	359.1846
44	1-Dehydro-[10]-gingerdione	14.246	+Na	369.2036	369.2038
45	Methyl acetoxy-[6]-gingerol	13.215	+NH4	368.2431	368.2444
46	[10]-Gingerol	13.845	+H	351.2530	351.2547
47	Acetoxy-[8]-gingerol	13.886	+Na	387.2142	387.2142
48	[12]-Gingerdione	14.401	+H	377.2686	377.2685
49	Methyl diacetoxy-[8]-gingerdiol	15.734	+NH4	440.3007	440.2997
50	[4]-Shogaol	10.86	+H	249.1485	249.1489
ESI（-）					
1	[4]-Shogaol	11.573	-H	247.134	247.1347
2	Methyl-[4]-shogaol	11.475	-H	261.1496	261.15

3	Demethoxy-[6]-gingerol	10.371	-H	263.1653	263.1662
3	3-Acetoxy-[4]-gingerdiol	10.371	+HCO O	309.1707	309.1719
4	[4]-Gingerdiol	8.335	-H	267.1602	267.1607
5	[6]-Shogaol	12.693	-H	275.1653	275.166
6	Methoxy-[4]-gingerol	9.521	-H	279.1602	279.1608
6	Methyl-[4]-gingerol	9.521	-H	279.1602	279.1608
7	[6]-Gingerdione	9.717	-H	291.1602	291.1615
7	6-Hydroxy-[6]-shogaol	9.717	-H	291.1602	291.1615
7	1-Dehydro-[6]-gingerol	9.717	-H	291.1602	291.1615
7	6-Dehydro-[6]-gingerol	9.717	-H	291.1602	291.1615
8	1-Hydroxy-[6]-paradol	10.453	+HCO O	339.1813	339.1826
8	[6]-Gingerol	10.453	+HCO O	339.1813	339.1826
9	[8]-Gingerdione	17.223	-H	319.1915	319.1919
9	6-Hydroxy-[8]-shogaol	17.223	-H	319.1915	319.1919
10	[8]-Gingerdiol	11.99	-H	323.2228	323.2233
11	[10]-Shogaol	16.283	-H	331.2279	331.2286
12	[10]-Gingerdione	13.151	-H	393.2283	393.2295
12	6-Hydroxy-[10]-shogaol	13.151	-H	393.2283	393.2295
12	1-Dehydro-3-dihydro-	13.151	-H	393.2283	393.2295

	[10]- gingerdione				
13	[10]-Gingerol	13.936	+HCO O	395.2439	395.2452
14	Acetoxy-[8]-gingerol	13.388	-H	363.2177	363.2165
24	Dihydro-[6]-paradol	12.767	-H	281.2122	281.213
25	1-Dehydro-[6]- gingerdione	12.702	-H	289.1809	289.1797
26	Methyl-[6]-paradol	11.59	-H	337.202	337.2037
27	Acetoxy-[4]-gingerol	10.379	-H	307.1551	307.1556
28	Methoxy-[6]-gingerol	11.271	-H	307.1915	307.1923
29	Methyl-[8]-shogaol	14.198	-H	317.2122	317.213
30	3-Acetoxy-[6]-gingerdiol	11.59	-H	337.202	337.2036
31	1-Dehydro-[10]- gingerdione	15.8	-H	345.2071	345.2086
32	[10]-Gingerdiol	13.634	-H	351.2541	351.2544
33	Methoxy-[10]-gingerol	14.697	-H	409.2596	409.2594
34	Methyl-[10]-gingerol	14.697	-H	409.2596	409.2594
35	Methyl diacetoxy- [4]-gingerdiol	8.319	-H	411.2024	411.2024
36	1-Dehydro-[12]- gingerdione	15.637	-H	373.2384	373.24

37	[12]-Gingerdione	14.402	-H	375.2541	375.2554
38	Diacetoxy-[6]-gingerdiol	12.473	-H	379.2126	379.2141
39	Acetoxy-[10]-gingerol	14.648	-H	391.249	391.2499
40	Methyl diacetoxy-[6]-gingerdiol	13.159	-H	393.2283	393.2294
41	Diacetoxy-[8]-gingerdiol	11.794	-H	407.2439	407.2449

Table S4. Compounds identified from total flavones in *Glycyrrhiza uralensis*

Labels	Compounds	Retention time(min)	M±X	m/z (expected)	m/z (experimental)
ESI(+)					
1	Kumatakenin A	10.933	+H	315.0863	315.0866
2	Licoflavone	10.352	+H	323.1278	323.129
3	Gancaonin O	8.177	+H	355.1176	355.118
4	Kumatakenin B	7.343	+H	255.0652	255.0659
5	Rutin	5.929	+Na	633.1426	633.1424
6	Quercetin	5.921	+H	303.0499	303.0508
7	Kaempferin -3-O-rutinoside	5.569	+H	595.1657	595.1656
8	Quercitrin	6.338	+H	449.1078	449.1088
9	Isorhamnetin-3-O-rutinoside	6.419	+Na	647.1583	647.1599
10	Licobenzofuran	10.45	+H	355.154	355.1545
11	Pinocembrin	6.084	+H	257.0808	257.0815
12	Liquiritin	7.18	+H	419.1337	419.1654
13	Cyclolicoflavanone	8.055	+H	341.1384	341.1384
14	Lliquiritigenin-4'-apiosyl (1-2)-	6.975	+H	551.1759	551.1778

	glucoside				
15	Gancaonin E	10.761	+H	425.1959	425.1957
16	Licochalcone A	11.382	+H	339.1591	339.1598
17	Uralenol-3-methylether	9.935	+H	385.1282	385.1271
18	Uralene	9.935	+H	385.1282	385.1271
19	Isoquercetin	5.929	+H	465.1028	465.1039
20	Uralenin	8.382	+H	357.1333	357.1335
21	Liquiritigenin	6.084	+H	257.0808	257.0815
22	Liquiritigenin-7,4'-diglucosid	5.634	+Na	603.1684	603.167
ESI(-)					
1	Gancaonin O	8.177	-H	353.1031	353.104
2	Licobenzofuran	10.941	-H	353.1394	353.1403
3	Uralenin	11.309	-H	355.1187	355.1187
4	Licochalcone A	11.383	-H	337.1445	337.1461
5	Echinatin	8.57	-H	269.0819	269.0829
6	Gancaonin A	11.497	-H	351.1238	351.1249
7	Gancaonin L	8.177	-H	353.1031	353.104
8	Licoflavone	10.361	-H	321.1132	321.1142
9	Quercitin-3,3'-dimethyleter	7.736	-H	329.0667	329.0669

10	Kumatakenin B	7.343	-H	253.0506	253.0515
11	Uralenol	5.774	+HCOO	415.1035	415.1051
12	Neouralenol	5.774	+HCOO	415.1035	415.1051
13	Quercitrin	7.115	-H	447.0933	447.0947
14	Gancaonin P	5.774	+HCOO	415.1035	415.1051
15	Liquiritin	7.303	-H	417.1191	417.1205
16	Liquiritigenin-7,4'-diglucosid	5.626	-H	579.1719	579.1729
17	Gancaonin E	10.769	-H	423.1813	423.1829
18	Formononetin	9.535	-H	267.0663	267.0671
19	Gancaonin B	11.178	-H	367.1187	367.1198
20	Gancaonin C	10.957	-H	337.1081	337.1095
21	Gancaonn M	11.497	-H	351.1238	351.1249
22	Gancaonin N	11.178	-H	367.1187	367.1202
23	Coumestrol	8.66	-H	267.0299	267.0302
24	Glycycoumarin	11.178	-H	367.1189	367.1202
25	Uralenol-3-methylether	9.927	-H	383.1136	383.1144
26	Uralene	9.927	-H	383.1136	383.1144
27	Cyclolicoflavanone	11.056	-H	339.1238	339.1254
28	Licoricone	11.522	-H	381.1344	381.1336

29	Gancaonin D	9.927	-H	383.1136	383.1144
30	Glycyrin	11.522	-H	381.1344	381.1336

Table S5. Compounds identified from total saponins in *Glycyrrhiza uralensis*

Labels	Compounds	Retention time(min)	M±X	m/z(expected)	m/z(experimental)
ESI(+)					
1	Glycyrrhizic acid	10.089	+H	823.4111	823.4143
2	Licoricesaponin A3	8.241	+H	985.4639	985.4662
3	Licoricesaponin G2	9.369	+H	839.406	839.4078
4	Licoricesaponin J2	10.334	+H	825.4267	825.43
5	18b-Glycyrrhetinic acid	10.931	+H	471.3469	471.3477
6	22b-Acetyoxy glybric zcid	8.552	+H	529.3524	529.3542
7	3-Oxo-glycyrrhizic acid	12.019	+H	469.3312	469.3333
8	24-Hydroxy glycyrrhetic acid	12.321	+H	487.3418	487.3426
9	Licoricesaponin E2	8.977	+H	821.3954	821.3968
10	24-Hydroxy glabrolide	14.929	+H	485.3262	485.3281
11	Licoricesaponin D3	9.328	+H	1013.4592	1013.4954
12	Licoricesaponin B2	9.239	+H	809.4318	809.4332
13	3-Acetyl glycyrrhetinic acid	16.81	+H	513.3575	513.3583
14	Uralsaponin B	10.089	+H	823.4111	823.4143
15	Glycyrrhizin	10.089	+H	823.4111	823.4143

16	Glabrolide	12.019	+H	469.3312	469.3333
17	Licoricesaponin C2	10.759	+H	807.4161	807.4156
18	Licoricesaponin K2	10.089	+H	823.4111	823.4141
19	3b-Hydroxy-olean-9(11), 12-dien-30-oic acid	14.177	+H	455.352	455.353
20	Betulic acid	14.177	+H	455.352	455.353
21	Uralenolide	12.019	+H	469.3312	469.3321
ESI(-)					
1	Glycyrrhizic acid	9.994	-H	821.3965	821.4006
2	Licoricesaponin A3	8.252	-H	983.4493	983.4533
3	Licoricesaponin B2	10.713	-H	807.4172	807.4212
4	Licoricesaponin G2	7.851	-H	837.3914	837.3939
5	18b-Glycyrrhetinic acid	14.851	+HCOO	515.3378	515.3375
6	24-Hydroxy glycyrrhetic acid	10.435	-H	485.3272	485.3291
7	24-Hydroxy glabrolide	14.932	-H	483.3116	483.3114
8	Licoricesaponin C2	11.408	-H	805.4016	805.4017
9	3b-Hydroxy-olean-9(11), 12-dien-30-oic acid	17.287	-H	453.3374	453.3388
10	Licoricesaponin D3	9.331	-H	1011.4806	1011.48

11	Licoricesaponin J2	10.108	-H	823.4122	823.4122
12	3-Acetyl glycyrrhetinic acid	15.382	-H	511.3429	511.3426
13	Uralsaponin B	9.994	-H	821.3965	821.4006
14	Glycyrrhizin	9.994	-H	821.3965	821.4006
15	Licoricesaponin E2	9.25	-H	819.3809	819.3817
16	Licoricesaponin F3	10.149	-H	951.4595	951.4607
17	Licoricesaponin K2	9.994	-H	821.3965	821.4006
18	Betulic acid	17.287	-H	453.3374	453.3388

Table S6. Compounds identified from *SND*

Labels	Compounds	Retention time(min)	M±X	m/z (expected)	m/z (experimental)
ESI(+)					
1	Mesaconine	4.181	+H	486.2698	486.2703
2	Senbusine A	4.337	+H	424.2694	424.2711
3	Fuziline	5.024	+H	454.2799	454.2817
4	Neoline	5.22	+H	438.285	438.2870
5	Benzoyldeoxyaconitine	8.016	+NH4	605.3433	605.3427
6	Hypaconitine	8.777	+H	616.313	616.3135
7	Isodelphinine	8.883	+H	600.3167	600.3177
8	Salsolinol	1.033	+H	180.1019	180.1016
9	[6]-Gingerdiol	10.232	+Na	319.1880	319.1885
10	Methoxy-[6]-gingerol	10.584	+NH4	326.2326	326.2330
11	[8]-Gingerdione	13.388	+H	321.206	321.2069
12	[10]-Gingerdione	14.443	+H	349.2373	349.2379
13	[12]-Gingerdione	15.808	+H	377.2686	377.2672
14	Methyl-3-acetoxy-[6]-gingerdiol	12.554	+Na	375.2142	375.2149
15	[6]-Shogaol	12.693	+H	277.1798	277.1808
16	[8]-Shogaol	12.333	+H	305.2111	305.2120
17	[10]-Shogaol	13.936	+H	333.2424	333.2435

18	Methyl diacetoxy-[6]-gingerdiol	14.328	+Na	417.2248	417.2260
19	Glycyrrhizic acid	9.57	+H	823.4111	823.4131
20	Licoricesaponin A3	8.245	+H	985.4639	985.4653
21	Licoricesaponin J2	10.33	+H	825.4267	825.4276
22	3-Oxo-glycyrrhizic acid	8.67	+H	469.3312	469.3321
23	3-Acetyl glycyrrhetinic acid	9.324	+H	513.3575	513.3582
24	Pinocembrin	6.013	+H	257.0808	257.0814
25	Liquiritin	7.182	+H	419.1337	419.1350
26	Cyclolicoflavanone	11.262	+H	341.1384	341.1379
27	Ononin	7.272	+H	431.1337	431.1346
28	Gancaonin B	10.772	+H	369.1333	369.1340
29	Gancaonin L	11.123	+H	355.1176	355.1186
30	Licoricidin	13.143	+H	425.2323	425.2312
31	Karakoline	4.443	+H	378.2639	378.2647
32	Senbusine B	4.337	+H	424.2694	424.2711
33	Chuanfumine	4.165	+H	394.2588	394.2586
34	Aconine	4.631	+H	500.2854	500.2864
35	Songorine	4.688	+H	358.2377	358.2386
36	Hypaconine	4.991	+H	470.2748	470.2756
37	Kaempferin -3-O-rutinoside	5.163	+H	595.1657	595.1671
38	Karakanine	5.408	+H	376.2482	376.2480

39	Liquiritigenin-7,4'-diglucosid	5.784	+H	581.1865	581.1870
40	Isoliquiritigenin	6.013	+H	257.0808	257.0814
41	Liquiritigenin	6.013	+H	257.0808	257.0814
42	Songoramine	6.127	+H	356.222	356.2225
43	14-O-acetylneoline	6.209	+H	480.2956	480.2959
44	Lliquiritigenin-4'-apiosyl (1-2)-glucoside	6.97	+H	551.1759	551.1774
45	Neolicuroside	6.97	+H	551.1759	551.1774
46	Kumatakenin B	7.346	+H	255.0652	255.0654
47	Licochalcone B	7.55	+H	287.0914	287.0918
48	3b-Hydroxy-olean-9(11), 12-dien-30-oic acid	7.787	+H	455.352	455.3529
49	Betulic acid	7.787	+H	455.352	455.3529
50	Beiwutine	7.836	+H	648.3015	648.3029
51	5-O-Methylglycyrol	8.033	+H	381.1333	381.1351
52	24-Hydroxy glabrolide	8.196	+H	485.3262	485.3265
53	Mesaconitine	8.204	+H	632.3065	632.3073
54	Licoricesaponin B2	8.237	+H	809.4318	809.4319
55	Aconifine	8.327	+H	662.3171	662.3183
56	[4]-Shogaol	8.621	+H	249.1485	249.1489
57	Glabrolide	8.67	+H	469.3312	469.3321
58	Uralenolide	8.67	+H	469.3312	469.3321

59	14-O-anisoylneoline	8.728	+H	572.3218	572.3224
60	24-Hydroxy glycyrrhetic acid	9.169	+H	487.3418	487.3430
61	Licoricesaponin G2	9.169	+H	839.406	839.4095
62	Deoxyaconitine	9.259	+H	630.3273	630.3286
63	Glycyrol	9.496	+H	367.1176	367.1188
64	Neoglycyrol	9.496	+H	367.1176	367.1188
65	Noglycyrolisomer	9.496	+H	367.1176	367.1188
66	Formononetin	9.529	+H	269.0808	269.0812
67	18b-Glycyrrhetinic acid	9.57	+H	471.3469	471.3482
68	Licoricesaponin K2	9.57	+H	823.4111	823.4131
69	Glycyrrhizin	9.57	+H	823.4111	823.4131
70	Uralsaponin B	9.57	+H	823.4111	823.4131
71	Licoricesaponin D3	9.864	+H	1013.4952	1013.4933
72	Licoricesaponin E2	9.897	+H	821.3954	821.3955
73	Dihydrocurcumin	10.052	+H	371.1489	371.1495
74	[6]-Paradol	10.232	+H	279.1955	279.1958
75	Echinatin	10.265	+H	271.0965	271.0969
76	Licoflavone	10.363	+H	323.1278	323.1289
77	Demethoxy-[6]-shogaol	10.387	+H	247.1693	247.1693
78	1-Hydroxy-[6]-paradol	10.461	+Na	317.1723	317.1732
79	[6]-Gingerol	10.461	+Na	317.1723	317.1732
80	Licoricesaponin C2	10.747	+H	807.4161	807.4170

81	Glycycoumarin	10.772	+H	369.1333	369.1340
82	Gancaonin N	10.772	+H	369.1333	369.1340
83	Kumatakenin A	11.066	+H	315.0863	315.0871
84	Gancaonin O	11.409	+H	355.1176	355.1186
85	Licobenzofuran	11.467	+H	355.154	355.1535
86	Bikhaconine	11.516	+H	468.2956	468.2979
87	Licoricone	11.524	+H	383.1489	383.1501
88	Glycyrin	11.524	+H	383.1489	383.1501
89	1-Dehydro-[6]-gingerdione	11.548	+H	291.1955	291.1960
90	Gancaonin C	11.851	+H	339.1227	339.1237
91	Methyl-[8]-gingerol	11.736	+H	337.2373	337.2359
92	Methoxy-[8]-gingerol	11.884	+H	337.2373	337.2359
93	[8]-Shogaol	12.333	+H	305.2111	305.2120
94	[10]-Gingerdiol	12.938	+H	353.2686	353.2690
95	Licorisoflavan B	13.143	+H	425.2323	425.2312
96	Methyl-[8]-shogaol	13.265	+H	319.2268	319.2264
97	1-Dehydro-[6]-gingerol	13.315	+H	293.1747	293.1749
98	6-Hydroxy-[6]-shogaol	13.315	+H	293.1747	293.1749
99	[6]-Gingerdione	13.315	+H	293.1747	293.1749
100	6-Dehydro-[6]-gingerol	13.315	+H	293.1747	293.1749
101	6-Hydroxy-[8]-shogaol	13.388	+H	321.206	321.2069
102	Gancaonin E	13.47	+H	425.1959	425.1959

103	Methyl-[6]-shogaol	13.593	+H	291.1591	291.1598
104	[10]-Gingerol	13.936	+H	351.253	351.2534
105	Licorisoflavan A	14.942	+H	439.2479	439.2496
106	1-Dehydro-[8]-gingerdione	15.113	+H	319.1904	319.1910
107	[12]-Shogaol	15.432	+H	361.2737	361.2744
108	6-Hydroxy-[10]-shogaol	16.291	+H	349.2373	349.2379
109	1- Dehydro-3-dihydro-[10]-gingerdione	16.291	+H	349.2373	349.2379
110	1-Dehydro-[10]-gingerdione	16.438	+H	347.2217	347.2226
111	Methoxy-[10]-gingerol	13.928	+NH4	382.2952	382.2945
112	1-Dehydro-[12]-gingerdione	5.547	+NH4	392.2795	392.2805
113	Acetoxy-[4]-gingerol	10.706	+Na	331.1516	331.1507
114	Acetoxy-[6]-gingerol	12.366	+Na	359.1829	359.1838
115	Methyl acetoxy-[6]-gingerol	3.756	+Na	373.1985	373.1977
116	Acetoxy-[10]-gingerol	15.359	+Na	415.2455	415.2470
117	3-Acetoxy-[6]-gingerdiol	11.606	+H	339.2166	339.2182
118	Diacetoxy-[6]-gingerdiol	13.396	+Na	403.2091	403.2099
119	Diacetoxy-[8]-gingerdiol	13.388	+NH4	426.2850	426.2860
120	[4]-Gingerol	8.621	+Na	289.1410	289.1416
121	Methyl-[6]-gingerol	10.584	+NH4	326.2326	326.2330
122	[8]-Gingerol	12.325	+H	323.2217	323.2211
123	Glabridin	5.302	+NH4	342.1700	342.1708

ESI(-)

1	Isodelphinine	11.501	-H	598.3022	598.3016
2	Echinatin	8.565	-H	269.0819	269.0823
3	[6]-Shogaol	8.042	-H	275.1653	275.1663
4	1-Dehydro-[10]-gingerdione	16.439	-H	345. 2071	345. 2088
5	Methyl-[6]-shogaol	13.594	-H	289.1445	289.1458
6	1-Hydroxy-[6]-paradol	10.585	+Cl	329.1525	329.1528
7	[10]-Gingerol	13.945	-H	349.2384	349.2402
8	Glycyrrhizic acid	10.013	-H	821.3965	821.3999
9	Licoricesaponin B2	9.939	-H	807.4172	807.4200
10	Licoricesaponin G2	8.672	-H	837.3914	837.3944
11	Licoricesaponin J2	10.34	-H	823.4122	823.4136
12	Licoricesaponin E2	9.489	-H	819.3809	819.3845
13	Methyl-[4]-shogaol	11.476	-H	261.1496	261.1504
14	Liquiritigenin	9.293	+HCOO	301.0718	301.0721
14	Isoliquiritigenin	9.293	+HCOO	301.0718	301.0721
15	Kaempferin -3-O-rutinoside	5.156	-H	593.1512	593.1541
16	Licobenzofuran	11.149	-H	353.1394	353.1408
17	Liquiritigenin-7,4'-diglucosid	4.894	+Cl	615.1509	615.1486
18	3-Acetoxy-[6]-gingerdiol	8.459	-H	337.2020	337.2024
19	Licorisoflavan A	14.935	-H	437.2333	437.2344
20	Aconine	5.344	-H	498.2709	498.2729

21	Kumatakenin B	7.346	+HCOO	299.0561	299.0575
22	Benzoylhypaconine	7.625	+HCOO	618.292	618.2940
23	Mesaconine	4.621	+HCOO	530.2607	530.2616
24	Gancaonin A	11.885	-H	351.1238	351.1249
25	Senbusine A	4.354	+HCOO	468.2603	468.2616
25	Senbusine B	4.354	+HCOO	468.2603	468.2616
26	Kaempferin -3-O-rutinoside	5.156	-H	593.1512	593.1541
27	Liquiritigenin-7,4'-diglucosid	4.894	+Cl	615.1509	615.1486
28	Hokbusine B	3.879	+HCOO	436.2341	436.2346
29	Benzoylaconine	7.388	+HCOO	648.3025	648.3040
30	Isoglycyrol	4.224	+HCOO	409.0929	409.0931
31	[8]-Gingerdiol	7.895	+HCOO	369.2283	369.2275
32	Methoxy-[4]-gingerol	9.522	-H	279.1602	279.1611
33	Methyl-[6]-paradol	10.585	-H	291.1966	
34	[8]-Paradol	10.241	+HCOO	351.2177	351.2191
35	Methyl-[4]-gingerol	9.522	-H	279.1602	279.1611
36	Licoricesaponin F3	8.009	+HCOO	997.465	997.4631
37	Licochalcone A	14.109	-H	337.1445	337.1458
38	Glycycoumarin	10.626	-H	367.1187	367.1199
39	Fuziline	5.025	+HCOO	498.2709	498.2729
40	Neoline	5.524	+HCOO	482.2759	482.2780
41	Benzoyldeoxyaconitine	8.001	+HCOO	632.309	632.3091

42	Salsolinol	6.562	+HCOO	224.0928	224.0939
43	Chuanfumine	2.531	+HCOO	438.2497	438.2513
44	[6]-Gingerdiol	9.955	+HCOO	341.1970	341.1987
45	[10]-Gingerdiol	13.332	+HCOO	397.2615	397.2596
46	Methoxy-[8]-gingerol	11.214	+HCOO	381.2283	381.2275
47	[6]-Gingerdione	9.726	-H	291.1602	291.1610
48	3-Acetoxy-[6]-gingerdiol	8.459	-H	337.2020	337.2024
49	6-Hydroxy-[6]-shogaol	9.726	+HCOO	337.1657	337.1668
50	Demethoxy-[6]-shogaol	9.726	+HCOO	291.1602	291.1609
51	1-Dehydro-[6]-gingerol	9.726	-H	291.1602	291.1610
52	Methyl-[8]-gingerol	11.214	+HCOO	381.2283	381.2275
53	6-Dehydro-[6]-gingerol	9.726	+HCOO	337.1657	337.1668
54	Licoricesaponin D3	9.857	-H	1011.4806	1011.4816
55	18b-Glycyrrhetinic acid	14.591	-H	469.3323	469.3342
56	22b-Acetyoxy glybric acid	12.727	-H	527.3378	527.3391
57	3-Oxo-glycyrrhizic acid	15.188	-H	467.3167	467.3182
58	24-Hydroxy glycyrrhetic acid	12.024	-H	485.3272	485.3289
59	Uralsaponin B	9.57	-H	821.3965	821.3999
60	Glycyrrhizin	9.57	-H	821.3965	821.3999
61	Glabrolide	15.188	-H	467.3167	467.3182
62	Licoricesaponin C2	10.552	-H	805.4016	805.4032
63	Licoricesaponin K2	10.013	-H	821.3965	821.3999

64	Uralenolide	15.188	-H	467.3167	467.3182
65	Kumatakenin A	11.075	-H	313.0718	313.0733
66	Licoflavone	10.626	+HCOO	367.1187	367.1196
67	Formononetin	11.075	-H	267.0663	267.0675
68	Gancaonin B	10.626	-H	367.1187	367.1199
69	Gancaonin C	11.844	-H	337.1081	337.1097
70	Gancaonin N	10.626	-H	367.1187	367.1199

Quantitive Fingerprint Study of active components in *SND* and *SND*

Chromatographic separation of quantified fingerprint of active components in *SND* and *SND* was performed on an Waters Terra C_{18} column (3.0 mm × 100 mm, 3.5 μm) using an Agilent 1100series HPLC system (Agilent), equipped with a binary solvent delivery system, an autosampler, and a DAD detector. The column was maintained at room temperature and eluted at a flow rate of 0.5 ml/min, using a mobile phase of (A) acetonitrile and (B) water (5mM ammonium acetate). The gradient program was optimized as follows: 0-10 min, 15% A to 26% A; 10-20 min, 26% A to 30% A; 20-25 min, 30% A. Detection wavelength: 235 nm. Column temperature: 25℃; Injection volume: 5μL.

Table S7 Contents of major constituents in active components in *SND* and *SND*

Components	Peak Area (Mean ± S.D.)				
	SND	**TA**	**TG**	**TF**	**TS**
Benzoylmesaconine	31358210 ± 491898	84667167 ± 564658	——	——	——
Benzoylaconine	5666954 ± 29052	15412775 ± 35642	——	——	——
Mesaconine	40603670 ± 952579	108629909 ± 856932	——	——	——
6-gingerol	978249 ± 11828	——	4012996 ± 25437	——	——

Liquiritigenin	59198220 ± 1380282	——	——	159835194 ± 1450312	——
Glycyrrhizin	16313060 ± 49258	——	——	——	43042262± 38217

Table S8 62 identified biomarkers of DOX-induced cardiomyopathy and their metabolism pathways.

mode	No.	R.T.(min)	Ion(m/z)	Identification	Trend[a]	Related pathway
GC/MS	1	8.82	117.0204	Lactate[b]	↓	Glycolysis
	2	34.41	319.1629	D-Glucose[b]	↑	Glycolysis
	3	23.88	156.0749	L-proline[b]	↑	α-amino acids metabolism
	4	10.23	116.069	L-Alanine[b]	↓	α-amino acids metabolism
	5	17.07	174.107	glycine[b]	↓	α-amino acids metabolism
	6	27.01	246.167	glutamine[b]	↓	α-amino acids metabolism
	7	24.05	232.1413	L-Aspartate[b]	↓	α-amino acids metabolism
	8	38.07	313.2688	Palmitic acid[b]	↓	Fatty acids metabolism

	9	42.14	341.3394	Stearic acid[b]	↓	Fatty acids metabolism
	10	16.16	205.1155	glycerol[b]	↓	Glycerophospholipid metabolism
	11	15.12	147.0861	urea[b]	↓	Urea cycle
	12	23.11	147.0729	malate[b]	↓	Energy metabolism
	13	16.01	158.1297	phosphate[b]	↑	Energy metabolism
	14	31.88	265.0865	9H-Purine	↑	Not known
	15	45.79	371.3575	monopalmitin	↓	Not known
	16	47.21	399.3489	monostearin	↓	Not known
	17	11.49	149.1025	1-methoxy-1,3 -propanediol	↓	Not known
	18	24.83	115.0611	Creatinine[b]	↓	Not known
ESI(+)	19	16.21	255.2323	7-Hexadecenoic acid	↓	Fatty acids metabolism
	20	15.78	279.2323	Pinolenic acid	↓	Fatty acids metabolism
	21	10.74	298.2746	3-ketosphingosine	↑	Not known
	22	15.68	303.2324	Eicosapentaenoic acid[b]	↓	Fatty acids metabolism
	23	13.75	455.3933	29:3	↓	Fatty acids metabolism
	24	15.10	466.3302	PE(18:1/0:0)	↑	Glycerophospholipid metabolism
	25	12.29	494.3252	LPC(16:1)	↓	Glycerophospholipid metabolism

	26	14.00	506.358	PC(18:2/0:0)	↑	Glycerophospholipid metabolism
	27	0.75	144.101579	unknown	↓	Not known
	28	15.80	377.2671909	unknown	↓	Not known
	29	15.68	325.2142337	unknown	↓	Not known
	30	13.30	1017.688141	unknown	↓	Not known
ESI(－)	31	0.71	259.0236	D-Glucose-6P	↑	Glycolysis
	32	3.95	181.0505	Hydroxyphenyllactic acid	↓	Fatty acids metabolism
	33	16.20	253.2184	Hexadecenoic acid	↓	Fatty acids metabolism
	34	15.07	275.2023	Stearidonic acid	↓	Fatty acids metabolism
	35	15.78	277.2186	Pinolenic acid	↓	Fatty acids metabolism
	36	15.68	301.2191	5,6-dehydro Arachidonic acid	↓	Fatty acids metabolism
	37	15.68	302.2222	N-Lauroylglycine	↓	Not kown
	38	17.07	355.2659	24:6	↓	Fatty acids metabolism
	39	12.17	450.2642	LPE(16:1/0:0)	↓	Glycerophospholipid metabolism
	40	13.62	524.3384	PC(16:1/0:0)	↑	Glycerophospholipid metabolism
	41	15.13	552.3684	PC(18:1/0:0)	↑	Glycerophospholipid metabolism

42	16.20	254.2215	Palmitic amide	↓	Glycerophospholipid metabolism
43	3.25	663.1610	unknown	↓	Not known
44	15.78	577.4179	unknown	↓	Not known
45	16.18	338.1963	unknown	↓	Not known
46	15.68	625.4224	unknown	↓	Not known
47	12.29	539.3204	unknown	↓	Not known
48	16.16	315.2341	unknown	↓	Not known
49	13.56	271.2288	unknown	↓	Not known
50	5.02	544.2433	unknown	↓	Not known
51	17.07	356.2692	unknown	↓	Not known
52	15.78	278.2219	unknown	↓	Not known
53	0.67	199.9397	unknown	↓	Not known
54	12.48	608.3464	unknown	↓	Not known
55	13.38	817.5741	unknown	↓	Not known
56	13.37	816.5764	unknown	↓	Not known
57	15.78	345.2063	unknown	↓	Not known
58	12.60	554.3040	unknown	↓	Not known
59	9.98	193.0834	unknown	↓	Not known
60	16.93	372.3135	unknown	↑	Not known
61	0.99	271.0574	unknown	↑	Not known
62	13.10	548.3371	unknown	↑	Not known

[a]”↑”represents up-regulated compared with control group,”↓”down-regulated compared with control group .[b] Metabolites that were validated with authentic standards.

Table S9 regulated extent of 7 treated groups on 62 identified biomarkers.

No	**Compound**	***SND***	**TAFSG**	**TAG**	**TAFS**	**TA**	**TG**	**TFS**
GC/MS								
1	Lactate	++	++	+	+	+		+
2	L-Alanine	+	+	+				
3	1- methox-1,3-propanediol		+	+				+
4	Urea	+	++	+	+	+	+	
5	Phosphate				+	+	+	
6	Glycerol	+	+	+	+	+		
7	Glycine	+	+	+	+	+		+
8	Malate	+	+	+	+	+		
9	L-proline		+			+	+	
10	L-Aspartic acid							
11	creatinine		++	+				+
12	glutamine	+			+			
13	9H-purine	+	+		+	+	+	+
14	d-glucose	++	+	+	+	+	+	+
15	Palmitic acid	+	+					

16	Stearic acid	+	+					
17	1-Monopalmitin	+	+	+				
18	1-Monostearin	+	+	+				
LC/MS								
19	Hydroxyphenyl lactic acid	+			+			+
20	7-Hexadecenoic acid	++	+					
21	Palmitic amide	+	+					
22	D-Glucose-6-phosphate	+	+					
23	Stearidonic acid	++	+	+	+	+	+	
24	Pinolenic acid	+	+					
25	5,6-dehydro arachidonic acid	+	+					
26	N-Lauroylglycine	+						
27	Tetracosahexaenoic acid							
28	LPE(16:1/0:0)	++	+			+		+
29	PC(16:1/0:0)	++	++	++	+	+	+	+
30	PC(18:1/0:0)	++	+					
31	7-Hexadecenoic acid							
32	Pinolenic acid							
33	3-ketosphingosine	+	+					
34	EPA							

35	29:3	+	+					
36	PE(18:1/0:0)	++	++	+				
37	LPC(16:1)	++	++	+	+	+	+	+
38	PC(18:2/0:0)	++	++	+	+	+	+	
39	0.75(144.101579)	+						
40	15.80(377.2671909)							
41	15.68(325.2142337)							
42	13.30(1017.688141)							
43	3.25(663.1610)	++	+	++	++	+	+	+
44	15.78(577.4179)	+	+					
45	16.18(338.1963)							
46	15.68(625.4224)	+						
47	12.29(539.3204)	+	+					
48	16.16(315.2341)	+						
49	13.56(271.2288)	+	+	++	+			+
50	5.02(544.2433)	+	+	+	++	+		
51	17.07(356.2692)							
52	15.78(278.2219)	+						
53	0.67(199.9397)	+	++	+	+		+	
54	12.48(608.3464)		+					
55	13.38(817.5741)	+	+			+		
56	13.37(816.5764)	+	+					

57	15.78(345.2063)							
58	12.60(554.3040)							
59	9.98(193.0834)			++				
60	16.93(372.3135)							
61	0.99(271.0574)	++					+	
62	13.10(548.3371)	++	++	++	++	++	++	++

Note:"+" means a relief from DOX group to control group to some extent,"++" represents *p*<0.05,compared to the DOX group

Table S10 potential targets found by molecular docking

Item	Gene ID	Protein Definition	PDB ID	Target Class	Gene Ontology (GO)	Properties and implications for the therapy of cardiovascular diseases
1	OAT	Ornithine aminotransferase, mitochondrial	2oat 1oat 2can	A	Ornithine-oxo-acid transaminase activity	Enzyme associated with amino-acid biosynthesis.
2	PIK3CG	Phosphoinositide 3-kinase gamma	2a4z 1e8z	E	G-protein coupled receptor protein signaling pathway	PIK3CG appears to negatively control cardiac contractility, thus becoming a possible drug target for the treatment of critical human cardiac pathologies, such as infarction or heart failure.[1]
3	RXRB	Retinoic acid receptor RXR-beta	1h9u	A	Regulation of transcription, DNA-dependent	Nuclear hormone receptor. Involved in the retinoic acid response pathway.
4	mTOR	Mammalian target of rapamycin	2fap	U	Phosphoinositide 3-kinase complex	mTOR functions in the regulation of cardiac

					Protein serine/threonine kinase activity	growth. Inhibition of mTOR attenuates the development of pressure overload cardiac hypertrophy and regresses established cardiac hypertrophy.[2]
5	MAPK12 (ERK6)	Mitogen-activated protein kinase p38 gamma	1cm8	E	MAP kinase activity Ras protein signal transduction	It is highly likely that p38 and JNK are bothrequired to generate a hypertrophic or apoptotic response in overloaded hearts. It has been known that MAP kinases are sensitive to oxidative stress and antioxidants preferentially inhibit JNK and p38.[3]
6	INSR	Insulin receptor	1ir3	A	Activation of MAPK activity	INSR binds insulin and mediates metabolic functions of insulin. Can activate PI3K either directly by binding to the p85

						regulatory subunit, or indirectly via IRS1. PI3K signaling plays a fundamental role in the regulation of myocardial contractility and hypertrophy.[4]
7	BST1	ADP-ribosyl cyclase 2	1isg	E	Humoral immune response	ADPR-cyclase synthesizes cyclic ADP-ribose, a second messenger that elicits calcium release from intracellular stores. BST1 is an important mediator of cardiac hypertrophy, and inhibition of ADPR-cyclase attenuates angiotensin II-induced cardiac hypertrophy.[5]
8	MAPK14	Mitogen-activated protein kinase p38 alpha	1wbv	E	MAP kinase activity Ras protein signal transduction	It is highly likely that p38 and JNK are bothrequired to generate a hypertrophic or apoptotic response in

						overloaded hearts. It has been known that MAP kinases are sensitive to oxidative stress and antioxidants preferentially inhibit JNK and p38.[3]
9	ACE	Angiotensin-converting enzyme	1o86 1uze	AC	Regulation of vasoconstriction	Regulation of vasodilation ACE inhibitors are widely used in the treatment of cardiovascular diseases, including congestive heart failure, coronary artery disease and hypertension. [6]
10	F2	Prothrombin	1awh	AC	Positive regulation of blood coagulation	Drug target of anticoagulants. Involved in blood clotting cascade. [6]
11	KIT	Mast/stem cell growth factor receptor	1t46	A	Transmembrane receptor protein tyrosine kinase signaling pathway	This is the receptor for stem cell factor (mast cell growth factor). It has a tyrosine-protein kinase activity. Binding of ligands leads to the autophosphorylation of

						KIT and its association with substrates such asphosphatidylinositol 3-kinase (PI3K).
12	DAPK1	Death-associated protein kinase 1	1ig1	E	Induction of apoptosis by extracellular signals Calmodulin binding	DAPK is a calmodulin-regulated serine/threonine protein kinase implicated in diverse apoptosis pathways, including those involved in neuronal cell death and tumour suppression. DAPK could be a potential therapeutic target for diseases characterized by rapid neurodegeneration, such as stroke or traumatic brain injury. [7]
13	GCK	Glucokinase	1v4s	E	Positive regulation of insulin secretion	GCK intervenes in the regulation of glucose metabolism. [8]
14	MAPK8 (JNK1)	c-Jun N-terminal kinase 1	2no3	U	JUN kinase activity JUN	See MAPK12 (Item 5).

					phosphorylation	
15	FGFR1	Basic fibroblast growth factor receptor 1	1agw	A	MAPKKK cascade	Fibroblast growth factor 2 (FGF2) plays an important role in inducing cardiac hypertrophy. Many of the effects of FGF-2 are mediated by binding and activating FGFR. The FGF2-FGFR1 axis needs to be considered as a potential target for the management of hypertrophy.[9]
16	RAC3	RAS-related C3 botulinum toxin substrate 3	2g0n	U	GTPase activity Small GTPase mediated signal transduction	Rac3 is a member of the Rho family of small GTP-binding proteins. Small G proteins are implicated in regulation ofendothelial function, smooth muscle cell contraction, proliferation and migration, as well as cardiomyocyte hypertrophy. Targeting

						small G proteins could constitute promising therapeutic approaches in cardiovascular disorders.[10]
17	MME	Neprilysin	1r1i	A	Cell-cell signaling	MME is implicated in the pathogenesis of arterial hypertension, congestive heart failure,left ventricular remodeling after myocardial infarction and other cardiovascular diseases. It is a novel target for the treatment of heart diseases. [11]

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Table S11 Dockscores of protein with cocrystallized ligands

PDB ID of Protein	Dockscore with cocrystallized ligands
2oat	133.681
1oat	89.1023
2can	101.927
2a4z	103.441
1e8z	132.295
1h9u	130.895
2FAP	172.394
1cm8	127.434
1ir3	131.222
1isg	151.137
1WBV	129.508
1O86	152.241
1UZE	137.321
1AWH	138.72
1T46	146.304
1IG1	135.488
1V4S	118.948

2no3	97.4273
1agw	98.5342
2g0n	163.273
1R1I	137.988