Table S1 Biochemistry parameters of clinical liver function

index / groups	ALT (U/L)	AST (U/L)	ALP (U/L)	D-Bili (μmol/L)	T-Bili (μmol/L)	γ-GT (U/gprot)	TBA (μmol/L)	T-SOD (U/mgprot)	MDA (nmol/mgprot)	GSH-Px (μmol/L)
Control	89.79 ±25.68	164.51 ±15.39	99.26 ±8.11	1.23 ±0.52	1.21 ±0.50	5.64 ±2.35	5.09 ±1.53	20.24 ±3.90	117.40 ±30.83	123.58 ±31.99
YHS	147.1 ±34.49**	224.83 ±42.66**	203.26 ±64.73**	2.41 ±0.99*	1.93 ±0.47*	7.38 ±2.40	9.26 ±2.71**	18.56 ±3.58	133.28 ±20.92	90.90 ±9.74*
GEN	96.42 ±3.86#	164.73 ±39.10#	108.00 ±8.71#	1.24 ±0.52#	1.31 ±0.30#	5.36 ±0.62	5.80 ±0.60#	19.97 ±1.23	113.73 ±16.90	125.79 ±16.54##

Note: *P<0.05，**P<0.01 compared with the control group

#P<0.05，##P<0.01 compared with the YHS group

Table S2 Identification and trends of change for differential metabolites

NO	Rt(min)	m/z determined	m/z calculated	Error （mDa）	Ion form	Molecular Formula	Metabolite Name	Trend	VIP	T'TEST
1	0.57	146.1653	146.1657	-0.4	$[M+H]^+$	$C_7H_{19}N_3$	Spermidine	↓	1.00	0.0069
2	0.86	126.0222	126.0225	-0.3	$[M+H]^+$	$C_2H_7NO_3S$	Taurine	↓	3.00	0.0062
3	1.96	314.1202	314.1240	-3.8	$[M+H]^+$	$C_{14}H_{19}NO_7$	Tyramine glucuronide	↓	1.13	0.0297
4	2.10	188.0911	188.0923	-1.2	$[M+H]^+$	$C_8H_{13}NO_4$	2-Keto-6-acetamidocaproate	↓	1.39	0.0096
5	2.70	122.0263	122.0276	-1.3	$[M+H]^+$	$C_3H_7NO_2S$	L-Cysteine	↓	1.42	0.0001
6	3.17	109.0286	109.0290	-0.4	$[M+H]^+$	$C_6H_4O_2$	1,2-Benzoquinone	↑	1.45	0.0143
7	3.32	168.0662	168.0661	0.1	$[M+H]^+$	$C_8H_9NO_3$	Pyridoxal	↓	1.42	0.0010
8	3.33	315.1193	315.1206	-1.3	$[M+H]^+$	$C_{14}H_{14}N_6O_3$	7,8-Dihydropteroic acid	↓	1.61	0.0006
9	3.74	210.0742	210.0766	-2.4	$[M+H]^+$	$C_{10}H_{11}NO_4$	Hydroxyphenylacetylglycine	↓	4.90	0.0041
10	3.92	184.0972	184.0974	-0.2	$[M+H]^+$	$C_9H_{13}NO_3$	Epinephrine	↑	2.46	0.0442
11	4.67	474.1725	474.1737	-1.2	$[M+H]^+$	$C_{20}H_{23}N_7O_7$	10-Formyltetrahydrofolate	↑	1.54	0.0060
12	4.87	235.1081	235.1083	-0.2	$[M+H]^+$	$C_{12}H_{14}N_2O_3$	5-Methoxytryptophan	↑	1.38	0.0038
13	4.87	281.1146	281.1137	0.9	$[M+H]^+$	$C_{13}H_{16}N_2O_5$	L-beta-aspartyl-L-phenylalanine	↑	1.31	0.0284
14	5.10	190.0504	190.0504	0	$[M+H]^+$	$C_{10}H_7NO_3$	Kynurenic acid	↓	8.04	0.0010
15	5.11	130.0637	130.0657	-2.0	$[M+H]^+$	C_9H_7N	3-Methylene-indolenine	↑	1.39	0.0011
16	5.64	247.0949	247.0930	1.9	$[M+H]^+$	$C_9H_{14}N_2O_6$	5,6-Dihydrouridine	↓	1.20	0.0040
17	6.22	233.1281	233.1290	-0.9	$[M+H]^+$	$C_{13}H_{16}N_2O_2$	Melatonin	↑	1.24	0.0013
18	6.38	247.1293	247.1294	-0.1	$[M+H]^+$	$C_{10}H_{18}N_2O_5$	L-beta-aspartyl-L-leucine	↑	1.02	0.0075
19	6.75	385.1694	385.1685	0.9	$[M+H]^+$	$C_{19}H_{28}O_6S$	3b,16a-Dihydroxyandrostenone sulfate	↓	1.16	0.0364
20	7.37	300.0913	300.0944	-3.1	$[M+H]^+$	$C_{10}H_{13}N_5O_6$	8-Hydroxyguanosine	↓	1.28	0.0024

21	0.65	177.0400	177.0399	0.1	$[M-H]^-$	$C_6H_{10}O_6$	L-Gulonolactone	↓	1.79	0.0241
22	0.65	195.0505	195.0505	0	$[M-H]^-$	$C_6H_{12}O_7$	Gluconic acid	↓	7.42	0.0215
23	3.18	347.0977	347.0992	-1.5	$[M-H]^-$	$C_{15}H_{16}N_4O_6$	Riboflavin reduced	↑	3.04	0.0077
24	3.49	252.0850	252.0872	-2.2	$[M-H]^-$	$C_{12}H_{15}NO_5$	N-Acetylvanilalanine	↑	1.02	0.0003
25	3.72	176.0375	176.0381	-0.6	$[M-H]^-$	$C_6H_{11}NO_3S$	N-Formyl-L-methionine	↓	1.23	0.0394
26	3.78	259.1292	259.1292	-0.2	$[M-H]^-$	$C_{11}H_{20}N_2O_5$	L-gamma-glutamyl-L-leucine	↑	1.31	0.0083
27	4.52	137.0602	137.0603	-0.1	$[M-H]^-$	$C_8H_{10}O_2$	Tyrosol	↑	2.08	0.0263
28	4.52	167.0341	167.0344	-0.3	$[M-H]^-$	$C_8H_8O_4$	Homogentisic acid	↑	3.44	0.0036
29	5.16	175.0607	175.0607	0.1	$[M-H]^-$	$C_7H_{12}O_5$	2-Isopropylmalic acid	↑	2.37	0.0259
30	5.61	163.0393	163.0395	0.1	$[M-H]^-$	$C_9H_8O_3$	Phenylpyruvic acid	↑	2.45	0.0040
31	6.76	194.0452	194.0453	-0.1	$[M-H]^-$	$C_9H_9NO_4$	Dopaquinone	↑	1.87	0.0024
32	6.96	172.0975	172.0974	1.7	$[M-H]^-$	$C_8H_{15}NO_3$	Isovalerylalanine	↑	11.8	0.0015
33	7.31	211.0600	211.0606	-0.6	$[M-H]^-$	$C_{10}H_{12}O_5$	Vanillactic acid	↓	1.03	0.0104

Note: ↑, ↓ compared with the control group

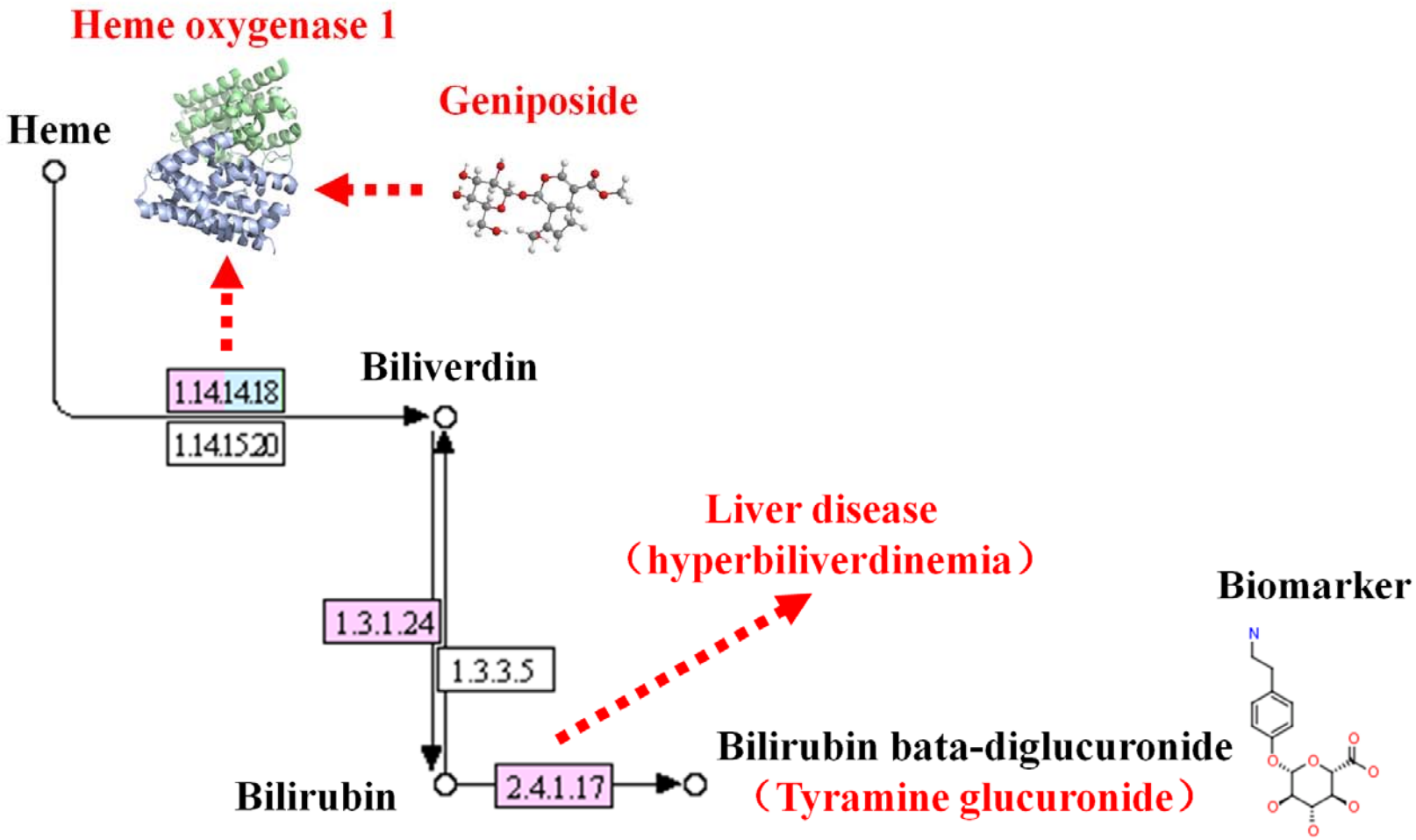

Fig. S1 The integrated analysis of metabolomics and network pharmacology

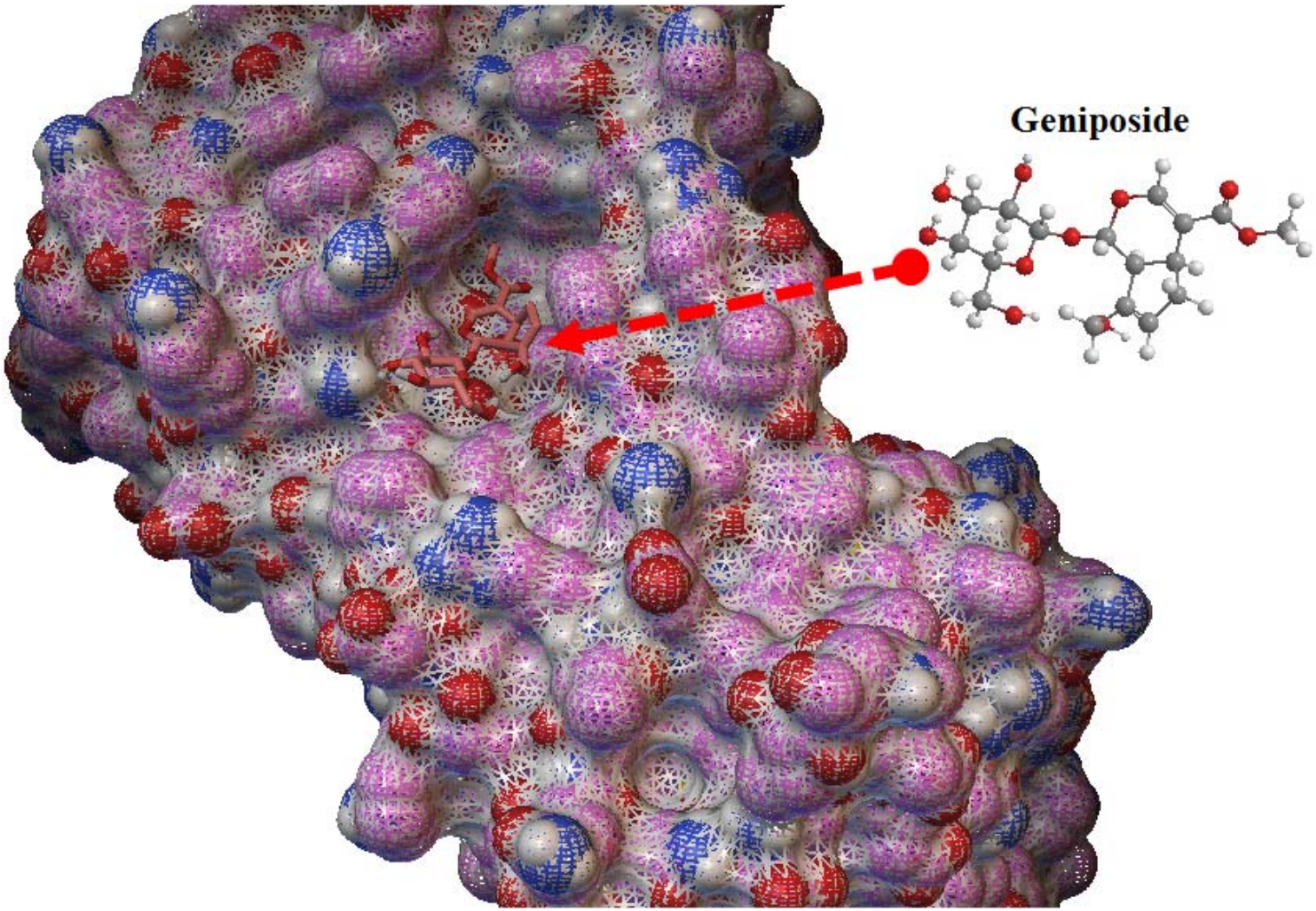

Fig. S2 The molecular docking result between heme oxygenase 1 and geniposide