Supplementary Figure

Fig. S1

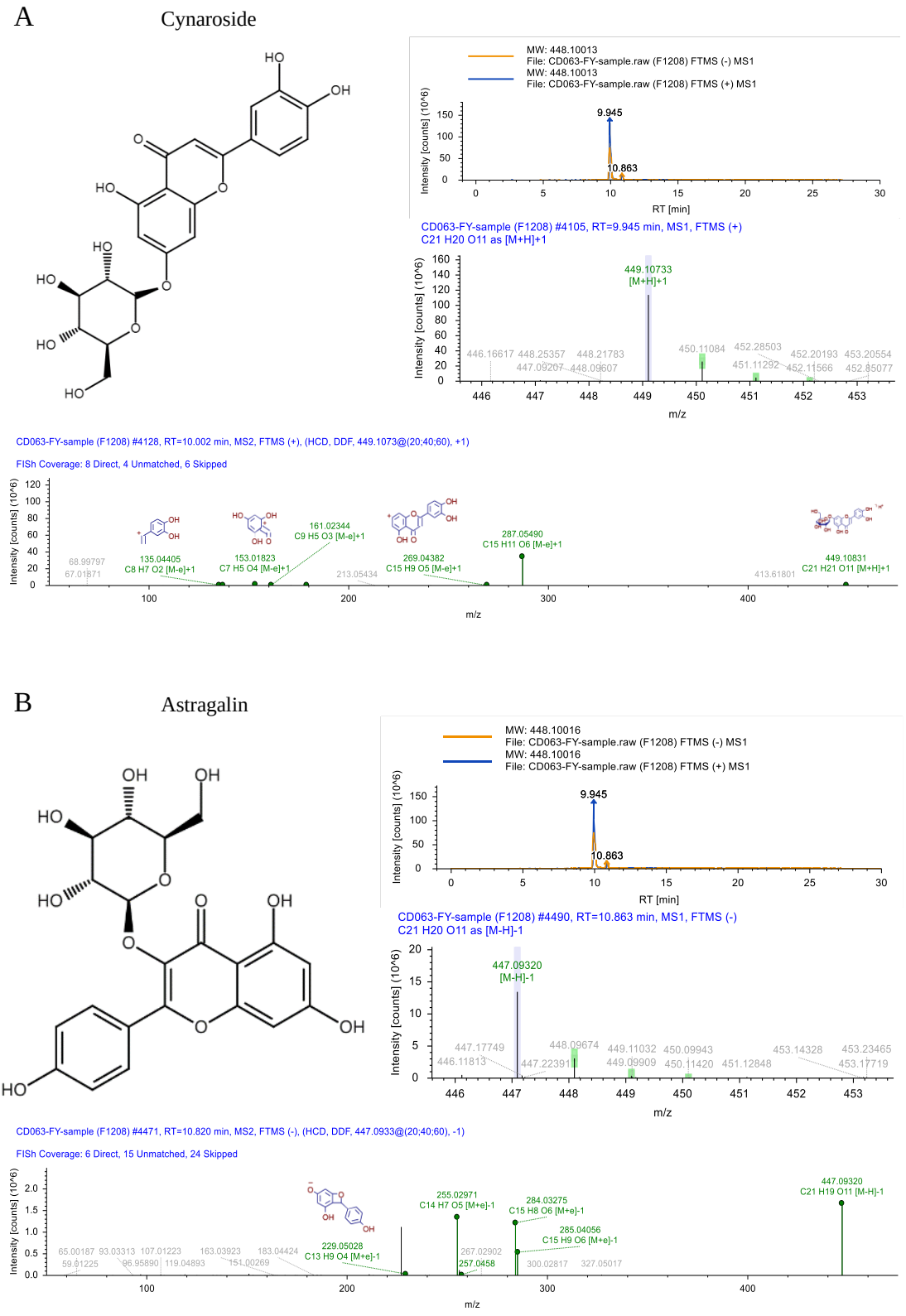
Supplementary figure legends and tables

Supplementary A

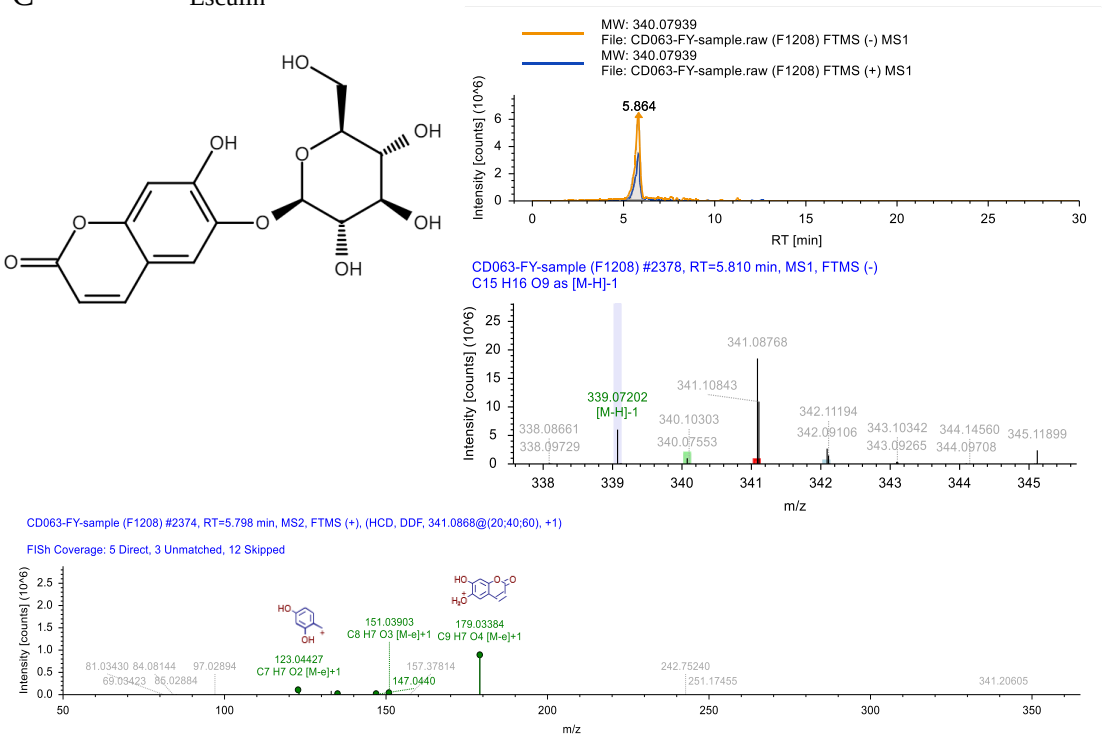
Fig. S1. The chromatography and mass spectrum for eight compounds from CQCQD

Fig. S2. Total ion flow spectrum of HBG

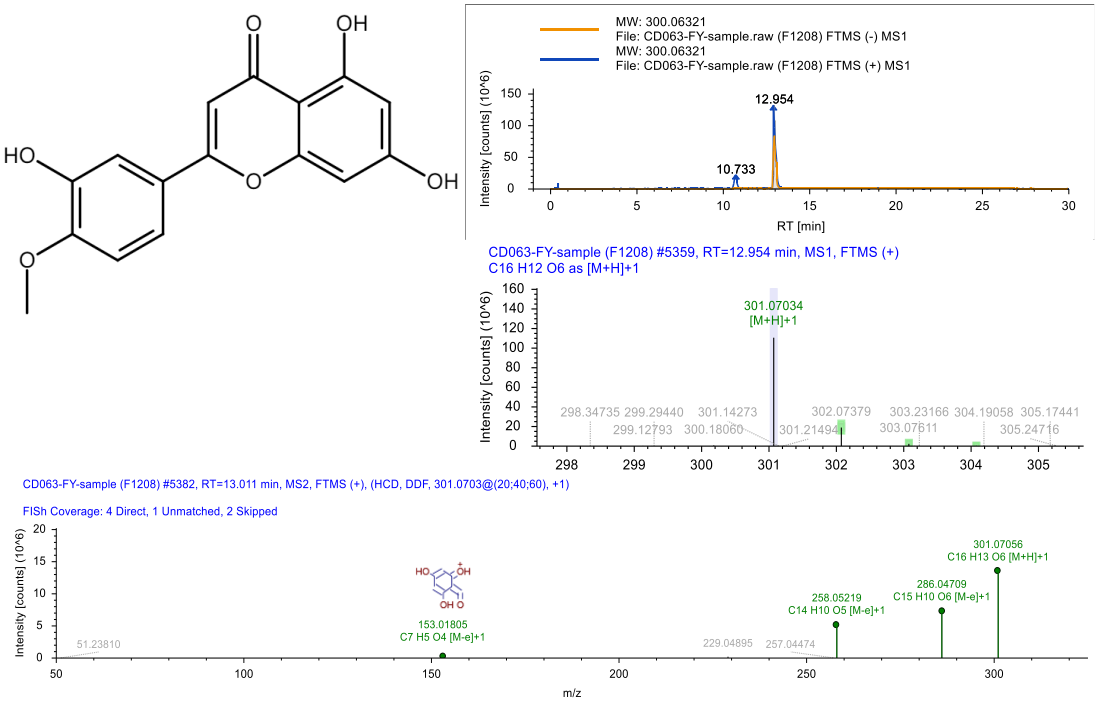
Fig. S3. The flowchart of pharmacology network construction.

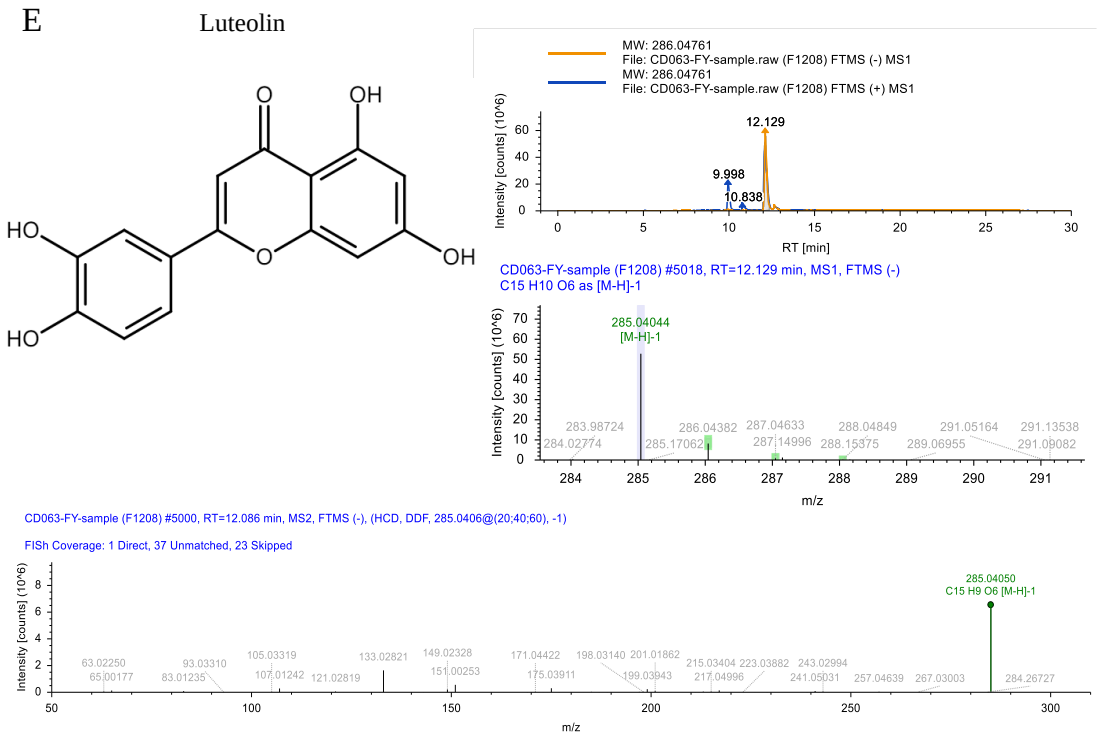


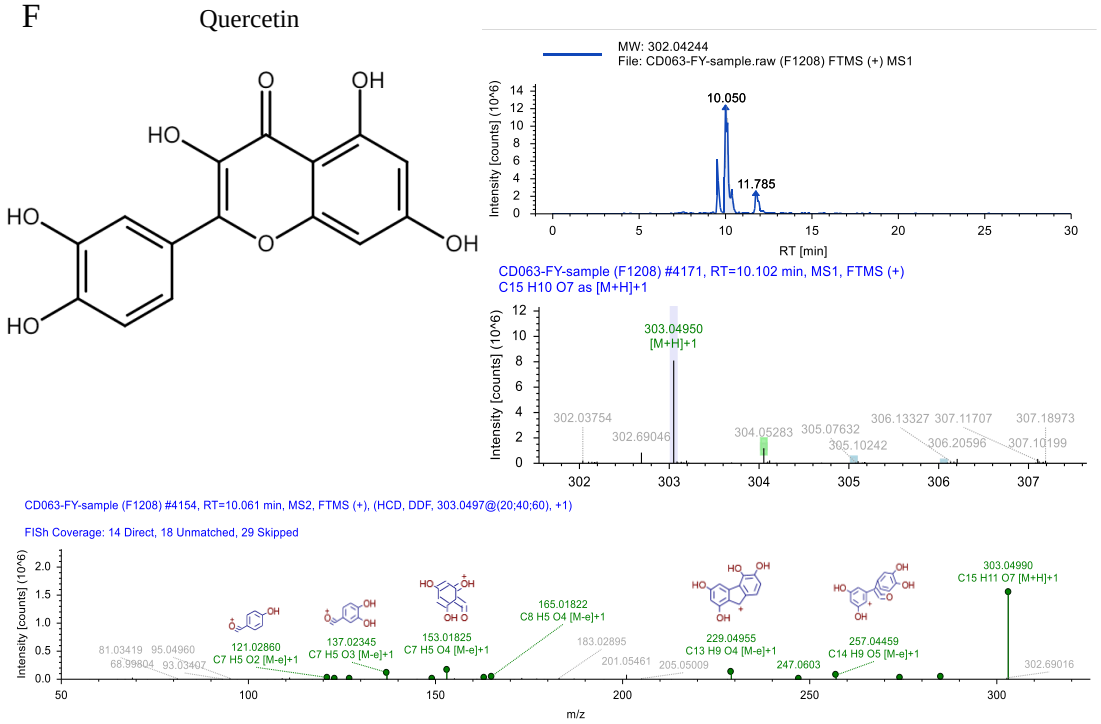
C Esculin



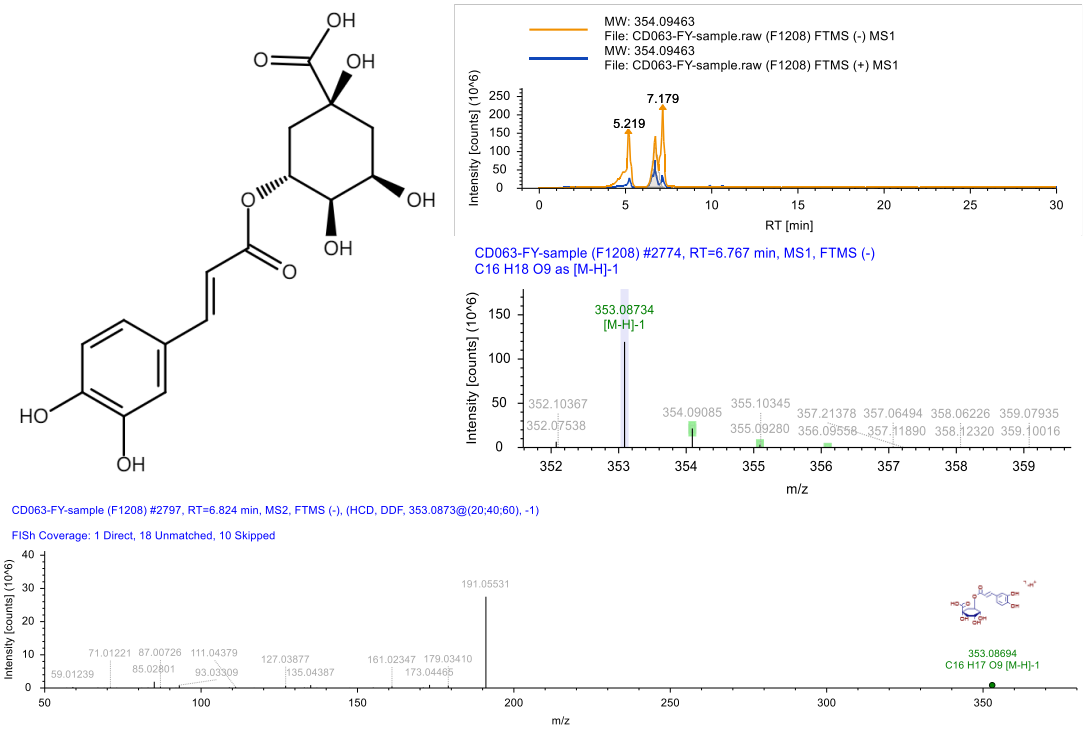
D Diosmetin



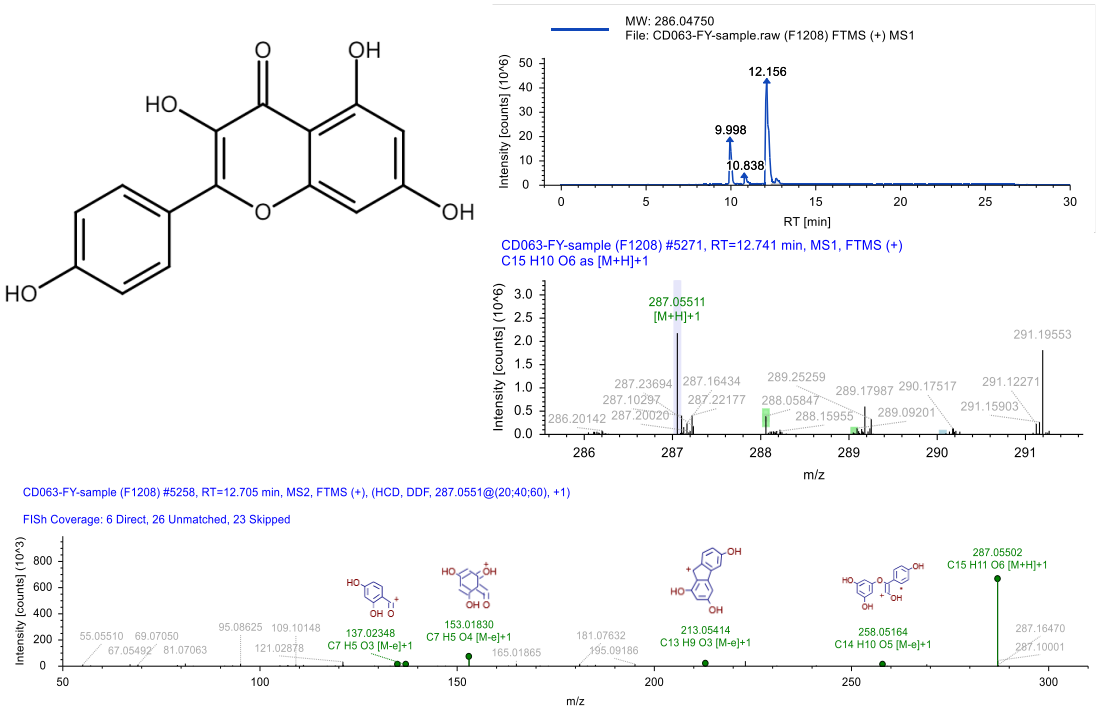

E
Luteolin
MW: 286.04761
File: CD063-FY-sample.raw (F1208) FTMS (-) MS1
MW: 286.04761
File: CD063-FY-sample.raw (F1208) FTMS (+) MS1
Intensity [counts] (10^6)
12.129
9.998
10.838
RT [min]
CD063-FY-sample (F1208) #5018, RT=12.129 min, MS1, FTMS (-)
C15 H10 O6 as [M-H]-1
285.04044
[M-H]-1
m/z
CD063-FY-sample (F1208) #5000, RT=12.086 min, MS2, FTMS (-), (HCD, DDF, 285.0406@(20;40;60), -1)
FISh Coverage: 1 Direct, 37 Unmatched, 23 Skipped
285.04050
C15 H9 O6 [M-H]-1


F
Quercetin
MW: 302.04244
File: CD063-FY-sample.raw (F1208) FTMS (+) MS1
Intensity [counts] (10^6)
10.050
11.785
RT [min]
CD063-FY-sample (F1208) #4171, RT=10.102 min, MS1, FTMS (+)
C15 H10 O7 as [M+H]+1
303.04950
[M+H]+1
m/z
CD063-FY-sample (F1208) #4154, RT=10.061 min, MS2, FTMS (+), (HCD, DDF, 303.0497@(20;40;60), +1)
FISh Coverage: 14 Direct, 18 Unmatched, 29 Skipped
303.04990
C15 H11 O7 [M+H]+1
121.02860
C7 H5 O2 [M-e]+1
137.02345
C7 H5 O3 [M-e]+1
153.01825
C7 H5 O4 [M-e]+1
165.01822
C8 H5 O4 [M-e]+1
229.04955
C13 H9 O4 [M-e]+1
257.04459
C14 H9 O5 [M-e]+1

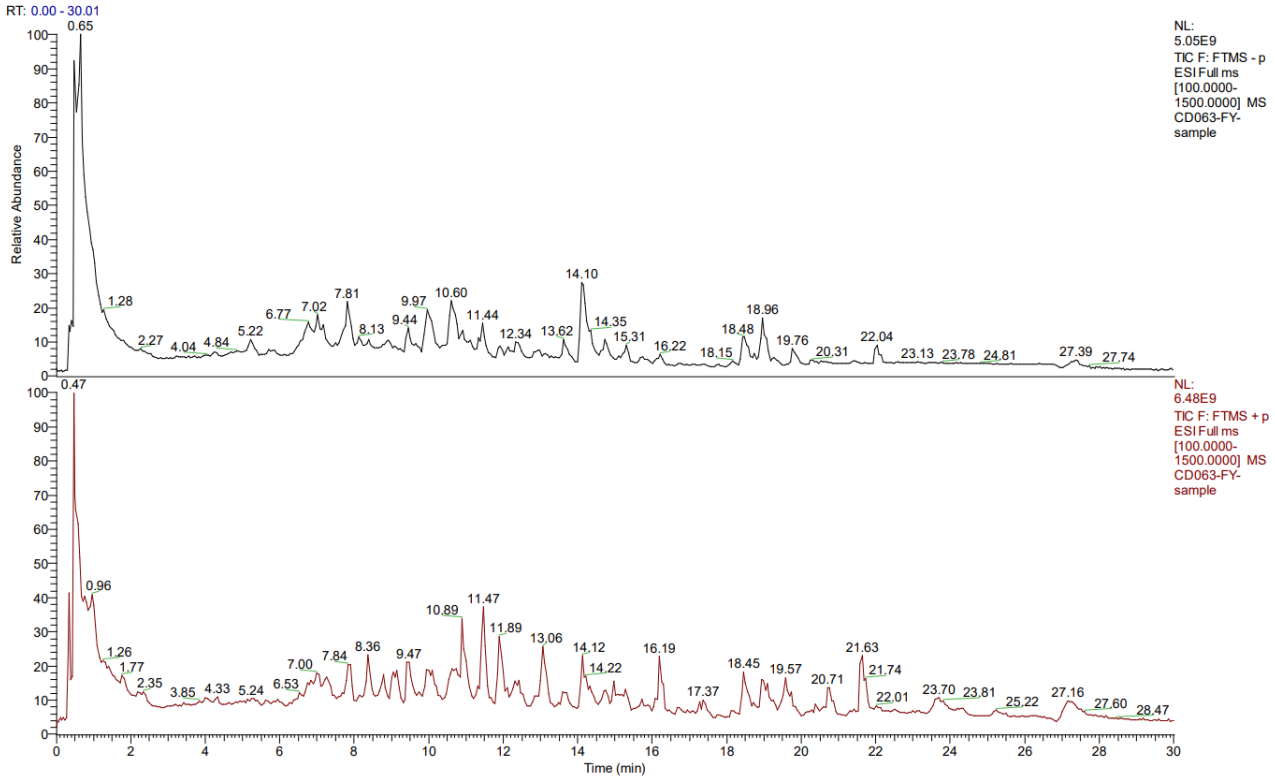
G Chlorogenic acid

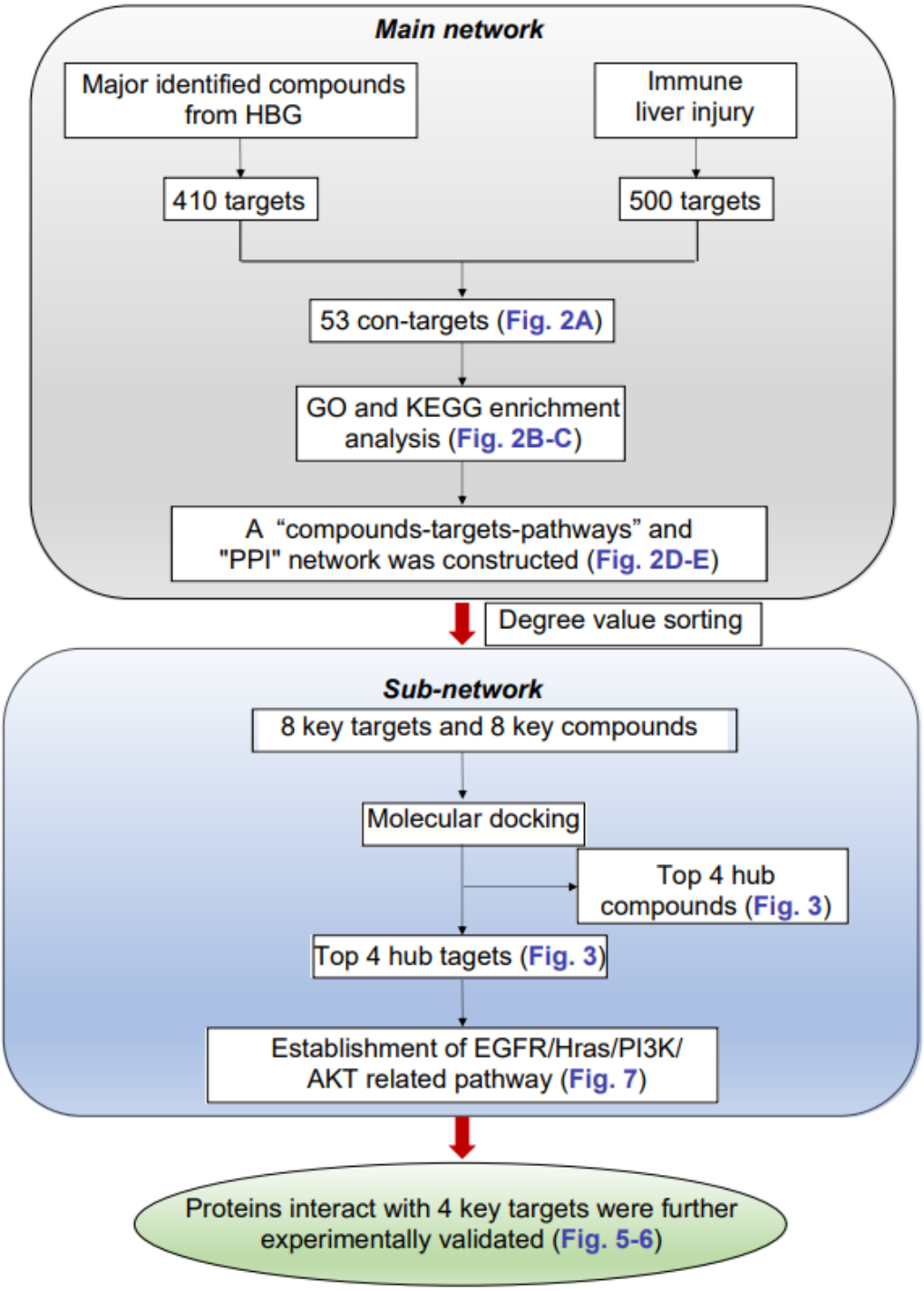


H Kaempferol



Supplementary Figure Fig. S2




Main network
Major identified compounds from HBG
Immune liver injury
410 targets
500 targets
53 con-targets (Fig. 2A)
GO and KEGG enrichment analysis (Fig. 2B-C)
A "compounds-targets-pathways" and "PPI" network was constructed (Fig. 2D-E)
Degree value sorting
Sub-network
8 key targets and 8 key compounds
Molecular docking
Top 4 hub compounds (Fig. 3)
Top 4 hub tagets (Fig. 3)
Establishment of EGFR/Hras/PI3K/ AKT related pathway (Fig. 7)
Proteins interact with 4 key targets were further experimentally validated (Fig. 5-6)

Supplementary B

Supplementary Table 1. Identified compounds with high intensity (mzCloud score> 80) from HBG by LC-ESI-QTOF/MS**.**

NO.	Comound name	Formula	Retention time	[M+H]+/[M-H]- (mDa, ppm)	mzCloud score	Fragment ions (m/z)
1	Diosmetin	$C_{16}H_{12}O_6$	12.98	301.0703	97.9	(+) 286.0471, 258.0522, 153.0181
2	Quercetin	$C_{15}H_{10}O_7$	10.10	303.0495	91.6	(+) 257.0446, 229.0496, 153.0813
3	Luteolin	$C_{15}H_{10}O_6$	12.13	285.0404	85.3	(-) 199.0394, 175.0391, 151.0025, 133.0282
4	Kaempferol	$C_{15}H_{10}O_6$	12.74	287.0551	82.4	(+) 258.0516, 213.0541, 165.0187, 153.0183, 137.0235
5	Cynaroside	$C_{10}H_8O_4$	9.95	449.1073	94.7	(+) 287.0549, 269.0438, 161.0234,153.0182
6	Apigenin	$C_{15}H_{10}O_5$	12.85	271.0600	95.0	(+) 153.0182, 145.0286, 119.0494
7	Astragalin	$C_{21}H_{20}O_{11}$	10.86	447.0932	89.4	(-) 285.0406, 284.0328, 257.0458, 255.0297, 229.0503
8	Esculin	$C_{15}H_{16}O_9$	5.81	341.0868	91.2	(+) 179.0338, 151.0390, 123.0443
9	Esculetin	$C_9H_6O_4$	6.59	179.0338	86.1	(+) 151.0389, 133.0285, 123.0442
10	Apigetrin	$C_{21}H_{20}O_{10}$	10.63	433.1123	94.0	(+) 271.0599, 153.0182, 145.0284, 119.0494
11	Chlorogenic acid	$C_{16}H_{18}O_9$	7.84	353.0873	89.0	(-) 191.0553, 173.0447, 93.0331
12	Vanillin	$C_8H_8O_3$	7.21	153.0545	85.3	(+) 153.0545, 125.0598, 111.0443, 93.0340, 65.0394
13	Caffeic acid	$C_9H_8O_4$	6.82	179.0339	82.2	(-) 135.0439, 134.0361, 117.0331, 107.0489
14	Scopoletin	$C_{10}H_8O_4$	8.42	193.0494	89.4	(+) 178.0260, 165.0548, 137.0596, 133.0284
15	Isoquercetin	$C_{21}H_{20}O_{12}$	10.08	463.0882	94.9	(-) 301.0356, 300.0277, 271.0249, 151.0026
16	Citric acid	$C_6H_8O_7$	0.69	191.0188	82.0	(-) 129.0180, 111.0074, 87.0073, 85.0280
17	Nicotinic acid	$C_6H_5NO_6$	0.77	124.0396	92.5	(+) 80.0502, 78.0344, 53.0395

18	Nootkatone	$C_{15}H_{22}O$	13.11	219.1742	89.4	(+) 201.1639, 163.1118, 109.1016, 81.0706
19	Azelaic acid	$C_9H_{16}O_4$	10.60	187.0966	83.8	(-) 125.0959, 97.0645
20	Palmitic acid	$C_{16}H_{32}O_2$	20.31	256.24	99.4	(-) 255.2328, 237.2212
21	Adenosine	$C_{10}H_{13}N_5O_4$	1.78	258.1040	98.0	(+) 137.0458, 136.0618, 119.0350
22	L-Phenylalanine	$C_9H_{11}NO_2$	2.20	166.0864	97.1	(+) 131.0492, 120.0809, 103.0546
23	Methoxsalen	$C_{12}H_8O_4$	11.05	217.0493	96.8	(+) 189.0547, 185.0235, 173.0599
24	Erucamide	$C_{22}H_{43}NO$	19.36	338.3412	96.1	(+) 321.3151, 149.1323, 121.1015
25	Stearamide	$C_{18}H_{37}NO$	20.39	284.2944	95.3	(+) 284.2947
26	D-Sphingosine	$C_9H_{11}NO_3$	15.23	300.2894	92.8	(+) 282.2790, 252.2683, 211.2043
27	L-Tyrosine	$C_{18}H_{37}NO_2$	1.04	182.0813	90.6	(+) 165.0546, 147.0440, 136.0756, 123.0442
28	Maltol	$C_6H_6O_3$	3.96	127.0396	90.3	(+) 109.0288, 81.0324, 55.0188, 53.0395
29	Choline	$C_5H_{13}NO$	0.45	104.1074	89.9	(+) 60.0816, 59.0738, 58.0660
30	Neochlorogenic acid	$C_{16}H_{18}O_9$	4.89	353.0876	88.9	(-) 191.0553, 179.0340
31	Uridine	$C_9H_{12}N_2O_6$	1.23	243.0620	86.3	(-) 200.0557, 182.0447, 111.0187, 110.0233
32	Hypoxanthine	$C_5H_4N_4O$	2.35	137.0460	85.1	(+) 119.0490, 95.0860, 81.0706,
33	Dibutyl phthalate	$C_{16}H_{22}O_4$	16.19	279.1588	83.3	(+) 205.0863, 149.0233
34	Betaine	$C_5H_{11}NO_2$	0.63	118.0866	83.1	(+) 59.0739, 58.0660
35	3-Phenyllactic acid	$C_9H_{10}O_3$	7.86	165.0546	82.0	(-) 147.0440, 119.0489,
36	Hesperidin	$C_{28}H_{34}O_{15}$	10.50	609.1826	81.7	(-) 301.0717, 286.0483, 242.0582
37	Suberic acid	$C_8H_{14}O_4$	8.92	173.0810	81.4	(-) 129.0909, 111.0802, 83.0487
38	Psoralen	$C_{11}H_6O_3$	10.80	187.0389	80.4	(+) 159.0440, 143.0491, 131.0492, 115.0545

Supplementary Table 2. The list of 16 accurately identified compounds from HBG.

No.	Compound	Formula	Source
1	**Diosmetin**	**$C_{16}H_{12}O_6$**	*Apium graveolens L.*
2	**Quercetin**	**$C_{15}H_{10}O_7$**	*Cuscuta chinensis Lam.*
			Foeniculum vulgare Mill.
			Cichorium intybus L.
3	**Luteolin**	**$C_{15}H_{10}O_6$**	*Apium graveolens L.*
			Foeniculum vulgare Mill.
4	**Kaempferol**	**$C_{15}H_{10}O_6$**	*Apium graveolens L.*
			Cuscuta chinensis Lam.
			Foeniculum vulgare Mill.
			Cichorium intybus L.
5	**Cynaroside**	**$C_{10}H_8O_4$**	*Apium graveolens L.*
			Cichorium intybus L.
6	**Apigenin**	**$C_{15}H_{10}O_5$**	*Apium graveolens L.*
7	**Astragalin**	**$C_{21}H_{20}O_{11}$**	*Cuscuta chinensis Lam.*
8	**Esculin**	**$C_{15}H_{16}O_9$**	*Cichorium intybus L*
9	**Esculetin**	**$C_9H_6O_4$**	*Cichorium intybus L*
10	**Apigetrin**	**$C_{21}H_{20}O_{10}$**	*Apium graveolens L.*
11	**Chlorogenic acid**	**$C_{16}H_{18}O_9$**	*Apium graveolens L.*
12	**Vanillin**	**$C_8H_8O_3$**	*Cichorium intybus L.*
13	**Caffeic acid**	**$C_9H_8O_4$**	*Cichorium intybus L.*
14	**Scopoletin**	**$C_{10}H_8O_4$**	*Foeniculum vulgare Mill.*
15	**Isoquercetin**	**$C_{21}H_{20}O_{12}$**	*Cuscuta chinensis Lam.*
16	**Citric acid**	**$C_6H_8O_7$**	*Cichorium intybus L.*

Supplementary Table 3. The specific result of molecular docking.

Compound	Libdock score							
	HRAS (4XVR)	EGFR (6LUD)	AKT1 (4EJN)	PIK3R1 (4L23)	MAPK14 (6ANL)	AKT2 (3D0E)	MAPK1 (2OJJ)	MAPK8 (4L7F)
Cynaroside	169.85	154.22	155.06	148.14	127.356	134.732	129.942	126.701
Astragalin	146.41	130.01	128.66	133.60	114.014	116.025	111.691	107.498
Esculin	139.28	130.80	122.06	119.84	109.742	112.36	116.065	112.933
Diosmetin	129.78	115.96	114.70	115.33	113.927	104.154	104.17	108.695
Luteolin	121.42	120.45	117.39	112.15	101.379	105.345	107.593	102.128
Quercetin	123.54	115.51	110.33	111.28	106.636	105.121	104.954	105.114
Chlorogenic acid	126.43	114.09	105.28	107.51	104.946	100.377	107.285	97.614
Kaempferol	113.01	111.68	111.99	101.51	101.379	99.217	94.709	100.84
Prednisolone	128.43	100.59	116.86	108.46	109.14	105.62	104.54	105.50