Table S1 Candidate compounds and the degree values

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Table S5 The crystal structure of target protein and the docking fraction with the optimal ligand

Figure S1 The “candidate compounds-targets” network

Figure S2 The body weight change and relative liver weight of female mice

Figure S3 The H&E stain **(A)** and serum biochemical indexes **(B)** of female mice

Table S1 Candidate compounds and the degree values

ID	Name	Degree
1	Ribalinine	153
2	3-(2-hydroxyethyl)-4-methoxy-2(1*H*)-quinolinone	111
3	Isodictamnine	29
4	8-methoxymyrtopsine	188
5	4-hydroxy-1-methyl-2(1*H*)-quinolinone	43
6	4-methoxy-2(1*H*)-quinolinone	264
7	(+)-cis-7,8-dimethoxymyrtopsine	12
8	*Iso*-*γ*-fagarine	79
9	Myrtopsine	105
10	Araliopsinine	151
11	8-hydroxy-platydesmine	93
12	1,2-dihydro-4-methoxy-1-methyl-2-oxo-, methyl ester-3-quinolinecarboxylic acids	98
13	(+)-7,8-dimethoxymyrtopsine	128
14	4-methoxy-1-methyl-2(1*H*)-quinolinone	70
15	Platydesmine	104
16	Haplopine	80
17	6-methoxydictamnine	43
18	Dasycarine D	139
19	7,8-dimethoxyplatydesmine	108
20	*γ*-fagarine	47
21	Skimmianine	62
22	2,6-dihydro-8-hydroxy-7-methoxy-2,2,6-trimethyl-5*H*-pyrano[3,2-c]quinolin-5-one	108
23	Dictamnine	34
24	Dihydroflindersine	104
25	2,4-hydroxy-3-(3'-methyl-2'-butenyl)-quinolin	140
26	Flindersine	100
27	8-methoxyflindersine	90
28	2-hydroxy-4-methoxy-3-(3'-methyl-2'-butenyl)-quinolin	147

29	2,6-dihydro-2,2,7-trimethyl-5*H*-pyrano[3,2-c]quinolin-5 one	73
30	Preskimmianine	168
31	8-methoxy-*N*-methylflindersine	71
32	*N*-metilatanina	24
33	Furo[2,3-b]quinoline-4,7-diol	61
34	2,3,4,10-tetrahydro-3-hydroxy-2,2-dimethyl-5*H*-pyrano[2,3-b]quinolin-5-one	137
35	2,3,4,10-tetrahydro-3,7-dihydroxy-2,2,10-trimethyl-5*H*-pyrano[2,3-b]quinolin-5-one	135
36	2,6-dihydro-8-hydroxy-2,2,6-trimethyl-5*H*-Pyrano[3,2-c]quinolin-5-one	90

Table S2 The targets of candidate compounds related with hepatotoxicity

ID	Uniprot ID	Gene name	Protein name
1	P02766	TTR	Transthyretin
2	P06737	PYGL	Glycogen phosphorylase, liver form
3	P00439	PAH	Phenylalanine-4-hydroxylase
4	P00374	DHFR	Dihydrofolate reductase
5	P11712	CYP2C9	Cytochrome P450 2C9
6	P05089	ARG1	Arginase-1
7	P02768	ALB	Serum albumin
8	Q00796	SORD	Sorbitol dehydrogenase
9	P04179	SOD2	Superoxide dismutase [Mn], mitochondrial
10	P00491	PNP	Purine nucleoside phosphorylase
11	P09211	GSTP1	Glutathione S-transferase P
12	P80188	LCN2	Neutrophil gelatinase-associated lipocalin
13	P00390	GSR	Glutathione reductase, mitochondrial
14	Q6ZQW0	IDO2	Indoleamine 2,3-dioxygenase 2
15	Q71U36	TUBA1A	Tubulin alpha-1A chain
16	P36897	TGFBR1	TGF-beta receptor type-1
17	P07451	CA3	Carbonic anhydrase 3
18	O00204	SULT2B1	Sulfotransferase 2B1

19	P49888	SULT1E1	Sulfotransferase 1E1
20	Q14994	NR1I3	Nuclear receptor subfamily 1 group I member 3
21	Q96RI1	NR1H4	Bile acid receptor
22	P08253	MMP2	72 kDa type IV collagenase
23	P32298	GRK4	G protein-coupled receptor kinase 4
24	P02774	GC	Vitamin D-binding protein
25	P01375	TNF	Tumor necrosis factor
26	O60427	FADS1	Acyl-CoA
27	P05177	CYP1A2	Cytochrome P450 1A2
28	P35869	AHR	Aryl hydrocarbon receptor
29	P08183	ABCB1	ATP-dependent translocase ABCB1
30	Q92887	ABCC2	Canalicular multispecific organic anion transporter 1
31	O60656	UGT1A9	UDP-glucuronosyltransferase 1A9
32	P08684	CYP3A4	Cytochrome P450 3A4
33	P05181	CYP2E1	Cytochrome P450 2E1
34	P17931	LGALS3	Galectin-3
35	P20309	CHRM3	Muscarinic acetylcholine receptor M3

Table S3 GO analysis results

Type	**No.**	**Name**	**Target number**	**-log$_{10}$*P***
BP	GO:0006805	xenobiotic metabolic process	7	8.00
	GO:0016098	monoterpenoid metabolic process	4	6.82
	GO:0055114	oxidation-reduction process	11	6.78
	GO:0008202	steroid metabolic process	5	5.79
	GO:0017144	drug metabolic process	4	4.67
	GO:0042493	response to drug	7	4.53
	GO:0042737	drug catabolic process	3	4.23
	GO:0046483	heterocycle metabolic process	3	4.23
	GO:0071222	cellular response to lipopolysaccharide	5	4.11

	GO:0070989	oxidative demethylation	3	3.59
	GO:0042738	exogenous drug catabolic process	3	3.59
	GO:0019373	epoxygenase P450 pathway	3	3.22
	GO:0046686	response to cadmium ion	3	2.94
	GO:2001237	negative regulation of extrinsic apoptotic signaling pathway	3	2.57
	GO:0000302	response to reactive oxygen species	3	2.55
MF	GO:0008144	drug binding	7	8.08
	GO:0019825	oxygen binding	6	7.45
	GO:0016491	oxidoreductase activity	7	5.58
	GO:0004497	monooxygenase activity	5	5.27
	GO:0005506	iron ion binding	6	4.89
	GO:0034875	caffeine oxidase activity	3	4.63
	GO:0020037	heme binding	5	3.80
	GO:0016712	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen	3	3.39
	GO:0008395	steroid hydroxylase activity	3	2.91
	GO:0004879	RNA polymerase II transcription factor activity	3	2.62
	GO:0002060	purine nucleobase binding	2	2.40
	GO:0016705	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	3	2.23
	GO:0050294	steroid sulfotransferase activity	2	2.10
	GO:0004887	thyroid hormone receptor activity	2	1.80
	GO:0032052	bile acid binding	2	1.80
CC	GO:0070062	extracellular exosome	17	4.87
	GO:0005829	cytosol	17	3.96
	GO:0005615	extracellular space	10	3.21
	GO:0031090	organelle membrane	3	1.94
	GO:0043231	intracellular membrane-bounded organelle	5	1.71

	GO:0005789	endoplasmic reticulum membrane	6	1.68
	GO:0043209	myelin sheath	3	1.49
	GO:0070062	extracellular exosome	17	4.87

Table S4 KEGG analysis results

No.	**Pathway**	**Targets number**	**-log$_{10}$*P***	**Target name**
hsa00140	Steroid hormone biosynthesis	6	5.60	SULT2B1, SULT1E1, CYP1A2, CYP2E1, UGT1A9, CYP3A4
hsa00982	Drug metabolism - cytochrome P450	6	5.26	CYP2C9, GSTP1, CYP1A2, CYP2E1, UGT1A9, CYP3A4
hsa00980	Metabolism of xenobiotics by cytochrome P450	6	5.07	CYP2C9, GSTP1, CYP1A2, CYP2E1, UGT1A9, CYP3A4
hsa05204	Chemical carcinogenesis	6	4.91	CYP2C9, GSTP1, CYP1A2, CYP2E1, UGT1A9, CYP3A4
hsa00591	Linoleic acid metabolism	4	3.73	CYP2C9, CYP1A2, CYP2E1, CYP3A4
hsa00830	Retinol metabolism	4	2.72	CYP2C9, CYP1A2, UGT1A9, CYP3A4
hsa01100	Metabolic pathways	12	2.38	DHFR, CYP2C9, PNP, ARG1, PAH, CYP1A2, SORD, CYP2E1, PYGL, UGT1A9, CYP3A4, IDO2
hsa04976	Bile secretion	3	1.53	ABCB1, ABCC2, NR1H4

Table S5 The crystal structure of target protein and the docking fraction with the optimal ligand

Target	**PDB**	**Ligand**	**Docking score**
FXR	1OSV	Obeticholic acid	-14.688
TNF	2AZ5	6,7-dimethyl-3-[[methyl[2-[methyl[[1-	-7.222

		[3-(trifluoromethyl)phenyl]-1*H*-indol-3-yl]methyl]amino]ethyl]amino]methyl]-4*H*-1-benzopyran-4-one	
PXR	3R8D	6-chloro-2-(1-furo[2,3-c]pyridin-5-yl-ethylsulfanyl)-pyrimidin-4-ylamine	-9.451
ALB	6HSC	Aristolochic acid	-12.171
CDK2	6INL	Cvt-313	-11.519
IDH2	5I96	Enasidenib	-15.831
GSR	1XAN	3,6-dihydroxy-xanthene-9-propionic acid	-3.979
P53	4XZV	Maltose	-11.183
CYP1A2	2HI4	Alpha-naphthoflavone	-8.948
CYP2C9	4NZ2	(2*R*)-*N*-[4-(3-bromophenyl)sulfonyl-2-chlorophenyl]-3,3,3-trifluoro-2-hydroxy-2-methylpropanamide	-6.308
CYP3A4	2V0M	Ketoconazole	-8.386
CYP2E1	3E6I	1*H*-indazole	-5.681

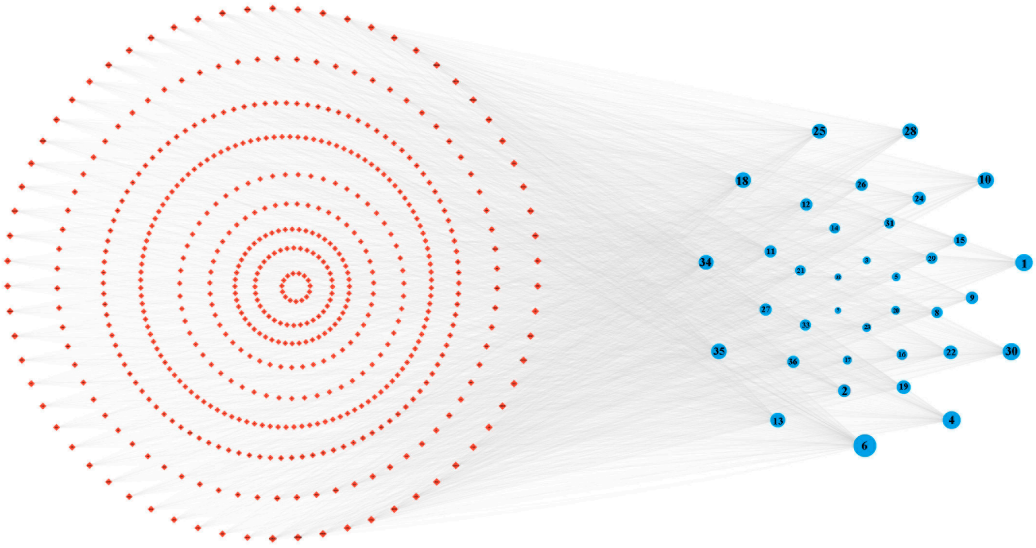


Figure S1 The “candidate compounds-targets” network

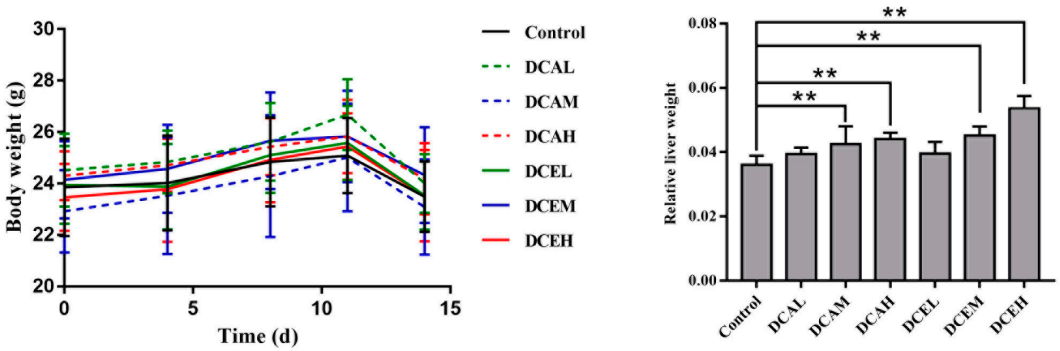


Figure S2 The body weight change and relative liver weight of female mice

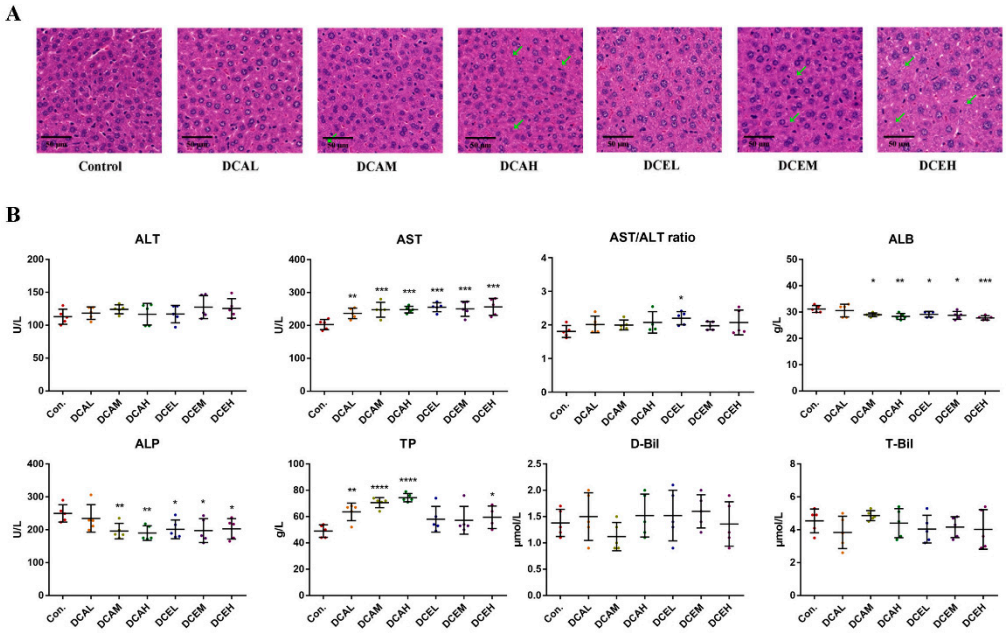


Figure S3 The H&E stain and weight change and relative liver weight of female mice