

## **Supplementary data**

# **Network Pharmacology-based Strategy for Predicting Active Ingredients and Potential Targets of LiuWei DiHuang Pill for Treating Type 2 Diabetes Mellitus**

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**Table S1: Compounds database of six herb in LiuWei DiHuang Pill**

Mol ID	Compound	MW	OB (%)	DL	Medicine	Database
MOL000359	sitosterol	414.79	36.91	0.75	SDH, SZY, MDP, ZX	TCMSP
MOL000449	Stigmasterol	412.77	43.83	0.76	SDH, SZY, SY,, ZX	TCMSP
MOL001494	Mandenol	308.56	42	0.19	SZY	TCMSP
MOL001495	Ethyl linolenate	306.54	46.1	0.2	SZY	TCMSP
MOL001771	poriferast-5-en-3beta-ol	414.79	36.91	0.75	SZY	TCMSP
MOL002879	Diop	390.62	43.59	0.39	SZY	TCMSP
MOL002883	Ethyl oleate (NF)	310.58	32.4	0.19	SZY	TCMSP
MOL003137	Leucanthoside	462.44	32.12	0.78	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL000358	beta-sitosterol	414.79	36.91	0.75	SZY	TCMSP
MOL005360	malkangunin	432.56	57.71	0.63	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL005481	2,6,10,14,18-pentamethylcosa-2,6,10,14,18-pentaene	342.67	33.4	0.24	SZY	TCMSP
MOL005486	3,4-Dehydrolycopene-16-al	548.92	46.64	0.49	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL005489	3,6-Digalloylglucose	484.4	31.42	0.66	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL005503	Cornudentanone	378.56	39.66	0.33	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL005530	Hydroxygenkwanin	300.28	36.47	0.27	SZY	TCMSP
MOL005531	Telocinobufagin	402.58	69.99	0.79	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL008457	Tetrahydroalstonine	352.47	32.42	0.81	SZY	TCMSP, Taiwan, BATMAN-TCM
MOL000554	gallic acid-3-O-(6'-O-galloyl)-glucoside	484.4	30.25	0.67	SZY, MDP	TCMSP, Taiwan
MOL005552	gemin D	634.49	68.83	0.56	SZY	TCMSP
MOL005557	lanosta-8,24-dien-3-ol,3-acetate	468.84	44.3	0.82	SZY	TCMSP
MOL000098	quercetin	302.25	46.43	0.28	MDP	TCMSP
MOL000211	betulinic acid	456.78	55.38	0.78	MDP	TCMSP
MOL000422	kaempferol	286.25	41.88	0.24	MDP	TCMSP

MOL000492	(+)-catechin	290.29	54.83	0.24	MDP	TCMSP
MOL001925	paeoniflorin_qt	318.35	68.18	0.4	MDP	TCMSP
MOL007003	benzoyl paeoniflorin	584.62	31.14	0.54	MDP	TCMSP
MOL007369	4-O-methylpaeoniflorin_qt	332.38	67.24	0.43	MDP	TCMSP
MOL007374	5-[[5-(4-methoxyphenyl)-2-furyl]methylene]barbituric acid	312.3	43.44	0.3	MDP	TCMSP
MOL007382	mudanpioside-h_qt 2	336.37	42.36	0.37	MDP	TCMSP
MOL007384	paeonianin_qt	330.41	65.31	0.35	MDP	TCMSP
MOL007025	isobenzoylpaeoniflorin	584.62	31.14	0.54	MDP	Taiwan, BATMAN-TCM
MOL001924	paeoniflorin	480.51	53.87	0.79	MDP, FL	BATMAN-TCM
MOL002222	Sugiol	300.48	36.11	0.28	MDP	BATMAN-TCM, Taiwan
MOL001559	piperlonguminine	273.36	30.71	0.18	SY	TCMSP
MOL001736	(-)taxifolin	304.27	60.51	0.27	SY	TCMSP
MOL000310	Denudatin B	356.45	61.47	0.38	SY	TCMSP
MOL000322	Kadsurenone	356.45	54.72	0.38	SY	TCMSP
MOL005429	hancinol	372.5	64.01	0.37	SY	TCMSP
MOL005430	hancinone C	400.51	59.05	0.39	SY	TCMSP
MOL005435	24-Methylcholest-5-enyl-3beta-O-glucopyranoside_qt	400.76	37.58	0.72	SY	TCMSP
MOL005438	campesterol	400.76	37.58	0.71	SY	TCMSP, BATMAN-TCM
MOL005440	Isofucosterol	412.77	43.78	0.76	SY	TCMSP
MOL005458	Dioscoreside C_qt	444.72	36.38	0.87	SY	TCMSP
MOL000546	diosgenin	414.69	80.88	0.81	SY	TCMSP,BATMAN-TCM
MOL005461	Doradexanthin	584.96	38.16	0.54	SY	TCMSP
MOL005463	Methylcimicifugoside_qt	556.81	31.69	0.24	SY	TCMSP
MOL005465	AIDS180907	394.45	45.33	0.77	SY	TCMSP
MOL000953	CLR	386.73	37.87	0.68	SY	TCMSP
MOL004580	cis-Dihydroquercetin	304.27	66.44	0.27	SY	BATMAN-TCM

MOL000273	16 $\alpha$ -Hydroxydehydrotrametenolic acid	470.76	30.93	0.81	FL	TCMSP
MOL000275	trametenolic acid	456.78	38.71	0.8	FL	TCMSP
MOL000276	7,9(11)-dehydropachymic acid	526.83	35.11	0.81	FL	TCMSP, Taiwan
MOL000279	Cerevisterol	430.74	37.96	0.77	FL	TCMSP
MOL000280	Dehydrotumulosic acid	484.79	31.07	0.82	FL	TCMSP
MOL000282	5-Dihydroergosterol	398.74	43.51	0.72	FL	TCMSP
MOL000283	Ergosterol peroxide	430.74	40.36	0.81	FL	TCMSP
MOL000285	Dehydrotumulosic acid	482.77	38.26	0.82	FL	TCMSP
MOL000287	3beta-Hydroxy-24-methylene-8-lanostene-21-oic acid	470.81	38.7	0.81	FL	TCMSP
MOL000289	pachymic acid	528.85	33.63	0.81	FL	TCMSP.Taiwan
MOL000290	Poricoic acid A	498.77	30.61	0.76	FL	TCMSP,Taiwan
MOL000291	Poricoic acid B	484.74	30.52	0.75	FL	TCMSP,Taiwan
MOL000292	poricoic acid C	482.77	38.15	0.75	FL	TCMSP,Taiwan
MOL000296	hederagenin	414.79	36.91	0.75	FL	TCMSP
MOL000300	dehydroeburicoic acid	453.75	44.17	0.83	FL	TCMSP,Taiwan
MOL000073	ent-Epicatechin	290.29	48.96	0.24	FL	Taiwan
MOL001921	Lactiflorin	462.49	49.12	0.8	FL	Taiwan
MOL000854	alisol C	486.76	32.7	0.82	FL, ZX	Taiwan
MOL000830	Alisol B	472.78	34.47	0.82	FL, ZX	Taiwan
MOL000831	Alisol B monoacetate	514.82	35.58	0.81	ZX	TCMSP,Taiwan,BATMAN-TCM
MOL000849	16 $\beta$ -methoxyalisol B monoacetate	544.85	32.43	0.77	ZX	TCMSP
MOL000856	alisol C monoacetate	514.77	33.06	0.83	ZX	TCMSP
MOL002464	1-Monolinolein	354.59	37.18	0.3	ZX	TCMSP
MOL000862	Alisol B 23-acetate	514.82	35.58	0.81	FL, ZX	TCMSP, Taiwan
MOL001396	PENTADECYLIC ACID	242.45	20.18	0.08	SDH	TCMSP
MOL001501	Daturic acid	270.51	18.51	0.12	SDH,SZY,	TCMSP

MOL001772	Dihydro-beta-ionone	194.35	26.25	0.05	SDH	TCMSP
MOL000003	MTL	182.2	17.73	0.03	SDH	TCMSP
MOL000305	lauric acid	200.36	23.59	0.04	SDH,SZY,FL	TCMSP
MOL000346	succinic acid	118.1	29.62	0.01	SDH	TCMSP
MOL003694	Cerebrosid	266.29	13.81	0.11	SDH	TCMSP
MOL003697	methyl 9,10-methylene-hexadecanoate	282.52	22.94	0.15	SDH	TCMSP
MOL003707	jioglutin C	232.26	2.55	0.13	SDH	TCMSP
MOL003719	methyl-2,6,10-trimethyltridecanoate	269.5	24.86	0.1	SDH	TCMSP
MOL003722	(3aS,4R,6aS)-4-hydroxy-6,6a-dimethylol-3a,4-dihydro-3H-cyclopenta furan-2-one	200.21	29.92	0.08	SDH	TCMSP
MOL003731	Rehmaglutin A	202.23	29.7	0.1	SDH	TCMSP,BATMAN-TCM
MOL000284	L-uridine	244.23	23.4	0.11	SDH,FL	TCMSP,BATMAN-TCM
MOL000105	protocatechuic acid	154.13	25.37	0.04	SZY,FL	TCMSP
MOL001393	myristic acid	228.42	21.18	0.07	SZY	TCMSP
MOL001394	Oktadekan	254.56	9.81	0.09	SZY	TCMSP
MOL001562	Nonadecene	266.57	5.23	0.11	SZY	TCMSP
MOL001600	copaene	204.39	29.47	0.12	SZY	TCMSP
MOL001618	Pellitorin	223.4	23.81	0.06	SZY,SY	TCMSP,Taiwan
MOL001619	UPL	268.59	8.52	0.11	SZY	TCMSP
MOL001681	loganetin	228.27	29.99	0.1	SZY	TCMSP
MOL001683	morroniside_qt	244.27	1.68	0.12	SZY	TCMSP,BATMAN-TCM
MOL001816	Amide HPL	255.5	19.79	0.1	SZY	TCMSP
MOL000223	caffeic acid	180.17	25.76	0.05	SZY,MDP	TCMSP
MOL002343	tetrandrine	622.82	26.64	0.1	SZY	TCMSP
MOL002534	1,6-dimethyl-4-isopropyl-1,2,3,4,4a,7-hexahydronaphthalene	204.39	17.14	0.08	SZY	TCMSP
MOL000261	Myristicin	192.23	17.99	0.07	SZY	TCMSP

MOL000269	Elemicin	208.28	21.94	0.06	SZY	TCMSP,BATMAN-TCM
MOL000027	alpha-Curcumene	202.37	4.68	0.06	SZY	TCMSP
MOL002703	OCTADECENE	252.54	19.21	0.09	SZY	TCMSP
MOL003080	2-METHYLPENTADECANE	226.5	4.35	0.06	SZY	TCMSP
MOL000034	2-[(1R,3S,4S)-3-isopropenyl-4-methyl-4-vinylcyclohexyl]propan-2-ol	222.41	19.03	0.07	SZY	TCMSP
MOL003484	PEY	178.24	25.7	0.1	SZY	TCMSP
MOL003573	calacorene	200.35	16.2	0.08	SZY	TCMSP
MOL003940	Stearamide	283.56	18.44	0.14	SZY	TCMSP
MOL004284	2-Nonadecanone	282.57	14.38	0.14	SZY	TCMSP
MOL000431	coumarin	146.15	29.17	0.04	SZY	TCMSP
MOL004590	2-METHYLHEXADECANE	240.53	4.19	0.07	SZY	TCMSP
MOL004784	Stenol	270.56	12.66	0.11	SZY	TCMSP
MOL000052	Gulutamine	147.15	6.66	0.02	SZY,SY	TCMSP
MOL005306	Acetal	118.2	26.4	0.01	SZY	TCMSP
MOL005470	Durol	134.24	17.74	0.03	SZY	TCMSP
MOL005473	1,5-DIACETYLNAPHTHALENE	212.26	11.6	0.1	SZY	TCMSP
MOL005474	1-Acetyl-4,6,8-trimethylazulene	212.31	27.02	0.09	SZY	TCMSP
MOL005475	Chloroicosane	317.06	10.43	0.15	SZY	TCMSP
MOL005477	Eicosene	280.6	17.83	0.13	SZY	TCMSP
MOL005488	3,5-Di-t-butyl-4-hydroxybenzaldehyde	234.37	27.19	0.08	SZY	TCMSP
MOL005494	6-Tetradecanesulfonic acid, butyl ester	334.63	21.36	0.13	SZY	TCMSP
MOL005495	6-ethyl-2,5-dihydroxy-1,4-naphthoquinone	218.22	20.58	0.1	SZY	TCMSP
MOL005498	7-Hydroxycadalene	214.33	29.3	0.09	SZY	TCMSP
MOL005501	Green Oil	178.24	17.74	0.1	SZY	TCMSP
MOL005504	Cornusiin A	1557.19	7.95	0.01	SZY	TCMSP,Taiwan
MOL005505	Cornusiin B	1086.77	17.84	0.01	SZY	TCMSP,Taiwan

MOL005506	Cornusiin C	784.57	3.01	0.14	SZY	TCMSP,Taiwan,BATMAN-TCM
MOL005507	Cornusiin G	1725.3	6.95	0.01	SZY	TCMSP,Taiwan
MOL005510	D-1-O-Methyl mucoinositol	194.21	25.11	0.05	SZY	TCMSP,Taiwan
MOL005514	Ethyl,alpha-hydroxymyristate	272.48	18.71	0.11	SZY	TCMSP
MOL005515	Eugenone	252.29	18.7	0.1	SZY	TCMSP,Taiwan,BATMAN-TCM
MOL005516	Fluoren	166.23	18.94	0.08	SZY	TCMSP
MOL005517	2-METHYLHEPTADECANE	254.56	10.57	0.09	SZY	TCMSP
MOL005518	Heptadecane,3-methyl	254.56	10.57	0.09	SZY	TCMSP
MOL005519	(7R)-7-methylheptadecane	254.56	10.57	0.08	SZY	TCMSP
MOL005520	Heptadecane,8-methyl	254.56	10.57	0.08	SZY	TCMSP
MOL005521	phytane	282.62	13.86	0.11	SZY	TCMSP
MOL005523	Nonadecane,2,3-di methyl	296.65	11.6	0.15	SZY	TCMSP
MOL005525	Octadecane,2,6,10,14-tetramethyl	310.68	13.58	0.15	SZY	TCMSP
MOL005526	Octadecane,3-methyl	268.59	10.42	0.11	SZY	TCMSP
MOL005527	Octadecane,6-methyl	268.59	10.42	0.1	SZY	TCMSP
MOL005528	2,6,10,14-tetramethylpentadecane	268.59	3.6	0.09	SZY	TCMSP
MOL005529	Pentadecane,2,6,10-trimethyl	254.56	13.33	0.08	SZY	TCMSP
MOL005532	Tetradecane,2,6,10-trimethyl	240.53	3.93	0.06	SZY	TCMSP
MOL005537	Z-5-Nonadecene	266.57	18.81	0.11	SZY	TCMSP
MOL005539	Acenaphthylene	152.2	28.55	0.07	SZY	TCMSP
MOL005540	alpha-Corocalene	200.35	13.97	0.08	SZY	TCMSP,Taiwan,BATMAN-TCM
MOL005542	camptothin A	1571.17	6.27	0.02	SZY	TCMSP
MOL005543	camptothin B	1086.77	3.01	0.04	SZY	TCMSP
MOL005545	cornin_qt	226.25	25.1	0.1	SZY	TCMSP
MOL005548	cornusiin E	1857.37	7.37	0	SZY	TCMSP
MOL005550	Vanirom	166.19	28.07	0.04	SZY	TCMSP

MOL007019	Eugenin	938.7	10.06	0.13	SZY	TCMSP,BATMAN-TCM
MOL005554	i-Butanol	74.14	28.26	0	SZY	TCMSP,BATMAN-TCM
MOL005555	isoterchebin	954.7	3.01	0.09	SZY	TCMSP,BATMAN-TCM
MOL005556	1-tert-Butyl-7-methoxynaphthalene	214.33	27.46	0.09	SZY	TCMSP
MOL005561	Anisylacetone	178.25	19.69	0.04	SZY	TCMSP
MOL005565	Uretan	89.11	3.97	0	SZY	TCMSP
MOL005567	vitamin a	286.5	19.53	0.16	SZY	TCMSP,BATMAN-TCM
MOL000610	TRD	184.41	17.89	0.03	SZY	TCMSP
MOL000644	swertiamarin_qt	212.22	2.58	0.09	SZY	TCMSP
MOL000069	palmitic acid	256.48	19.3	0.1	SZY,FL	TCMSP
MOL000704	styrene	104.16	29.55	0.01	SZY	TCMSP
MOL000860	stearic acid	284.54	17.83	0.14	SZY,ZX	TCMSP
MOL000864	MYS	212.47	13.98	0.05	SZY	TCMSP
MOL000865	hexadecane	226.5	12.32	0.06	SZY	TCMSP
MOL000867	Heptadekan	240.53	8.64	0.07	SZY	TCMSP
MOL000879	methyl palmitate	270.51	18.09	0.12	SZY	TCMSP
MOL000885	Dodekan	170.38	17.74	0.02	SZY	TCMSP
MOL000886	tetradecane	198.44	15.94	0.04	SZY	TCMSP
MOL000890	(+)-alpha-Curcumene	202.37	26.56	0.06	SZY	TCMSP
MOL000971	Ethylpalmitate	284.54	18.99	0.14	SZY	TCMSP
MOL008254	Isotetrandrine	622.82	10.42	0.1	SZY	Taiwan,BATMAN-TCM
MOL006077	Vitamin B1	265.4	19.87	0.11	SZY	Taiwan,BATMAN-TCM
MOL003549	1-Allyl-2,4,5-Trimethoxy-Benzene	208.28	22.76	0.06	SZY	Taiwan,BATMAN-TCM
MOL000394	choline	104.2	0.47	0.01	ZX	TCMSP,Taiwan
MOL000550	meso-galactitol	182.2	10.69	0.03	ZX	TCMSP
MOL000734	GLO	180.18	24.44	0.03	ZX	TCMSP

MOL000823	1h-indole-3-carboxylic,acid	161.17	25.83	0.05	ZX	TCMSP
MOL000844	Sulfoorientalol A	302.48	28.14	0.16	ZX	TCMSP,BATMAN-TCM
MOL011782	Ligustilide	190.26	23.5	0.07	FL	Taiwan

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**Table S3: Type 2 Diabetes Mellitus target genes interacting with compounds with a combined score $\geq$ 0.700**

No.	Symbol name	Gene name	No.	Symbol name	Gene name	No.	Symbol name	Gene name
1	ACACA	Acetyl-CoA carboxylase 1	56	PARP1	Poly [ADP-ribose] polymerase 1	111	CHRM1	Muscarinic acetylcholine receptor M1
2	AKT1	RAC-alpha serine/threonine-protein kinase	57	PLA2G4A	Cytosolic phospholipase A2	112	CHRM2	Muscarinic acetylcholine receptor M2
3	BCL2	Apoptosis regulator Bcl-2	58	PPARA	Peroxisome proliferator-activated receptor alpha	113	CHRM5	Muscarinic acetylcholine receptor M5
4	BCL2L1	Bcl-2-like protein 1	59	PRKCA	Protein kinase C alpha type	114	CRP	C-reactive protein
5	BIRC5	Baculoviral repeat-containing protein 5	IAP 60	PTGS2	Prostaglandin G/H synthase 2	115	CTRB1	Chymotrypsinogen B
6	CASP8	Caspase-8	61	RB1	Retinoblastoma-associated protein	116	CTSD	Cathepsin D
7	CAV1	Caveolin-1	62	RUNX2	Runt-related transcription factor 2	117	DRD2	D(2) dopamine receptor
8	CCNA2	Cyclin-A2	63	SLC2A4	Solute carrier family 2, facilitated glucose transporter member 4	118	F3	Tissue factor
9	CDKN1A	Cyclin-dependent kinase inhibitor 1	64	SPP1	Osteopontin	119	GJA1	Gap junction alpha-1 protein
10	CHUK	Inhibitor of nuclear factor kappa-B kinase subunit alpha	65	STAT1	Signal transducer and activator of transcription 1-alpha/beta	120	GSTP1	Glutathione S-transferase P
11	CYP1A1	Cytochrome P450 1A1	66	TOP1	DNA topoisomerase 1	121	INSR	Insulin receptor
12	E2F1	Transcription factor E2F1	67	ADRA1A	Alpha-1A adrenergic receptor	122	MAOA	Amine oxidase [flavin-containing] A
13	E2F2	Transcription factor E2F2	68	CHEK2	Serine/threonine-protein kinase Chk2	123	MGAM	Maltase-glucoamylase, intestinal
14	EGFR	Epidermal growth factor receptor	69	CXCL10	C-X-C motif chemokine 10	124	NOS3	Nitric oxide synthase, endothelial
15	ERBB2	Receptor tyrosine-protein kinase erbB-2	70	CYP1A2	Cytochrome P450 1A2	125	OPRM1	Mu-type opioid receptor
16	ESR1	Estrogen receptor	71	CYP1B1	Cytochrome P450 1B1	126	POR	NADPH--cytochrome P450 reductase
17	F7	Coagulation factor VII	72	CYP3A4	Cytochrome P450 3A4	127	PPP3CA	Serine/threonine-protein phosphatase

18	IGF2	Insulin-like growth factor II	73	GSTM1	Glutathione S-transferase Mu 1	128	PRSS1	2B catalytic subunit alpha isoform	Trypsin-1
19	IKBKB	Inhibitor of nuclear factor kappa-B kinase subunit beta	74	HSF1	Heat shock factor protein 1	129	PTGER3	Prostaglandin E2 receptor EP3 subtype	
20	IL10	Interleukin-10	75	ICAM1	Intercellular adhesion molecule 1	130	RASSF1	Ras association domain-containing protein 1	
21	IL1B	Interleukin-1 beta	76	IFNG	Interferon gamma	131	SCN5A	Sodium channel protein type 5 subunit alpha	
22	JUN	Transcription factor AP-1	77	IGFBP3	Insulin-like factor-binding protein 3	growth	132	THBD	Thrombomodulin
23	MAPK8	Mitogen-activated protein kinase 8	78	IL2	Interleukin-2		133	ABCG2	ATP-binding cassette sub-family G member 2
24	MYC	Myc proto-oncogene protein	79	LYZ	Lysozyme		134	ACHE	Acetylcholinesterase
25	NCOA1	Nuclear receptor coactivator 1	80	MAOB	Amine oxidase B		135	ADH1A	Alcohol dehydrogenase 1A
26	NCOA2	Nuclear receptor coactivator 2	81	MMP1	Interstitial collagenase		136	ADRA2A	Alpha-2A adrenergic receptor
27	NFE2L2	Nuclear factor erythroid 2-related factor 2	82	MMP3	Stromelysin-1		137	AHR	Aryl hydrocarbon receptor
28	PLAU	Urokinase-type plasminogen activator	83	MMP9	Matrix metalloproteinase-9		138	AKR1B1	Aldose reductase
29	RELA	Transcription factor p65	84	MPO	Myeloperoxidase		139	BAX	Apoptosis regulator BAX
30	RXRA	Retinoic acid receptor RXR-alpha	85	NFKBIA	NF-kappa-B inhibitor alpha		140	CCL2	C-C motif chemokine 2
31	SERPINE1	Plasminogen activator inhibitor 1	86	NOS2	Nitric oxide synthase, inducible		141	CHRM3	Muscarinic acetylcholine receptor M3
32	SOD1	Superoxide dismutase	87	NQO1	NAD(P)H dehydrogenase 1		142	DUOX2	Dual oxidase 2
33	VEGFA	Vascular endothelial growth factor A	88	NR1I3	Nuclear receptor subfamily 1 group I member 3		143	FASN	Fatty acid synthase
34	ADH1B	Alcohol dehydrogenase 1B	89	NR3C1	Glucocorticoid receptor		144	GRIA2	Glutamate receptor 2
35	ADH1C	Alcohol dehydrogenase 1C	90	NR3C2	Mineralocorticoid receptor		145	GSTM2	Glutathione S-transferase Mu 2
36	ALOX5	Arachidonate 5-lipoxygenase	91	PGR	Progesterone receptor		146	HK2	Hexokinase-2
37	AR	Androgen receptor	92	PPARG	Peroxisome proliferator activated receptor gamma		147	HMOX1	Heme oxygenase 1
38	CASP3	Caspase-3	93	PRKCB	Protein kinase C beta type		148	HSPB1	Heat shock protein beta-1

39	CASP9	Caspase-9	94	PTGS1	Prostaglandin G/H synthase 1	149	IL1A	Interleukin-1 alpha
40	CD14	Monocyte differentiation antigen CD14	95	RAF1	RAF proto-oncogene serine/threonine-protein kinase	150	KCNH2	Potassium voltage-gated channel subfamily H member 2
41	COL1A1	Collagen alpha-1(I) chain	96	RASA1	Ras GTPase-activating protein 1	151	LBP	Lipop polysaccharide-binding protein
42	COL3A1	Collagen alpha-1(III) chain	97	SELE	E-selectin	152	LTA4H	Leukotriene A-4 hydrolase
43	CXCL11	C-X-C motif chemokine 11	98	SLPI	Antileukoproteinase	153	MAPK1	Mitogen-activated protein kinase 1
44	CXCL2	C-X-C motif chemokine 2	99	VCAM1	Vascular cell adhesion protein 1	154	MMP2	72 kDa type IV collagenase
45	CXCL8	Interleukin-8	100	ABCC2	Canalicular multispecific organic anion transporter 1	155	NCF1	Neutrophil cytosol factor 1
46	EGF	Pro-epidermal growth factor	101	ADRA1B	Alpha-1B adrenergic receptor	156	NR1I2	Nuclear receptor subfamily 1 group I member 2
47	ELK1	ETS domain-containing protein Elk-1	102	ADRA1D	Alpha-1D adrenergic receptor	157	ODC1	Ornithine decarboxylase
48	ERBB3	Receptor tyrosine-protein kinase erbB-3	103	ADRA2C	Alpha-2C adrenergic receptor	158	PLAT	Tissue-type plasminogen activator
49	ESR2	Estrogen receptor beta	104	ADRB1	Beta-1 adrenergic receptor	159	PON1	Serum paraoxonase/arylesterase 1
50	FOS	Proto-oncogene c-Fos	105	ADRB2	Beta-2 adrenergic receptor	160	PPARD	Peroxisome proliferator-activated receptor delta
51	GSK3B	Glycogen synthase kinase-3 beta	106	AKR1C3	Aldo-keto reductase family 1 member C3	161	SLC6A2	Sodium-dependent noradrenaline transporter
52	HIF1A	Hypoxia-inducible factor 1-alpha	107	CAT	Catalase	162	SLC6A4	Sodium-dependent serotonin transporter
53	IL6	Interleukin-6	108	CCNB1	G2/mitotic-specific cyclin-B1	163	SULT1E1	Estrogen sulfotransferase
54	IRF1	Interferon regulatory factor 1	109	CCND1	G1/S-specific cyclin-D1			
55	MTOR	Serine/threonine-protein kinase mTOR	110	CD40LG	CD40 ligand			

**Table S4. The KEGG pathway analysis based on compound-Type 2 Diabetes Mellitus PPI network.** <sup>a,b, c</sup>

*a.* The detailed information of Cluster 1

Pathway ID	Pathway name	Gene count	P value	Gene
hsa04933	AGE-RAGE signaling pathway in diabetic complications	9	5.08E-15	AKT1,CCL2,CCND1,ICAM1,IL1B,IL6,JUN,NOS3,STAT1
hsa05200	Pathways in cancer	11	1.37E-12	AKT1,AR,CCND1,EGF,ERBB2,ESR1,HMOX1,IL6,JUN,MMP1,STAT1
hsa05418	Fluid shear stress and atherosclerosis	7	4.42E-10	AKT1,CCL2,HMOX1,ICAM1,IL1B,JUN,NOS3
hsa05164	Influenza A	7	1.61E-09	AKT1,CCL2,ICAM1,IL1B,IL6,JUN,STAT1
hsa05323	Rheumatoid arthritis	6	1.83E-09	CCL2,ICAM1,IL1B,IL6,JUN,MMP1
hsa04066	HIF-1 signaling pathway	6	3.69E-09	AKT1,EGF,ERBB2,HMOX1,IL6,NOS3
hsa05142	Chagas disease (American trypanosomiasis)	6	3.77E-09	AKT1,CCL2,IL10,IL1B,IL6,JUN
hsa04668	TNF signaling pathway	6	4.85E-09	AKT1,CCL2,ICAM1,IL1B,IL6,JUN
hsa05144	Malaria	5	7.67E-09	CCL2,ICAM1,IL10,IL1B,IL6
hsa05224	Breast cancer	6	2.31E-08	AKT1,CCND1,EGF,ERBB2,ESR1,JUN
hsa05321	Inflammatory bowel disease (IBD)	5	2.31E-08	IL10,IL1B,IL6,JUN,STAT1
hsa04630	Jak-STAT signaling pathway	6	3.14E-08	AKT1,CCND1,EGF,IL10,IL6,STAT1
hsa05212	Pancreatic cancer	5	4.54E-08	AKT1,CCND1,EGF,ERBB2,STAT1
hsa05167	Kaposi's sarcoma-associated herpesvirus infection	6	5.87E-08	AKT1,CCND1,ICAM1,IL6,JUN,STAT1
hsa04657	IL-17 signaling pathway	5	1.12E-07	CCL2,IL1B,IL6,JUN,MMP1

*b.* The detailed information of Cluster 2

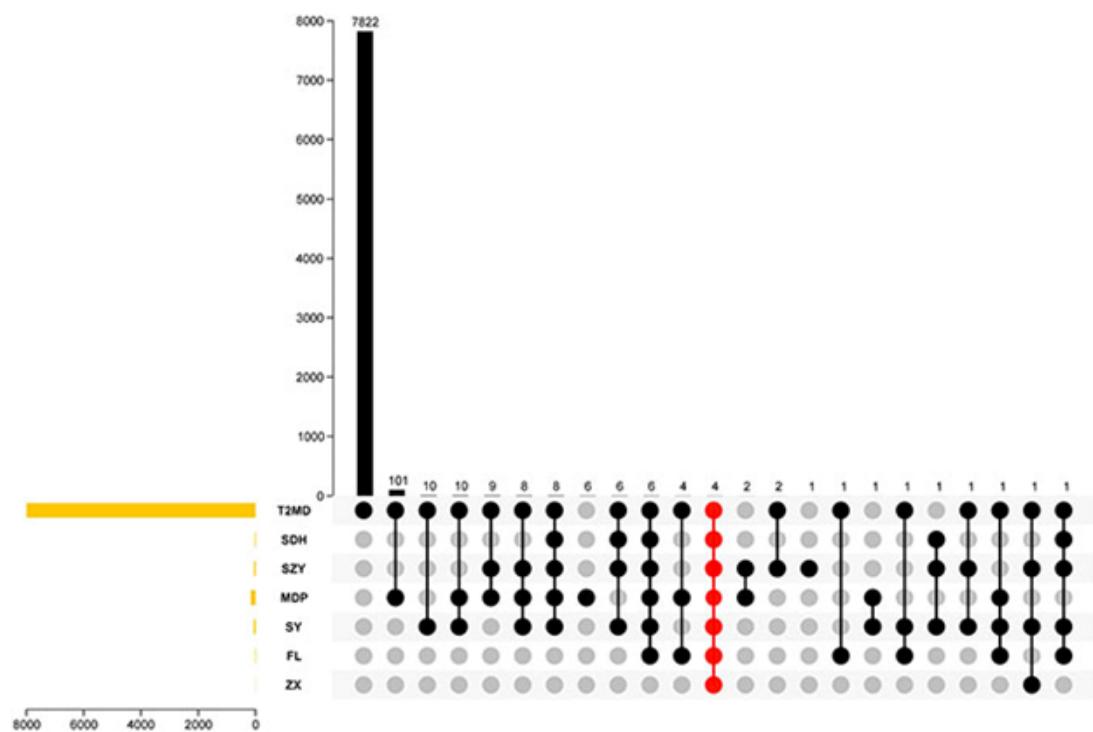
Pathway ID	Pathway name	Gene count	P value	Gene
hsa05200	Pathways in cancer	17	1.20E-16	BCL2L1,CASP3,CXCL8,EGFR,FOS,IFNG,IL2,MAPK1,MAPK8,MMP2,MMP9,MTOR,MYC,PPARG,PTGER3,PTGS2,VEGFA
hsa04657	IL-17 signaling pathway	10	4.57E-14	CASP3,CXCL2,CXCL8,FOS,IFNG,MAPK1,MAPK8,MMP3,MMP9,PTGS2
hsa04933	AGE-RAGE signaling pathway in diabetic complications	10	5.51E-14	CASP3,CXCL8,IL1A,MAPK1,MAPK8,MMP2,SELE,SERPINE1,VCAM1,VEGFA
hsa04668	TNF signaling pathway	10	1.03E-13	CASP3,CXCL2,FOS,MAPK1,MAPK8,MMP3,MMP9,PTGS2,SELE,VCAM1
hsa05167	Kaposi's sarcoma-associated herpesvirus infection	10	1.22E-11	CASP3,CXCL2,CXCL8,FOS,MAPK1,MAPK8,MTOR,MYC,PTGS2,VEGFA
hsa05219	Bladder cancer	7	2.90E-11	CXCL8,EGFR,MAPK1,MMP2,MMP9,MYC,VEGFA

hsa05418	Fluid shear stress and atherosclerosis	9	2.90E-11	FOS,IFNG,IL1A,MAPK8,MMP2,MMP9,SELE,VCAM1,VEGFA
hsa05132	Salmonella infection	7	2.37E-09	CXCL2,CXCL8,FOS,IFNG,IL1A,MAPK1,MAPK8
hsa05206	MicroRNAs in cancer	8	2.37E-09	CASP3,EGFR,MAPK1,MMP9,MTOR,MYC,PTGS2,VEGFA
hsa05210	Colorectal cancer	7	2.37E-09	CASP3,EGFR,FOS,MAPK1,MAPK8,MTOR,MYC
hsa01522	Endocrine resistance	7	3.88E-09	EGFR,FOS,MAPK1,MAPK8,MMP2,MMP9,MTOR
hsa05142	Chagas disease (American trypanosomiasis)	7	5.33E-09	CXCL8,FOS,IFNG,IL2,MAPK1,MAPK8,SERpine1
hsa05205	Proteoglycans in cancer	8	1.27E-08	CASP3,EGFR,MAPK1,MMP2,MMP9,MTOR,MYC,VEGFA
hsa04926	Relaxin signaling pathway	7	2.44E-08	EGFR,FOS,MAPK1,MAPK8,MMP2,MMP9,VEGFA
hsa04915	Estrogen signaling pathway	7	2.65E-08	EGFR,FOS,MAPK1,MMP2,MMP9,OPRM1,PGR

c. The detailed information of Cluster 3

Pathway ID	Pathway name	Gene count	P value	Gene
hsa00980	Metabolism of xenobiotics by cytochrome P450	7	2.09E-16	CYP1A1,CYP1A2,CYP1B1,CYP3A4,GSTM1, GSTM2,GSTP1
hsa05204	Chemical carcinogenesis	7	2.09E-16	CYP1A1,CYP1A2,CYP1B1,CYP3A4,GSTM1, GSTM2,GSTP1
hsa00982	Drug metabolism - cytochrome P450	5	7.20E-11	CYP1A2,CYP3A4,GSTM1,GSTM2,GSTP1
hsa00140	Steroid hormone biosynthesis	4	1.51E-08	CYP1A1,CYP1A2,CYP1B1,CYP3A4
hsa00983	Drug metabolism - other enzymes	4	3.41E-08	CYP3A4,GSTM1,GSTM2,GSTP1
hsa00380	Tryptophan metabolism	3	1.09E-06	CYP1A1,CYP1A2,CYP1B1
hsa00480	Glutathione metabolism	3	1.77E-06	GSTM1,GSTM2,GSTP1
hsa00830	Retinol metabolism	3	2.88E-06	CYP1A1,CYP1A2,CYP3A4
hsa01524	Platinum drug resistance	3	3.64E-06	GSTM1,GSTM2,GSTP1
hsa05418	Fluid shear stress and atherosclerosis	3	2.14E-05	GSTM1,GSTM2,GSTP1
hsa05225	Hepatocellular carcinoma	3	3.53E-05	GSTM1,GSTM2,GSTP1
hsa00591	Linoleic acid metabolism	2	8.03E-05	CYP1A2,CYP3A4
hsa04913	Ovarian steroidogenesis	2	0.0002	CYP1A1,CYP1B1
hsa05200	Pathways in cancer	3	0.00081	GSTM1,GSTM2,GSTP1
hsa01100	Metabolic pathways	3	0.0095	CYP1A1,CYP1A2,CYP3A4

**Figure S1. The veen information of compound- Type 2 Diabetes Mellitus**



A total of 7822 type 2 diabetes genes were obtained from the GeneCard and OMIM databases, with a total of 26, 46, 151, 57, 18 and 5 genes shared with SDH, SZY, MDP, SY, FL and ZX, respectively. The four genes (NCOA2, PGR, PTGS1, NR3C2), which painted in red, are shared by T2DM and the above six herbal of LWDH Pill.

**Figure S2. KEGG analysis of compound-Type 2 Diabetes Mellitus**

