

Table 1 Active Ingredients of TCM formulae

Medicine	Active Ingredients
Chishao	ellagic acid, paeoniflorgenone, Lactiflorin, paeoniflorin, paeoniflorin_qt, baicalein, Baicalin, beta-sitosterol, sitosterol, Spinasterol, Stigmasterol, (+)-catechin, (1S,2S,4R)-trans-2-hydroxy-1,8-cineole-B-D-glucopyranoside, (2R,3R)-4-methoxyl-distylin, 1-o-beta-d-glucopyranosyl-8-o-benzoylpaeonisuffrone_qt, 1-o-beta-d-glucopyranosylpaeonisuffrone_qt, stigmast-7-en-3-ol, benzoyl paeoniflorin, Albiflorin, Albiflorin_qt, 4-ethyl-paeoniflorin_qt, 4-o-methyl-paeoniflorin_qt, 8-debenzoylpaeonidanin, Paeoniflorigenone, 9-ethyl-neo-paeoniaflorin A_qt, evofolinB, isobenzoylpaeoniflorin, Ethyl oleate (NF), campest-5-en-3beta-ol
Dahuang	gallic acid-3-O-(6'-O-galloyl)-glucoside, Procyanidin B-5,3'-O-gallate, palmidin A, Daucosterol_qt, beta-sitosterol, Physciindiglucoside, Torachrysone-8-O-beta-D-(6'-oxayl)-glucoside, Emodin-1-O-beta-D-glucopyranoside, Toralactone, rhein, Mutatochrome, (-)-catechin, Sennoside E_qt, EUPATIN, Sennoside D_qt, aloe-emodin
Gancao	5,7-dihydroxy-3-(4-methoxyphenyl)-8-(3-methylbut-2-enyl)chromone, icos-5-enoic acid, gadelaic acid, (2S)-2-[4-hydroxy-3-(3-methylbut-2-enyl)phenyl]-8,8-dimethyl-2,3-dihydropyrano[2,3-f]chromen-4-one, Isotrifoliol, Phaseolinisoflavan, Kanzonol F, DFV, licorce glycoside E, Licocoumarone, 3,22-Dihydroxy-11-oxo-delta(12)-oleanene-27-alpha-methoxycarbonyl-29-oic acid, Sigmoidin-B, 2-[(3R)-8,8-dimethyl-3,4-dihydro-2H-pyrano[6,5-f]chromen-3-yl]-5-methoxyphenol, Euchrenone, (2S)-7-hydroxy-2-(4-hydroxyphenyl)-8-(3-methylbut-2-enyl)chroman-4-one, sitosterol, glycyroside, HMO, 7-Acetoxy-2-methylisoflavone, Licoisoflavone B, 6-prenylated eriodictyol, (E)-1-(2,4-dihydroxyphenyl)-3-(2,2-dimethylchromen-6-yl)prop-2-en-1-one, Inflacoumarin A, licochalcone a, (-)-Medicocarpin, 18 α -hydroxyglycyrrhetic acid, Glycyrrhiza flavonol A, Licoisoflavone, kaempferol, 7-Methoxy-2-methyl isoflavone, Eurycarpin A, 3'-Hydroxy-4'-O-Methylglabridin, 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chromone, Isoglycyrol, Glepidotin A, Isolicoflavonol, Glyasperin C, 3'-Methoxyglabridin, Glabrene, (E)-3-[3,4-dihydroxy-5-(3-methylbut-2-enyl)phenyl]-1-(2,4-dihydroxyphenyl)prop-2-en-1-one, quercetin, Quercetin der., Calycosin, 1,3-dihydroxy-9-methoxy-6-benzofurano[3,2-c]chromenone, Semilicoisoflavone B, Gancaonin B, Medicarpin, licochalcone G, isorhamnetin, Odoratin, Gancaonin H, kanzonols W, Jaranol, Gancaonin A, Lupiwighteone, licoisoflavanone, Glabrone,, Glycyrin, Glabranin, Glabridin, 8-prenylated eriodictyol,

dehydroglyasperins C, Xambioona, Mairin, Licoagroisoflavone, 8-(6-hydroxy-2-benzofuranyl)-2,2-dimethyl-5-chromenol, Licoagrocarpin, naringenin, 3-(2,4-dihydroxyphenyl)-8-(1,1-dimethylprop-2-enyl)-7-hydroxy-5-methoxy-coumarin, (2S)-6-(2,4-dihydroxyphenyl)-2-(2-hydroxypropan-2-yl)-4-methoxy-2,3-dihydrofuro[3,2-g]chromen-7-one, Gancaonin G, Glyzaglabrin, Glypallichalcone, 1,3-dihydroxy-8,9-dimethoxy-6-benzofurano[3,2-c]chromenone, Licoricone, Glepidotin B, glyasperin B, liquiritin, 3-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8-(3-methylbut-2-enyl)chromone, formononetin, 1-Methoxyphaseollidin, (2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one, Glyasperins M, Vestitol, Inermine, glyasperin F, Licochalcone B, Phaseol, shinpterocarpin, licopyranocoumarin, 7,2',4'-trihydroxy - 5-methoxy-3 - arylcoumarin, Glycyrol

Huangqin	Coptisine, wogonin, 5,2'-Dihydroxy-6,7,8-trimethoxyflavone, baicalein, Supraene, 5,7,2,5-tetrahydroxy-8,6-dimethoxyflavone, acacetin, 5,7,4'-Trihydroxy-8-methoxyflavone, 5,7,4'-trihydroxy-6-methoxyflavanone, sitosterol, beta-sitosterol, 5,8,2'-Trihydroxy-7-methoxyflavone, 5,7,2',6'-Tetrahydroxyflavone, rivularin, dihydrooroxylin A, 11,13-Eicosadienoic acid, methyl ester, Norwogonin, Dihydrobaicalin_qt, Carthamidin, Eriodictiol (flavanone), oroxylin a, epiberberine, bis[(2S)-2-ethylhexyl] benzene-1,2-dicarboxylate, Diop, Stigmasterol, Moslosooflavone, 5,2',6'-Trihydroxy-7,8-dimethoxyflavone, ent-Epicatechin, Salvigenin, (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one, Skullcapflavone II, DIHYDROOROXYLIN, 2,6,2',4'-tetrahydroxy-6'-methoxychaleone, 5,7,4'-trihydroxy-8-methoxyflavanone, Panicolin, NEOBAICALEIN
Mahuang	Mandenol, naringenin, Genkwanin, leucopelargonidin, kaempferol, (+)-catechin, Truflex OBP, eriodictyol, luteolin, Herbacetin, Resivit, (+)-Leucocyanidin, taxifolin, Diosmetin, quercetin, delphinidin, Pectolinarigenin, Supraene, campest-5-en-3beta-ol, poriferast-5-en-3beta-ol, beta-sitosterol, Stigmasterol, 24-Ethylcholest-4-en-3-one
Qinghao	EUPATIN, isorhamnetin, sitosterol, Tamarixetin, Patuletin, kaempferol, Stigmasterol, Areapillin, Artemetin, luteolin, Skrofulein, artemisitene, vicensin-2_qt, Cirsiliol, vitexin_qt, DMQT, [(2S)-2-[(2S)-2-(benzoylamino)-3-phenylpropanoyl]amino]-3-phenylpropyl] acetate, 6,8-di-c-glucosylapigenin_qt, artemisinin, dihydroartemisinin, deoxyartemisinin, quercetin
Tinglizi	11,14-eicosadienoic acid, hederagenin, isorhamnetin, beta-sitosterol, K-STROPHANTHOSIDE, evobioside, K-STROPHANTHOSIDE_qt, erysimoside, Cynotoxin, Dihomolinolenic acid, kaempferol, quercetin

Xingren	gondoic acid, Diisooctyl succinate, (6Z,10E,14E,18E)-2,6,10,15,19,23-hexamethyltetracos-2,6,10,14,18,22-hexaene, sitosterol, CLR, 11,14-eicosadienoic acid, Spinasterol, Stigmasterol, Glabridin, estrone, (+)-catechin, Mairin, liquiritin, Ziziphin_qt, Licochalcone B, Phaseol, Machiline, l-SPD, Glycyrol
Yuxingcao	1-methyl-2-nonacosyl-4-quinolone, Ruvoside_qt, quercetin, C09747, Isoramanone, kaempferol, Spinasterol,
Zhebeimu	Zhebeiresinol, pelargonidin, Chaksine, 6-Methoxyl-2-acetyl-3-methyl-1,4-naphthoquinone-8-O-beta-D-glucopyranoside, Ziebeimine, beta-sitosterol, Peimisine
Zhimu	Anemarsaponin E_qt, Timosaponin B III_qt, Anemarsaponin C_qt, Mangiferolic acid, Chrysanthemaxanthin, Icariin I, kaempferol, Stigmasterol, Anhydroicaritin, Hippastrine, diosgenin, asperglaucide, Anemarsaponin F_qt, coumaroyltyramine, (Z)-3-(4-hydroxy-3-methoxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide

Table 2 The list of 31 potential anti-influenza target genes for active components

UniProt ID	Protein name	Gene name
P25963	NF-kappa-B inhibitor alpha	NFKBIA
P10145	Interleukin-8	CXCL8
P98066	Tumor necrosis factor-inducible gene 6 protein	TNFAIP6
P23219	Prostaglandin G/H synthase 1	PTGS1 PTGS2PTGS1
P35354	Prostaglandin G/H synthase 2	PTGS2
P05412	Transcription factor AP-1	JUN
P42574	Caspase-3	CASP3
Q14790	Caspase-8	CASP8
P27338	Amine oxidase [flavin-containing] B	MAOB

P04637	Cellular tumor antigen p53	TP53
P12004	Proliferating cell nuclear antigen	PCNA
P01106	Myc proto-oncogene protein	MYC
P01584	Interleukin-1 beta	IL1B
P22303	Acetylcholinesterase	ACHE
O14920	Inhibitor of nuclear factor kappa-B kinase subunit beta	IKBKB
P45983	Mitogen-activated protein kinase 8	MAPK8
P42224	Signal transducer and activator of transcription 1- alpha/beta	STAT1
Q14994	Nuclear receptor subfamily 1 group I member 3	NR1I3
P27361	Mitogen-activated protein kinase 3	MAPK3
P28482	Mitogen-activated protein kinase 1	MAPK1
Q04828	Aldo-keto reductase family 1 member C1	AKR1C1
P23141	Liver carboxylesterase 1	CES1
P24385	G1/S-specific cyclin-D1	CCND1
P11021	Endoplasmic reticulum chaperone BiP	HSPA5
P13500	C-C motif chemokine 2	CCL2
P01579	Interferon gamma	IFNG
P01583	Interleukin-1 alpha	IL1A
P02778	C-X-C motif chemokine 10	CXCL10
O15111	Inhibitor of nuclear factor kappa-B kinase subunit alpha	CHUK
P48023	Tumor necrosis factor ligand superfamily member 6	FASLG
P11712	Cytochrome P450 2C9	CYP2C9

Table3 Top 10 degree of ingredient in formulae

	ID	ingredient	degree
1	MOL000098	quercetin	

2	MOL000006	luteolin
3	MOL000422	kaempferol
4	MOL000173	wogonin
5	MOL000471	aloe-emodin
6	MOL004328	naringenin
7	MOL001689	acacetin
8	MOL000358	beta-sitosterol
9	MOL000392	formononetin
1	MOL002714	baicalein
0		

Table 4 binding energy of three componets to target protein

compound	Affinity (kcal/mol)	
	JUN	IL-1B
quercetin	-8.4	-7.0
luteolin	-8.7	-7.7
naringenin	-8.6	-7.0

Fig1 Venn diagrams for influenza target. Based on Drugbank ,GeneCard, OMIM, TTD, PharmGkbdatabase, 229 influenza-related targets were found.

Fig2 Venn diagrams for the co-target between 242 targets of active ingredients and 229 influenza-related targets. 31 key targets were obtained after the duplicative terms deleted.

Fig3. Network diagram between active components and target genes. The circle hexagon nodes represent the active components, the blue hexagon nodes represent the target genes. Nodes size are proportional to their degree.

Fig4. PPI network construction and analysis. PPI network of the co-expressed genes. The PPI network was constructed via the Search Tool for the Retrieval of Interacting Genes online, degree values of 11 target proteins are higher than the average for further analysis.

Fig5.Top 10 GO enrichments in BP,CC,MF (fig 5) GO enrichment. X-axis is enrichment gene ratio, Y-axis is biological process, molecular function and cellular component analysis. Color represents the adjusted p-value, the bluer the color, the

smaller the adjusted p-value.

Fig6. KEGG pathway enrichment and top 30 KEGG pathways annotation. (fig 6). X-axis is enrichment gene count, Y-axis is KEGG pathway, and the color of bar chart represents the adjusted p-value.

Fig7-8. The docking complex of four targets and their strongest binding components. the active site residues are shown. (A) JUN. (B) ILIB.