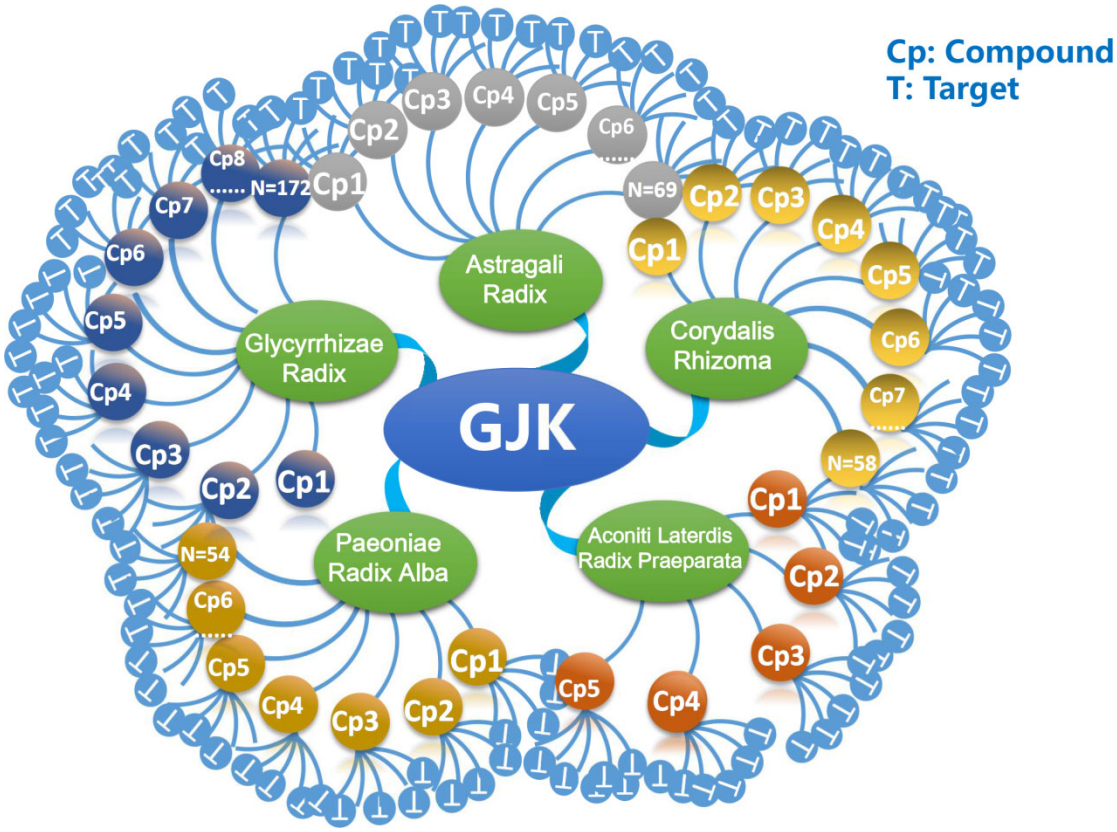
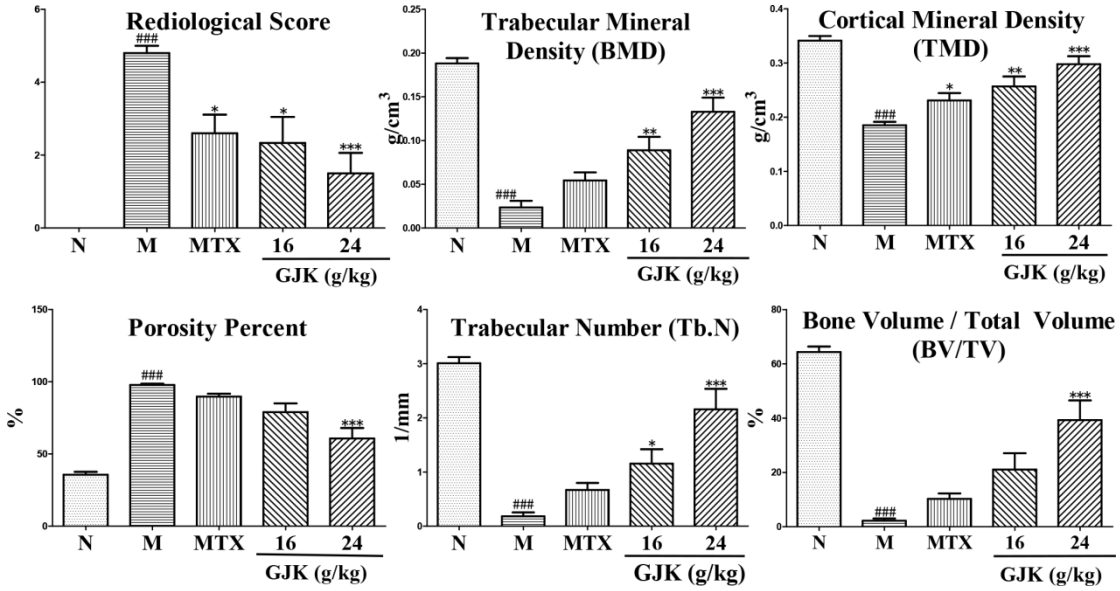
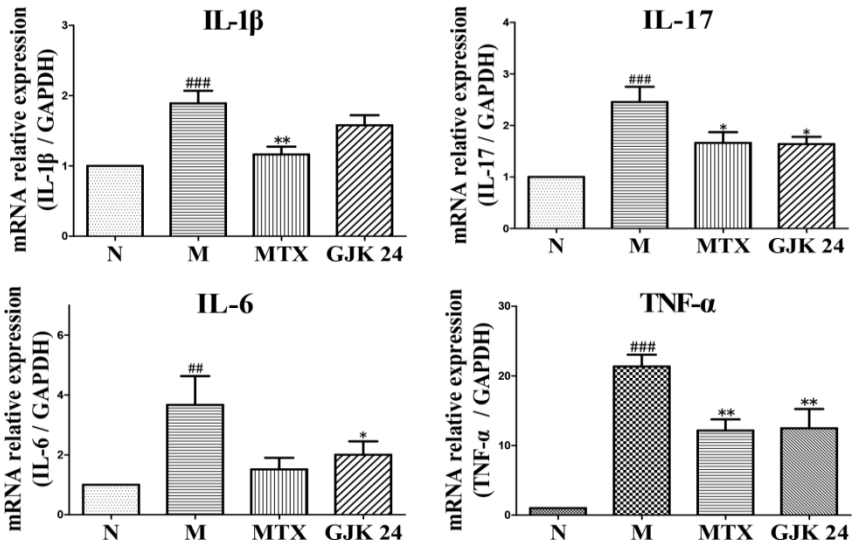


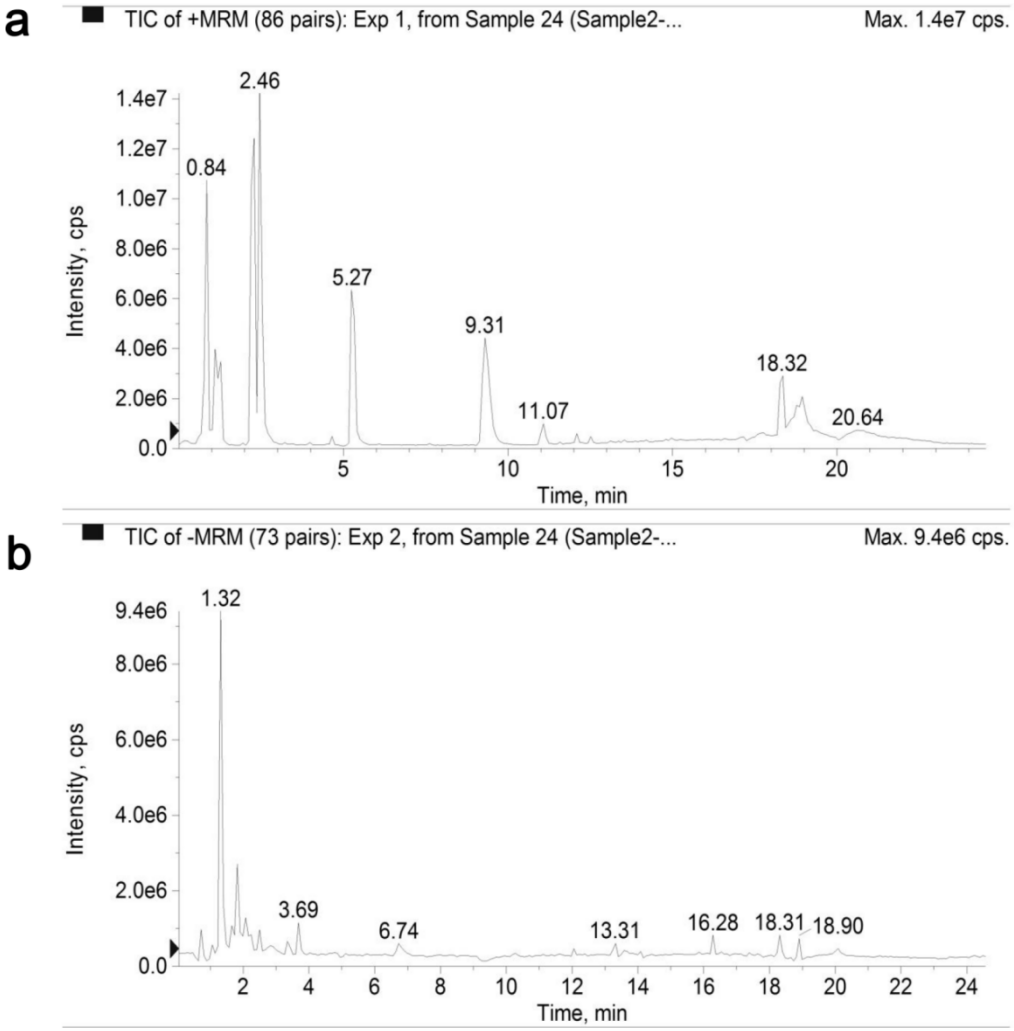
Supplementary Fig.1 The 358 compounds in the 5 herbs in GJK.



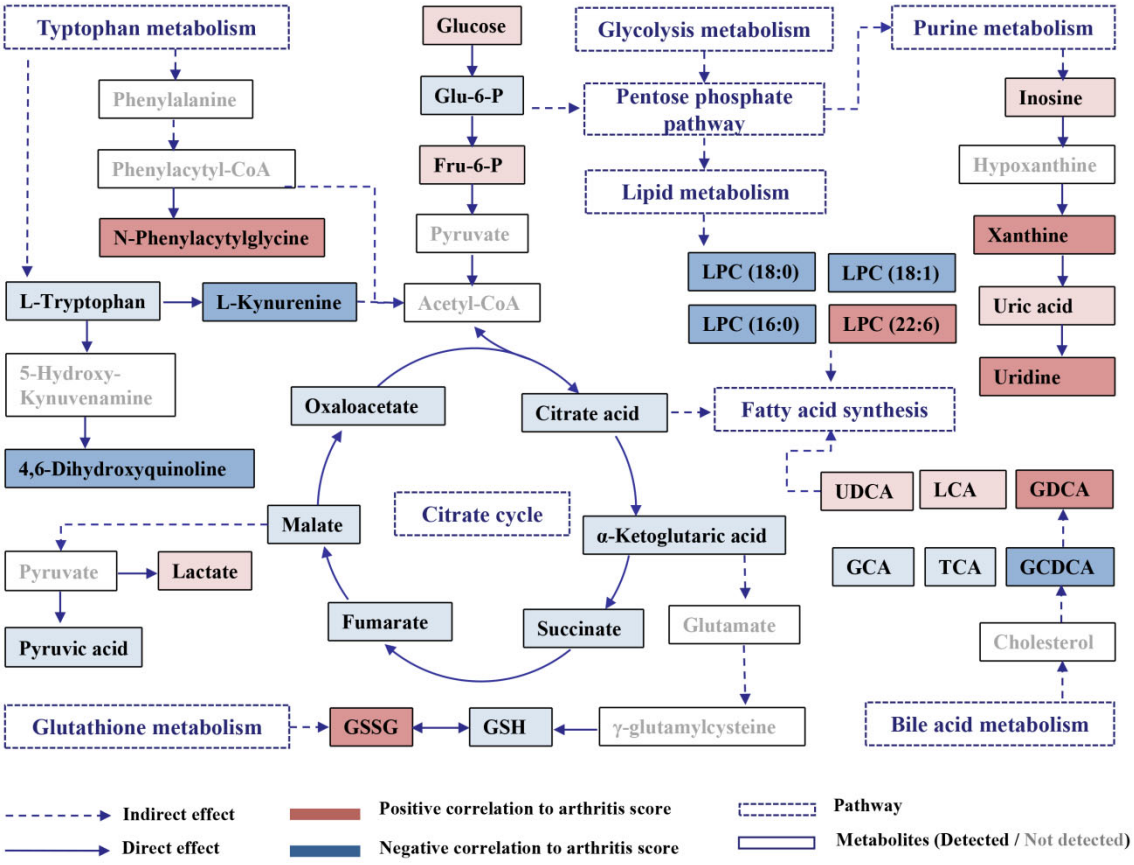
Supplementary Fig.2 Bone destruction indices analyzed by Micro CT (n=5~6). Difference between groups was analyzed by one-way ANOVA. (*P<0.05, **P<0.01, ***P<0.001 VS model) **(a)** Radiological score was assessed by observers according to the Micro CT photograph of ankles. **(b,c,d,e,f)** Trabecular mineral density (BMD), cortical mineral density (TMD), porosity percent, trabecular number (Tb.N) and bone volume/ total volume were analyzed by Micro CT analyzer.



Supplementary Fig.3 Gene expression levels of pro-inflammatory cytokines in bone tissue（upper end of tipia）（n=5~6）.Difference between groups was analyzed by one-way ANOVA. (*P<0.05, **P<0.01, ***P<0.001 VS model).



Supplementary Fig.4 Representative base peak intensity chromatogram of the rat plasma obtained in ESI positive mode (a) and ESI negative mode (b) based on LC- MS.



Supplementary Fig.5 KEGG pathways for the identified 17 arthritis-associated metabolic biomarkers. Box in red: positive correlation to arthritis score (r=0.6~0.8); light red: positive correlation to arthritis score ($P<0.05$); pink: positive correlation to arthritis score ($P\geqslant0.05$). Box in blue: negative correlation to arthritis score ($P<0.05$); light blue: negative correlation to arthritis score ($P\geqslant0.05$). Black in font: detected; grey: not detected. Abbreviation: GSSG, glutathione disulfide; GSH, glutathione; Glu-6-P, glucose 6-phosphatase; Fru-6-P, fructose 6-phosphate; LPC, lysophosphatidylcholine; UDCA, ursodeoxycholic acid; LCA, lithocholic acid; GDCA, glycodeoxycholic acid; GCA, glycocholic acid; TCA, taurocholic acid; GCDCA, glycochenodeoxycholic acid.

Supplementary Table 1. The 358 compounds in the 5 herbs.

Herb	Compond
Astragali Radix (HUANG QI)	(3r) -2', 3' -dihydroxy-7, 4' -dimethoxyisoflavone
Astragali Radix (HUANG QI)	(6ar, 11ar) -10-hydroxy-3, 9-dimethoxypterocarpane
Astragali Radix (HUANG QI)	medicarpin
Astragali Radix (HUANG QI)	2', 4' -dihydroxy-5
Astragali Radix (HUANG QI)	2'-hydroxy-3
Astragali Radix (HUANG QI)	2'-hydroxy-3',4'-dime thoxy-isoflavane-7-o-beta-d-glucoside
Astragali Radix (HUANG QI)	2-hydroxy-3-methoxystrychnine
Astragali Radix (HUANG QI)	20(r)-21,24-cyclo-3beta,25-dihydroxyl-dammar-23(24)-en-21-one
Astragali Radix (HUANG QI)	20-hexadecanoylingenol
Astragali Radix (HUANG QI)	3'-hydroxy-4--methoxyisoflavone-7-o-beta-d-glucos ide
Astragali Radix (HUANG QI)	3,5-dimethoxystilbene
Astragali Radix (HUANG QI)	3-o-beta-d-glucuronopyranosyl gypsogenin
Astragali Radix (HUANG QI)	4'-dimethoxyisoflavane-7-o-beta-d-glucoside
Astragali Radix (HUANG QI)	4-hydroxy-2,6-dimethyl-6-(3,7-dimethyl-2,6-octadie nyl)-8-(3-methyl-2-butenyl)-2h-1-benzopyran-5,7(3 h,6h)-dione
Astragali Radix (HUANG QI)	6-dimethoxy-isoflavane
Astragali Radix (HUANG QI)	9, 10-dimethoxypterocarpane-3-o-beta-d-glucoside
Astragali Radix (HUANG QI)	acetic acid(0.971)
Astragali Radix (HUANG QI)	acetyl astragaloside i
Astragali Radix (HUANG QI)	acetylastragaloside
Astragali Radix (HUANG QI)	adenine(0.667)
Astragali Radix (HUANG QI)	adeninenucleoside
Astragali Radix (HUANG QI)	astragaloside 1~8
Astragali Radix (HUANG QI)	astragaloside i
Astragali Radix (HUANG QI)	astragaloside ii
Astragali Radix (HUANG QI)	astragaloside iii
Astragali Radix (HUANG QI)	astragaloside iv
Astragali Radix (HUANG QI)	astragaloside v
Astragali Radix (HUANG QI)	astragaloside vi
Astragali Radix (HUANG QI)	astragaloside vii
Astragali Radix (HUANG QI)	astragaloside viii
Astragali Radix (HUANG QI)	astramembrannin
Astragali Radix (HUANG QI)	astramembrannin i
Astragali Radix (HUANG QI)	astramembrannin ii

Astragali Radix (HUANG QI)	beta-sitosterol(0.743)
Astragali Radix (HUANG QI)	betaine(0.907)
Astragali Radix (HUANG QI)	calycosin
Astragali Radix (HUANG QI)	canavanine(1)
Astragali Radix (HUANG QI)	choline(0.637)
Astragali Radix (HUANG QI)	chrysanthemaxanthin
Astragali Radix (HUANG QI)	cycloastragenol
Astragali Radix (HUANG QI)	cyclosieversigenin
Astragali Radix (HUANG QI)	folicacid
Astragali Radix (HUANG QI)	folinic acid(0.67)
Astragali Radix (HUANG QI)	foliosidine
Astragali Radix (HUANG QI)	formononentin
Astragali Radix (HUANG QI)	formononetin
Astragali Radix (HUANG QI)	gamma-sitosterol
Astragali Radix (HUANG QI)	glucuronicacid
Astragali Radix (HUANG QI)	guanosine(0.586)
Astragali Radix (HUANG QI)	hexadecanoicacid
Astragali Radix (HUANG QI)	isoastragaloside i
Astragali Radix (HUANG QI)	isoastragaloside ii
Astragali Radix (HUANG QI)	isoastragaloside1, 3
Astragali Radix (HUANG QI)	isorhamnetin(0.757)
Astragali Radix (HUANG QI)	kaempferol(0.778)
Astragali Radix (HUANG QI)	kumatakenin
Astragali Radix (HUANG QI)	kumugansine a
Astragali Radix (HUANG QI)	lupeol(0.967)
Astragali Radix (HUANG QI)	n-candicine
Astragali Radix (HUANG QI)	quercetin(0.883)
Astragali Radix (HUANG QI)	rhamnocitrin
Astragali Radix (HUANG QI)	rhamnocitrin
Astragali Radix (HUANG QI)	soyasapogenol b
Astragali Radix (HUANG QI)	soyasaponin 1
Astragali Radix (HUANG QI)	sucrose(0.807)
Astragali Radix (HUANG QI)	suffruticoside a
Astragali Radix (HUANG QI)	uridine(0.665)
Astragali Radix (HUANG QI)	β-sitosterol
Astragali Radix (HUANG QI)	βetaine
Glycyrrhizae Radix (GAN CAO)	(e)-1-[2,4-dihydroxy-3-(3-methyl-2-butenyl)phenyl]-3-(2,2-dimethyl-8-hydroxy-2h-benzo-pyran-6-yl)-2-propen-1-one
Glycyrrhizae Radix (GAN CAO)	(e)-1-[2,4-dihydroxy-3-(3-methyl-2-butenyl)phenyl]-3-(4-hydroxy-3-[3-methyl-2-butenyl)

	phenyl]-2-propen-1-one
Glycyrrhizae Radix (GAN CAO)	(e)-1-[2,4-dihydroxy-3-(3-methyl-2-butenyl)phenyl]-3-(4-hydroxy-3-[3-methyl-2-butenyl)phenyl]-2-propen-1-one
Glycyrrhizae Radix (GAN CAO)	18alpha-glycyrrhetinic acid
Glycyrrhizae Radix (GAN CAO)	18beta-glycyrrhetinic acid(0.71)
Glycyrrhizae Radix (GAN CAO)	2,4,4'-trihydroxychalcone
Glycyrrhizae Radix (GAN CAO)	2,5-dihydroxymethyl-3,4-dihydroxypyrrolidine(0.75)
Glycyrrhizae Radix (GAN CAO)	2-methyl-1,3,6-trihydroxyanthraquinone
Glycyrrhizae Radix (GAN CAO)	3'-(γ,γ-dimethylallyl)-kievitone
Glycyrrhizae Radix (GAN CAO)	3'-methoxyglabridin
Glycyrrhizae Radix (GAN CAO)	3,3'-dimethylquercetin
Glycyrrhizae Radix (GAN CAO)	3,4-dicaffeoyl-5-(3-hydroxy-3-methyl) glutaroyl quinic acid
Glycyrrhizae Radix (GAN CAO)	3-hydroxyglabrol
Glycyrrhizae Radix (GAN CAO)	3-hydroxyglabrol (ii)
Glycyrrhizae Radix (GAN CAO)	3-methyl-6,7,8-trihydropyrrolo[1,2-a]pyrimidin-2-one
Glycyrrhizae Radix (GAN CAO)	3-o-acetyl-glycyrrhetinicacid
Glycyrrhizae Radix (GAN CAO)	3-o-[β-d-glucuronopyranosyl-(1→2)-o-β-d-glucuronopyranosyl]-24-hydroxyglabrolide
Glycyrrhizae Radix (GAN CAO)	4'-o-methylglabridin
Glycyrrhizae Radix (GAN CAO)	5,6,7,8-tetrahydro-2, 4-dimethylquinoline
Glycyrrhizae Radix (GAN CAO)	5,6,7,8-tetrahydro-4-methylquinoline
Glycyrrhizae Radix (GAN CAO)	6,8-bis(c-β-glucosyl)-apigenin
Glycyrrhizae Radix (GAN CAO)	8-methoxy-5-o-glucoside flavone
Glycyrrhizae Radix (GAN CAO)	8-methyl-10-hydroxylycoctonine
Glycyrrhizae Radix (GAN CAO)	alpha-trihydroxy coprostanic acid
Glycyrrhizae Radix (GAN CAO)	astragalin
Glycyrrhizae Radix (GAN CAO)	berniarin
Glycyrrhizae Radix (GAN CAO)	corylifolinin
Glycyrrhizae Radix (GAN CAO)	dibutyl uralsaponin a ester
Glycyrrhizae Radix (GAN CAO)	dimethyl sebacate
Glycyrrhizae Radix (GAN CAO)	ethyl-n-buthy-uralsaponin a esters
Glycyrrhizae Radix (GAN CAO)	ferulic acid(0.8)
Glycyrrhizae Radix (GAN CAO)	formononetin(0.933)
Glycyrrhizae Radix (GAN CAO)	formononetin-7-glucoside
Glycyrrhizae Radix (GAN CAO)	gamma-sitosterol
Glycyrrhizae Radix (GAN CAO)	gancaonin a
Glycyrrhizae Radix (GAN CAO)	gancaonin b

Glycyrrhizae Radix (GAN CAO)	gancaonin c
Glycyrrhizae Radix (GAN CAO)	gancaonin d
Glycyrrhizae Radix (GAN CAO)	gancaonin e
Glycyrrhizae Radix (GAN CAO)	gancaonin f
Glycyrrhizae Radix (GAN CAO)	gancaonin i
Glycyrrhizae Radix (GAN CAO)	gancaonin p-3'-methylether
Glycyrrhizae Radix (GAN CAO)	gancaonin x
Glycyrrhizae Radix (GAN CAO)	ganoderic acid a(1)
Glycyrrhizae Radix (GAN CAO)	glabrolide
Glycyrrhizae Radix (GAN CAO)	glisoflavanone
Glycyrrhizae Radix (GAN CAO)	gloeosteretriol
Glycyrrhizae Radix (GAN CAO)	glyarallin b
Glycyrrhizae Radix (GAN CAO)	glycycoumarin
Glycyrrhizae Radix (GAN CAO)	glycyphyllin
Glycyrrhizae Radix (GAN CAO)	glycyrin
Glycyrrhizae Radix (GAN CAO)	glycyrol
Glycyrrhizae Radix (GAN CAO)	glycyroside
Glycyrrhizae Radix (GAN CAO)	glycyrrhetinic acid(0.71)
Glycyrrhizae Radix (GAN CAO)	glycyrrhetinicacid
Glycyrrhizae Radix (GAN CAO)	glycyrrhetol
Glycyrrhizae Radix (GAN CAO)	glycyrrhisoflavanone
Glycyrrhizae Radix (GAN CAO)	glycyrrhisoflavone
Glycyrrhizae Radix (GAN CAO)	glycyrrhiza-flavonol a
Glycyrrhizae Radix (GAN CAO)	glycyrrhizic acid(0.8)
Glycyrrhizae Radix (GAN CAO)	glycyrrhizicacid
Glycyrrhizae Radix (GAN CAO)	glycyrrhizin(0.8)
Glycyrrhizae Radix (GAN CAO)	glyeurysaponin
Glycyrrhizae Radix (GAN CAO)	glyurallin a
Glycyrrhizae Radix (GAN CAO)	glyuranolide
Glycyrrhizae Radix (GAN CAO)	glyyunnanprosapogenin d
Glycyrrhizae Radix (GAN CAO)	glyzaglabrin
Glycyrrhizae Radix (GAN CAO)	gmelofuran
Glycyrrhizae Radix (GAN CAO)	hispaglabridin a
Glycyrrhizae Radix (GAN CAO)	hispaglabridin b
Glycyrrhizae Radix (GAN CAO)	hispidulin(1)
Glycyrrhizae Radix (GAN CAO)	isoglycyrol
Glycyrrhizae Radix (GAN CAO)	isogosferol
Glycyrrhizae Radix (GAN CAO)	isolicoflavonol(1)
Glycyrrhizae Radix (GAN CAO)	isoliensinine
Glycyrrhizae Radix (GAN CAO)	isoliquiriligenin

Glycyrrhizae Radix (GAN CAO)	isoliquiritigenin(0.96)
Glycyrrhizae Radix (GAN CAO)	isoliquiritin
Glycyrrhizae Radix (GAN CAO)	isolobelanine
Glycyrrhizae Radix (GAN CAO)	isoononin
Glycyrrhizae Radix (GAN CAO)	isoorientin
Glycyrrhizae Radix (GAN CAO)	isoquercitrin(1)
Glycyrrhizae Radix (GAN CAO)	isoramanone
Glycyrrhizae Radix (GAN CAO)	isoschaftoside
Glycyrrhizae Radix (GAN CAO)	isotrifoliol
Glycyrrhizae Radix (GAN CAO)	isotrilobine
Glycyrrhizae Radix (GAN CAO)	kanzonol k
Glycyrrhizae Radix (GAN CAO)	kanzonol l
Glycyrrhizae Radix (GAN CAO)	lensinine
Glycyrrhizae Radix (GAN CAO)	licobenzofuran
Glycyrrhizae Radix (GAN CAO)	licobichalcone
Glycyrrhizae Radix (GAN CAO)	licochalcone a(1)
Glycyrrhizae Radix (GAN CAO)	licocoumarone
Glycyrrhizae Radix (GAN CAO)	licoflavone
Glycyrrhizae Radix (GAN CAO)	licofuranocoumarin
Glycyrrhizae Radix (GAN CAO)	licoisoflavaone
Glycyrrhizae Radix (GAN CAO)	licoisoflavone
Glycyrrhizae Radix (GAN CAO)	licoleafol
Glycyrrhizae Radix (GAN CAO)	licopyranocoumarin
Glycyrrhizae Radix (GAN CAO)	licoricesaponin a3
Glycyrrhizae Radix (GAN CAO)	licoricesaponin b2
Glycyrrhizae Radix (GAN CAO)	licoricesaponin c2
Glycyrrhizae Radix (GAN CAO)	licoricesaponin d3
Glycyrrhizae Radix (GAN CAO)	licoricesaponin e2
Glycyrrhizae Radix (GAN CAO)	licoricesaponin f3
Glycyrrhizae Radix (GAN CAO)	licoricesaponin g2
Glycyrrhizae Radix (GAN CAO)	licoricesaponin j2
Glycyrrhizae Radix (GAN CAO)	licoricesaponin k2
Glycyrrhizae Radix (GAN CAO)	licoricesaponine a3
Glycyrrhizae Radix (GAN CAO)	licoricesaponine c2
Glycyrrhizae Radix (GAN CAO)	licoricesaponine d3
Glycyrrhizae Radix (GAN CAO)	licoricesaponine f3
Glycyrrhizae Radix (GAN CAO)	licoricesaponine g2
Glycyrrhizae Radix (GAN CAO)	licoricesaponine h2
Glycyrrhizae Radix (GAN CAO)	licoricesaponine j2
Glycyrrhizae Radix (GAN CAO)	licoricesaponine k2

Glycyrrhizae Radix (GAN CAO)	licoricesaponinh2
Glycyrrhizae Radix (GAN CAO)	licoricidin
Glycyrrhizae Radix (GAN CAO)	licoricone
Glycyrrhizae Radix (GAN CAO)	licorisoflavan a
Glycyrrhizae Radix (GAN CAO)	liquiriligenin
Glycyrrhizae Radix (GAN CAO)	liquiritigenin(0.804)
Glycyrrhizae Radix (GAN CAO)	liquiritigenin-7,4'-diglucoside
Glycyrrhizae Radix (GAN CAO)	liquiritigenin-7-o-beta-d-(3-o-acetyl)-apiofuranosyl-4'-o-beta-d-glucopyranoside
Glycyrrhizae Radix (GAN CAO)	liquiritigenin4'-o-β-d-apio-d-furanosyl(1→2)-β-d-glucopyranoside
Glycyrrhizae Radix (GAN CAO)	liquiritin(1)
Glycyrrhizae Radix (GAN CAO)	liquoric acid
Glycyrrhizae Radix (GAN CAO)	lupiwighteone
Glycyrrhizae Radix (GAN CAO)	methyl 18α-hydroxyglycyrrhetate
Glycyrrhizae Radix (GAN CAO)	methyl 2-hydroxy-3,4-dimethoxy benzoate
Glycyrrhizae Radix (GAN CAO)	methyl 3-o-beta-d-glucopyranosyl polygalacate
Glycyrrhizae Radix (GAN CAO)	methyl linoleate(1)
Glycyrrhizae Radix (GAN CAO)	methyl-24-hydroxy-11-deoxoglycyrrhetate
Glycyrrhizae Radix (GAN CAO)	methyl-24-hydroxyglycyrrhetate
Glycyrrhizae Radix (GAN CAO)	methyl-n-butyl-uralsaponin a esters
Glycyrrhizae Radix (GAN CAO)	methylglycyrrhetate
Glycyrrhizae Radix (GAN CAO)	methylglyoxal
Glycyrrhizae Radix (GAN CAO)	monoammonium glycyrrhizinate(0.8)
Glycyrrhizae Radix (GAN CAO)	n-tricosane
Glycyrrhizae Radix (GAN CAO)	narcissin
Glycyrrhizae Radix (GAN CAO)	narwedine(1)
Glycyrrhizae Radix (GAN CAO)	neohancoside a
Glycyrrhizae Radix (GAN CAO)	neoisoliquiritin
Glycyrrhizae Radix (GAN CAO)	neoisopulegol
Glycyrrhizae Radix (GAN CAO)	neoliquiritin
Glycyrrhizae Radix (GAN CAO)	neomatatabiol
Glycyrrhizae Radix (GAN CAO)	neouralenol
Glycyrrhizae Radix (GAN CAO)	neowilforine
Glycyrrhizae Radix (GAN CAO)	nicotiflorin
Glycyrrhizae Radix (GAN CAO)	ononin(1)
Glycyrrhizae Radix (GAN CAO)	ononitol
Glycyrrhizae Radix (GAN CAO)	phaseollinisoflavan(1)
Glycyrrhizae Radix (GAN CAO)	phebalosin
Glycyrrhizae Radix (GAN CAO)	rutin(0.833)

Glycyrrhizae Radix (GAN CAO)	ruvoside
Glycyrrhizae Radix (GAN CAO)	schaftoside
Glycyrrhizae Radix (GAN CAO)	sigmoidin b
Glycyrrhizae Radix (GAN CAO)	sinapic acid
Glycyrrhizae Radix (GAN CAO)	tetrahydroharmine(1)
Glycyrrhizae Radix (GAN CAO)	tetrahydropalmatine(1)
Glycyrrhizae Radix (GAN CAO)	umbelliferone(1)
Glycyrrhizae Radix (GAN CAO)	uralene
Glycyrrhizae Radix (GAN CAO)	uralenin
Glycyrrhizae Radix (GAN CAO)	uralenneoside
Glycyrrhizae Radix (GAN CAO)	uralenol
Glycyrrhizae Radix (GAN CAO)	uralenol-3-methylether
Glycyrrhizae Radix (GAN CAO)	uralsaponin a
Glycyrrhizae Radix (GAN CAO)	uralsaponin b
Glycyrrhizae Radix (GAN CAO)	uralstilbene
Glycyrrhizae Radix (GAN CAO)	urea(0.832)
Glycyrrhizae Radix (GAN CAO)	vicianin
Glycyrrhizae Radix (GAN CAO)	β-sitosterol
Paeoniae Radix Alba(BAI SHAO)	(+)-catechin
Paeoniae Radix Alba(BAI SHAO)	(-)-catechin
Paeoniae Radix Alba(BAI SHAO)	(z)-(1s,5r)-beta-pinen-1-oxy-beta-vicianoside
Paeoniae Radix Alba(BAI SHAO)	1, 2, 3, 4, 6-pentagalloylglucose
Paeoniae Radix Alba(BAI SHAO)	1,2,3,4,6-pentagalloylglucose
Paeoniae Radix Alba(BAI SHAO)	1,2,3,6-tetra-o-galloyl-β-d-glucose
Paeoniae Radix Alba(BAI SHAO)	1,2,3-tri-o-galloyl-β-d-glucose
Paeoniae Radix Alba(BAI SHAO)	1,2,6-tri-o-galloyl-β-d-glucose
Paeoniae Radix Alba(BAI SHAO)	1,3,6-trigalloyl-β-d-glucose
Paeoniae Radix Alba(BAI SHAO)	1-o-galloyl-glucose
Paeoniae Radix Alba(BAI SHAO)	13-methyl tetradecanoicacid
Paeoniae Radix Alba(BAI SHAO)	2,3-o-(s)-hexahydroxydiphenoyl-d-gluco-pyranose
Paeoniae Radix Alba(BAI SHAO)	3-o-galloyl quinicacid
Paeoniae Radix Alba(BAI SHAO)	4-o-galloyl quinicacid
Paeoniae Radix Alba(BAI SHAO)	5-desgalloylstachyurin
Paeoniae Radix Alba(BAI SHAO)	acetic acid
Paeoniae Radix Alba(BAI SHAO)	albiflorin
Paeoniae Radix Alba(BAI SHAO)	albiflorinr1
Paeoniae Radix Alba(BAI SHAO)	benzoic acid
Paeoniae Radix Alba(BAI SHAO)	benzoicacid
Paeoniae Radix Alba(BAI SHAO)	benzoylpaeoniflorin
Paeoniae Radix Alba(BAI SHAO)	beta-sitosterol

Paeoniae Radix Alba(BAI SHAO)	casuarictin
Paeoniae Radix Alba(BAI SHAO)	casuariin
Paeoniae Radix Alba(BAI SHAO)	catechin
Paeoniae Radix Alba(BAI SHAO)	d-catechin
Paeoniae Radix Alba(BAI SHAO)	epigallocatechin
Paeoniae Radix Alba(BAI SHAO)	eugeniin
Paeoniae Radix Alba(BAI SHAO)	gallicacid
Paeoniae Radix Alba(BAI SHAO)	gallocatechin
Paeoniae Radix Alba(BAI SHAO)	gallotannin
Paeoniae Radix Alba(BAI SHAO)	lactiflorin
Paeoniae Radix Alba(BAI SHAO)	oxypaeoniflorin
Paeoniae Radix Alba(BAI SHAO)	paeonianiin e
Paeoniae Radix Alba(BAI SHAO)	paeonianin a
Paeoniae Radix Alba(BAI SHAO)	paeonianin b
Paeoniae Radix Alba(BAI SHAO)	paeonianin c
Paeoniae Radix Alba(BAI SHAO)	paeonianin d
Paeoniae Radix Alba(BAI SHAO)	paeoniflorigenone
Paeoniae Radix Alba(BAI SHAO)	paeoniflorin
Paeoniae Radix Alba(BAI SHAO)	paeonilactone a
Paeoniae Radix Alba(BAI SHAO)	paeonilactone b
Paeoniae Radix Alba(BAI SHAO)	paeonilactone c
Paeoniae Radix Alba(BAI SHAO)	paeonin
Paeoniae Radix Alba(BAI SHAO)	paeonol
Paeoniae Radix Alba(BAI SHAO)	palbinone
Paeoniae Radix Alba(BAI SHAO)	pedunculagin
Paeoniae Radix Alba(BAI SHAO)	peonin
Paeoniae Radix Alba(BAI SHAO)	phenol
Paeoniae Radix Alba(BAI SHAO)	pyrethrin i
Paeoniae Radix Alba(BAI SHAO)	pyrethrin ii
Paeoniae Radix Alba(BAI SHAO)	strictinin
Paeoniae Radix Alba(BAI SHAO)	tellimagrandin i
Paeoniae Radix Alba(BAI SHAO)	β-sitosterol
Corydalis Rhizoma (YAN HU SUO)	(+)-corybulbine
Corydalis Rhizoma (YAN HU SUO)	(+)-corydaline
Corydalis Rhizoma (YAN HU SUO)	(+)-n-methyl laurotetanine
Corydalis Rhizoma (YAN HU SUO)	(?)-tetrahydroberberine
Corydalis Rhizoma (YAN HU SUO)	(?)-tetrahydrocoptisine
Corydalis Rhizoma (YAN HU SUO)	1-tetrahydropal-matrine
Corydalis Rhizoma (YAN HU SUO)	allocryptopine
Corydalis Rhizoma (YAN HU SUO)	berberine

Corydalis Rhizoma (YAN HU SUO)	bicuculline
Corydalis Rhizoma (YAN HU SUO)	canadine
Corydalis Rhizoma (YAN HU SUO)	canaline
Corydalis Rhizoma (YAN HU SUO)	columbamine
Corydalis Rhizoma (YAN HU SUO)	columbianadin
Corydalis Rhizoma (YAN HU SUO)	coptisine
Corydalis Rhizoma (YAN HU SUO)	corchoroside a
Corydalis Rhizoma (YAN HU SUO)	corycavine
Corydalis Rhizoma (YAN HU SUO)	corydaline
Corydalis Rhizoma (YAN HU SUO)	corydalmine
Corydalis Rhizoma (YAN HU SUO)	corydamine
Corydalis Rhizoma (YAN HU SUO)	corydine
Corydalis Rhizoma (YAN HU SUO)	corylidin
Corydalis Rhizoma (YAN HU SUO)	corypalmine
Corydalis Rhizoma (YAN HU SUO)	corytuberine
Corydalis Rhizoma (YAN HU SUO)	dehydrocorybulbine
Corydalis Rhizoma (YAN HU SUO)	dehydrocorydaline
Corydalis Rhizoma (YAN HU SUO)	dehydrocorydalmine
Corydalis Rhizoma (YAN HU SUO)	dehydrocostus lactone
Corydalis Rhizoma (YAN HU SUO)	di-tetrahydropal-matrine
Corydalis Rhizoma (YAN HU SUO)	fumaricacid
Corydalis Rhizoma (YAN HU SUO)	glaucine
Corydalis Rhizoma (YAN HU SUO)	glaudine
Corydalis Rhizoma (YAN HU SUO)	isocorydine
Corydalis Rhizoma (YAN HU SUO)	isocorynoline
Corydalis Rhizoma (YAN HU SUO)	isocorypalmine
Corydalis Rhizoma (YAN HU SUO)	isocrotonylpterosin b
Corydalis Rhizoma (YAN HU SUO)	leonticine
Corydalis Rhizoma (YAN HU SUO)	lirioferine
Corydalis Rhizoma (YAN HU SUO)	methyl leptol b
Corydalis Rhizoma (YAN HU SUO)	norisocorydine
Corydalis Rhizoma (YAN HU SUO)	norjuzunal
Corydalis Rhizoma (YAN HU SUO)	palmatine
Corydalis Rhizoma (YAN HU SUO)	palmidin a
Corydalis Rhizoma (YAN HU SUO)	protopine
Corydalis Rhizoma (YAN HU SUO)	protoporphyrin
Corydalis Rhizoma (YAN HU SUO)	reticulin
Corydalis Rhizoma (YAN HU SUO)	reticuline
Corydalis Rhizoma (YAN HU SUO)	scoulerine
Corydalis Rhizoma (YAN HU SUO)	sculponeata a

Corydalis Rhizoma (YAN HU SUO)	stylopine
Corydalis Rhizoma (YAN HU SUO)	stypandrol
Corydalis Rhizoma (YAN HU SUO)	tetrahydrocannabinol delta8
Corydalis Rhizoma (YAN HU SUO)	tetrahydrocorysamine
Corydalis Rhizoma (YAN HU SUO)	tetrahydrocyperaguinone
Corydalis Rhizoma (YAN HU SUO)	tetrahydropalmatine
Corydalis Rhizoma (YAN HU SUO)	tetrahydropiperic acid
Corydalis Rhizoma (YAN HU SUO)	thaliporphine
Corydalis Rhizoma (YAN HU SUO)	yuanhunine
Corydalis Rhizoma (YAN HU SUO)	yuehchukene
Aconiti Laterdis Radix Praeparata (FU ZI)	aconitine(1)
Aconiti Laterdis Radix Praeparata (FU ZI)	coryneine chloride
Aconiti Laterdis Radix Praeparata (FU ZI)	higenamine(0.917)
Aconiti Laterdis Radix Praeparata (FU ZI)	hypaconitine
Aconiti Laterdis Radix Praeparata (FU ZI)	mesaconitine

Supplementary Table 2. Immune response pathways in the enriched 165 pathways.

Term	RT	Count	%	P-Value	Fold Enrichment	Benjamini
Toll-like receptor signaling pathway	RT	36	2.3	0.0000002	2.5	0.0000019
TNF signaling pathway	RT	35	2.2	0.000013	2.1	0.000066
PI3K-Akt signaling pathway	RT	80	5	0.000022	1.6	0.0001
T cell receptor signaling pathway	RT	34	2.1	0.000027	2.1	0.00012
NF-kappa B signaling pathway	RT	29	1.8	0.000061	2.2	0.00025
Inflammatory mediator regulation of TRP channels	RT	31	1.9	0.0013	1.8	0.0034

Natural killer cell mediated cytotoxicity	RT	27	1.7	0.002	1.8	0.0052
B cell receptor signaling pathway	RT	21	1.3	0.0021	2	0.0054
Cytokine-cytokine receptor interaction	RT	48	3	0.0044	1.5	0.011
NOD-like receptor signaling pathway	RT	17	1.1	0.0065	2	0.015
Leukocyte transendothelial migration	RT	28	1.8	0.017	1.6	0.036
Intestinal immune network for IgA production	RT	14	0.9	0.018	2	0.036
mTOR signaling pathway	RT	17	1.1	0.018	1.8	0.036
MAPK signaling pathway	RT	50	3.1	0.046	1.3	0.082

Supplementary Table 3. Calibration curves.

Compound	Standard curves	R2	Range
MDA	Y = 0.016X +0.008	R2=0.9949	20 -1400 ng/ml
GSH	Y =0.00007X-0.0056	R2=0.999	100-10000 ng/ml
GSSG	Y = 0.0013X+0.22	R2=0.9972	200-20000 ng/ml
L-Leu	Y = 0.016X+1.16	R2=0.9996	100-10000 ng/ml
L-Kyn	Y =0.020 X- 0.011	R2=0.9993	5-500 ng/ml
L-Try	Y =0.0025 X+ 0.83	R2=0.9952	600-60000 ng/ml
5-HTP	Y =0.053X - 0.0041	R2=0.9927	0.2-20 ng/ml
Cholic acid	Y =0.00003 X - 0.0003	R2=0.9986	40-4000 ng/ml
5-HT	Y =0.032 X+0.0062	R2=0.9985	0.8-80 ng/ml
N-phe	Y = 0.0094X+ 1.69	R2=0.9941	250-25000 ng/ml

Supplementary Table 4. Within-run and between-run precision, accuracy, recovery and stability values (n=6).

Cpd.	ng/ml	Accuracy %	Precision %	Recovery %	Repatbility %	Stability %	Matrix effect %
	5	84.4±4.7	5.6	85.9±8.4	9.8	2.5	82.6

	10	88.8±2.4	2.7	85.0±8.9	10.5	6.3	98.6
	1500	97.2±2.7	2.8	85.3±4.9	2.8	1.2	87.9
GSH	2000	98.0±8.9	9.1	85.0±3.9	9.1	0.3	88
	10000	102.7±4.3	4.2	92.1±8.3	4.2	2.5	83.4
	20	83.4±5.7	6.9	81.8±8.0	9.8	2.8	96.1
	40	96.6±5.2	5.3	96.4±6.8	7	0.3	99.1
	750	99.2±6.2	6.3	87.5±2.8	6.3	1.7	89.9
GSSG	1000	104.1±6.2	6	84.4±5.6	6	6	84.7
	5000	103.9±8.3	8	93.7±9.9	8	5.6	81.9
	1	110.7±1.3	1.2	100.4±11.4	11.3	14.6	96.8
	5	89.2±6.0	6.8	89.7±5.7	6.4	0.8	99
	750	98.2±4.7	4.8	91.9±7.9	4.8	0.4	88.4
L-Leu	1000	106.1±5.2	4.9	100.7±9.4	4.9	3.4	85.9
	5000	94.6±6.1	6.4	85.4±2.5	6.4	5.8	81.5
	0.5	97.0±3.5	3.6	98.6±4.0	4	2.3	93.8
	1	95.5±4.0	4.2	102.7±8.5	8.2	9.8	99.1
	37	95.8±4.2	4.3	89.5±8.7	4.3	0.1	88.7
L-Kyn	50	100.8±7.6	7.5	93.2±8.4	7.5	6.1	92.4
	250	99.1±4.6	4.6	93.5±7.0	4.6	1.5	84
	1	89.2±6.2	7	95.4±9.5	9.9	9.2	49.8
	10	90.2±8.6	9.6	100.6±12.9	12.9	14.6	96.5
	4500	94.0±3.38	3.6	86.9±6.8	3.6	3.4	86.5
L-Try	6000	97.9±4.4	4.5	94.2±8.4	4.5	3.9	85.6
	30000	98.1±6.6	6.8	91.7±10.6	6.8	4.6	82.2
	0.1	85.2±5.8	6.8	91.3±9.3	10.2	9.5	87
	0.2	90.3±9.6	10.6	95.7±10.5	11	8	98.6
	300	102.4±3.4	3.3	107.5±6.2	3.3	1.1	87.9
5-HTP	400	102.0±10.0	9.8	83.4±4.4	9.8	2.8	89.8
	2000	101.3±6.9	6.8	93.2±9.5	6.8	6.5	89
	10	95.2±7.0	7.3	94.8±9.9	10.4	0.5	83.9
	20	95.1±9.9	10.4	100.4±8.9	8.9	7.4	96.6
CA	300	97.7±4.4	4.5	85.8±5.1	4.5	3.9	91
	400	102.0±5.3	5.2	93.8±3.5	5.2	0.6	87.7
	2000	99.7±7.0	7	93.6±7.2	7	0.5	84.7
	5	114.6±6.0	5.2	108.9±8.8	8.1	7.4	87.4
	10	98.2±11.9	12.1	96.4±11.5	11.9	2.7	91.7
N-phe	1800	100.4±3.5	3.5	86.8±4.5	3.5	2	87.3
	2500	94.5±6.5	6.9	92.5±6.0	6.9	3.7	90.7

	12500	94.1±2.7	2.9	95.4±7.28	2.9	1.4	85.7
	0.5	92.2±9.8	10.6	97.8±11.1	14.1	10.5	86.3
	1	91.4±5.0	5.4	97.47±8.4	8.6	8.8	98.8
5-HT	6	99.6±1.2	1.3	84.03±2.4	1.3	1.2	89.4
	8	100.3±3.0	2.9	93.4±2.6	2.9	2	87
	40	101.9±2.4	2.3	88.1±4.9	2.3	1.9	83.9
	1	107.0±2.1	2	107.6±1.9	1.5	9.7	110.4
	10	90.8±6.7	7.7	89.0±3.0	6.7	9.8	108.4
MDA	180	103.6±6.2	6	92.3±9.1	6	0.4	107.2
	360	102.2±5.0	4.9	85.8±3.33	4.9	52	107.1
	720	91.6±4.2	4.6	106.4±5.6	4.6	49.4	97.5

Supplementary Table5. GJK-related targets -metabolism integrated pathways.

Pathway	Total	Expected	Hits	P.Value	Topology
Pyruvate metabolism	64	10.502	30	7.7881E-09	1.1304
Purine metabolism	234	38.398	69	1.0629E-07	1.3046
Glycolysis / Gluconeogenesis	91	14.933	35	2.202E-07	0.88136
Propanoate metabolism	52	8.5329	20	0.000096211	1.0244
Arginine and proline metabolism	102	16.738	32	0.0001001	0.73118
Cysteine and methionine metabolism	63	10.338	21	0.00065517	0.67273
Drug metabolism - other enzymes	77	12.635	24	0.00083182	0.70175
Citrate cycle (TCA cycle)	50	8.2047	17	0.0016608	1.4318
Linoleic acid metabolism	34	5.5792	13	0.0017469	1
Glycerophospholipid metabolism	119	19.527	32	0.0020657	0.85333
Nicotinate and nicotinamide metabolism	39	6.3997	14	0.0023672	1.027
Phenylalanine metabolism	29	4.7588	11	0.0042233	0.95455
beta-Alanine metabolism	50	8.2047	16	0.0045276	0.61905
Galactose metabolism	55	9.0252	17	0.005176	1.6531
Starch and sucrose metabolism	78	12.799	22	0.0054706	0.83333
Ether lipid metabolism	51	8.3688	16	0.005627	0.82759
Pyrimidine metabolism	142	23.301	35	0.0062362	1.0265

Porphyrin and chlorophyll metabolism	70	11.487	20	0.0067885	0.59574
Tyrosine metabolism	80	13.128	22	0.0075789	0.90805
Alanine, aspartate and glutamate metabolism	56	9.1893	16	0.01478	0.77551
Glutathione metabolism	75	12.307	20	0.015123	1.0755
Retinol metabolism	83	13.62	21	0.023345	0.69767
Arachidonic acid metabolism	100	16.409	24	0.029621	0.66667
Histidine metabolism	44	7.2202	12	0.045786	0.3125
Ascorbate and aldarate metabolism	35	5.7433	10	0.049089	0.66667