

Supporting Information

Exploring Anti-nonalcoholic Fatty Liver Disease Mechanism of Gardeniae Fructus by Network Pharmacology, Molecular docking, and Experiment Validation

Zhongyan Tang,¹ Lin Li,² Zhengxiang Xia^{3,*}

*Correspondence: Zhengxiang Xia, xzx5380537@163.com

Zhongyan Tang and Lin Li are the co-first authors.

¹Department of Emergency and Critical Care Medicine, Jin Shan Hospital, Fudan University, Shanghai, 201508, China.

Zhongyan Tang, ORCID: <https://orcid.org/0000-0002-9044-9180>

²Department of Operative Dentistry and Endodontics, School & Hospital of Stomatology, Shanghai Engineering Research Center of Tooth Restoration and Regeneration, Tongji University, 399 Middle Yan Chang Road, Shanghai, 200072, China.

³Department of Pharmacy, School & Hospital of Stomatology, Shanghai Engineering Research Center of Tooth Restoration and Regeneration, Tongji University, 399 Middle Yan Chang Road, Shanghai, 200072, China

*Zhengxiang Xia

Department of Pharmacy, School & Hospital of Stomatology, Shanghai Engineering Research Center of Tooth Restoration and Regeneration, Tongji University, 399 Middle Yan Chang Road, Shanghai, 200072, China

ORCID: <https://orcid.org/0000-0001-9042-9772>

Tel: +8621-66315500; E-mail: xzx5380537@163.com

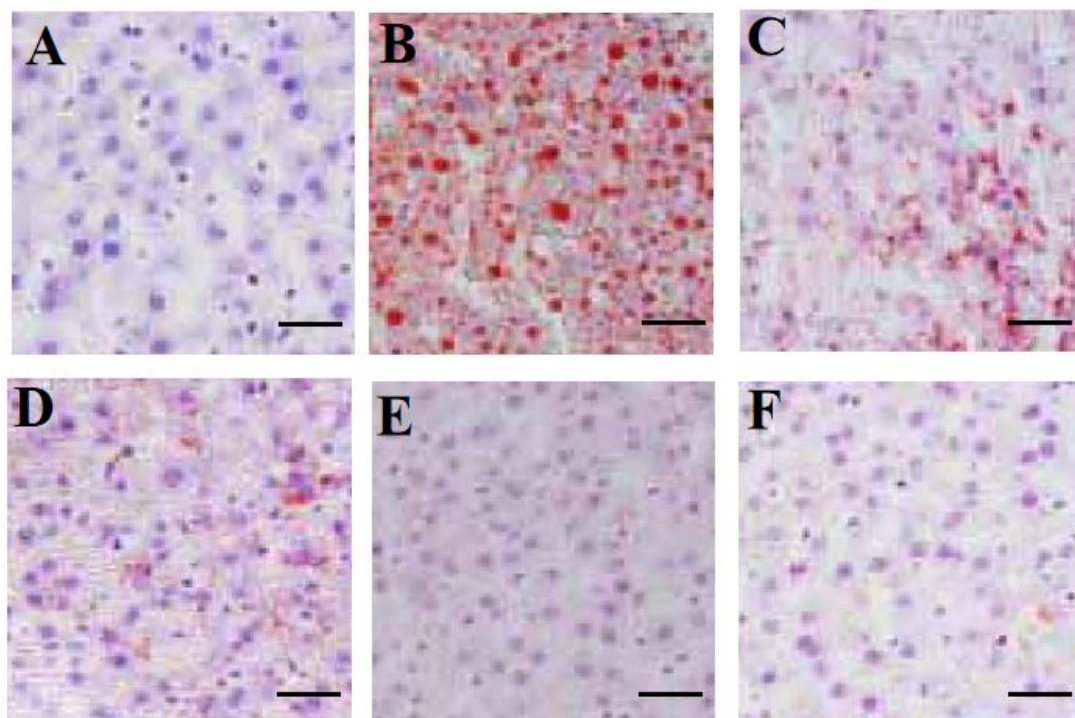


Figure S1. Liver tissue stained with haematoxylin and eosin (H&E). (A) Control group, (B) HFD-fed group; (C) HFD + 25 mg/kg GF; (D) HFD + 50 mg/kg GF; (E) HFD + 100 mg/kg GF; (F) HFD + Metformin. — Bar, 100 μ m.

Table S1. The relationship among compounds-targets-signal pathways

crocetin	ADRA1A
crocetin	ADRA1B
genipin	CA2
oceanolic acid	PPARA
oceanolic acid	FAS
oceanolic acid	PTPN1
quercetin	PPARG
quercetin	ADRB2
quercetin	MAOB
quercetin	PPARG
quercetin	ACACA
quercetin	PPARA
quercetin	PPARD
kaempferol	PPARG
kaempferol	SLC6A2
geniposide	AMPK
geniposide	GLP1R
geniposide	CA2
geniposide	GCG
chrysin	SLC6A4
PPARA	PPAR signaling pathway
PPARD	PPAR signaling pathway
PPARG	PPAR signaling pathway
ADRB2	Salivary secretion
ADRA1B	Salivary secretion
ADRA1A	Salivary secretion
ADRB2	Neuroactive ligand-receptor interaction
ADRA1B	Neuroactive ligand-receptor interaction
ADRA1A	Neuroactive ligand-receptor interaction
GLP1R	Neuroactive ligand-receptor interaction
GCG	Glucagon signaling pathway
PPARA	Glucagon signaling pathway
ACACA	Glucagon signaling pathway
PPARG	AMPK signaling pathway
ACACA	AMPK signaling pathway
ADRA1A	AMPK signaling pathway
ADRB2	Adrenergic signaling in cardiomyocytes 3
ADRA1B	Adrenergic signaling in cardiomyocytes 3
ADRA1A	Adrenergic signaling in cardiomyocytes 3
ADRB2	cGMP-PKG signaling pathway
ADRA1B	cGMP-PKG signaling pathway
ADRA1A	cGMP-PKG signaling pathway
ADRB2	Calcium signaling pathway

ADRA1B	Calcium signaling pathway
ADRA1A	Calcium signaling pathway
PPARA	cAMP signaling pathway
ADRB2	cAMP signaling pathway
GLP1R	cAMP signaling pathway

Table S2. The compounds' targets

Compound	targets
crocetinI	CHRM3
crocetinI	CHRM1
crocetinI	GABRA2
crocetinI	GABRA5
crocetinI	ADRA1A
crocetinI	GABRA3
crocetinI	ADRA1B
crocetinI	GABRA1
crocetinI	IGHG1
crocetinI	PTGS2
crocetinI	NCOA2
crocetinI	VCAM1
genipin	PTGS1
genipin	PTGS2
genipin	CA2
genipin	GABRA2
genipin	GABRA1
genipin	TK1
genipin	PRSS1
genipin	GRIA2
genipin	GABRA6
genipin	ABCC2
genipin	CA2
genipin	F2
Oeanolic acid	CASP3
Oeanolic acid	NAMPT
Oeanolic acid	NFE2L2
Oeanolic acid	NQO1
Oeanolic acid	PPARA
Oeanolic acid	PTGIR
Oeanolic acid	TOP1
Oeanolic acid	TOP2A
Oeanolic acid	UGT2B11
Oeanolic acid	UGT2B10
Oeanolic acid	BAX

Oeanolic acid	MMP2
Oeanolic acid	MMP9
Oeanolic acid	CDK4
Oeanolic acid	TNF
Oeanolic acid	JUN
Oeanolic acid	IL6
Oeanolic acid	CDK6
Oeanolic acid	CASP3
Oeanolic acid	TP53
Oeanolic acid	MAPK8
Oeanolic acid	PTGS2
Oeanolic acid	NFKBIA
Oeanolic acid	CASP8
Oeanolic acid	FAS
Oeanolic acid	MMP1
Oeanolic acid	MMP3
Oeanolic acid	MMP10
Oeanolic acid	ICAM1
Oeanolic acid	IL1B
Oeanolic acid	CREB1
Oeanolic acid	SELE
Oeanolic acid	PTGER3
Oeanolic acid	PTGS1
Oeanolic acid	MCL1
Oeanolic acid	PRKCG
Oeanolic acid	ATF2
Oeanolic acid	CSF2
Oeanolic acid	PECAM1
Oeanolic acid	VL
Oeanolic acid	BIRC5
Oeanolic acid	PTPN6
Oeanolic acid	GAP43
Oeanolic acid	DUOX2
Oeanolic acid	NOS3
Oeanolic acid	PTPN1
Oeanolic acid	INPPL1
Oeanolic acid	LITAF
Oeanolic acid	CCND2
Oeanolic acid	FASLG
Oeanolic acid	CASP1
Oeanolic acid	PLAU
Oeanolic acid	CTSB
Oeanolic acid	RELA
Oeanolic acid	STAT3

Oeanolic acid	VEGF
Oeanolic acid	CCND1
Oeanolic acid	Bcl2
Oeanolic acid	BCL2L1
Oeanolic acid	FOS
Oeanolic acid	CDKN1
Oeanolic acid	ENPP7
quercetin	ATP5B
quercetin	CYP1A1
quercetin	CYP1B1
quercetin	CYP2C8
quercetin	HCK
quercetin	HIBCH
quercetin	MCL1
quercetin	PIM1
quercetin	SLC2A2
quercetin	STK17B
quercetin	PTGS1
quercetin	AR
quercetin	PPARG
quercetin	PTGS2
quercetin	HSP90
quercetin	PIK3CG
quercetin	NCOA2
quercetin	DPP4
quercetin	AKR1B1
quercetin	PRSS1
quercetin	TOP2
quercetin	KCNA2
quercetin	SCN5A
quercetin	F10
quercetin	ADRB2
quercetin	MMP3
quercetin	F7
quercetin	NOS3
quercetin	RXRA
quercetin	ACHE
quercetin	GABRA1
quercetin	MAOB
quercetin	RELA
quercetin	EGFR
quercetin	AKT1
quercetin	VEGF
quercetin	CCND1

quercetin	BCL2
quercetin	BCL2L1
quercetin	FOS
quercetin	CDKN1
quercetin	EIF6
quercetin	BAX
quercetin	CASP9
quercetin	PLAU
quercetin	MMP2
quercetin	MMP9
quercetin	MAPK1
quercetin	IL10
quercetin	EGF
quercetin	E2F1
quercetin	TNF
quercetin	IL6
quercetin	AHSA1
quercetin	CASP3
quercetin	TP53
quercetin	ELK1
quercetin	NFKBIA
quercetin	POR
quercetin	ODC1
quercetin	XDH
quercetin	CASP8
quercetin	TOP1
quercetin	RAF1
quercetin	SOD1
quercetin	PRKCA
quercetin	MMP1
quercetin	HIF1A
quercetin	STAT1
quercetin	RUNX1T1
quercetin	CDC2
quercetin	Hspa5
quercetin	ERBB2
quercetin	PPARG
quercetin	ACACA
quercetin	HMOX1
quercetin	CYP3A4
quercetin	CYP1A2
quercetin	CAV1
quercetin	MYC
quercetin	F3

quercetin	GJA1
quercetin	CYP1A1
quercetin	ICAM1
quercetin	IL1B
quercetin	CCL2
quercetin	SELE
quercetin	VCAM1
quercetin	PTGER3
quercetin	IL8
quercetin	PRKCB
quercetin	BIRC5
quercetin	DUOX2
quercetin	NOS3
quercetin	HSPB1
quercetin	TGFB1
quercetin	SULT1E1
quercetin	MGAM
quercetin	IL2
quercetin	NR1I2
quercetin	CYP1B1
quercetin	CCNB1
quercetin	PLAT
quercetin	THBD
quercetin	SERPINE1
quercetin	COL1A1
quercetin	IFNG
quercetin	ALOX5
quercetin	PTEN
quercetin	IL1A
quercetin	MPO
quercetin	TOP2A
quercetin	NCF1
quercetin	ABCG2
quercetin	HAS2
quercetin	GSTP
quercetin	NFE2L2
quercetin	NQO1
quercetin	PARP1
quercetin	AHR
quercetin	PSMD11
quercetin	SLC2A4
quercetin	COL3A1
quercetin	TOP2A
quercetin	CXCL11

quercetin	DCAF5
quercetin	NR1I3
quercetin	CHEK2
quercetin	INSR
quercetin	CLDN4
quercetin	PPARA
quercetin	PPARD
quercetin	HSF1
quercetin	CRP
quercetin	CXCL10
quercetin	IKBKB
quercetin	SPP1
quercetin	RUNX2
quercetin	RASSF5
quercetin	E2F1
quercetin	E2F2
quercetin	ACPP
quercetin	CTSD
quercetin	IGFBP3
quercetin	IGF2
quercetin	CD40LG
quercetin	IRF1
quercetin	ERBB3
quercetin	PON1
quercetin	DIO1
quercetin	PCOLCE
quercetin	NPEPPS
quercetin	HK2
quercetin	NKX3-1
quercetin	RASA1
quercetin	PRXC1A
quercetin	GSTM1
quercetin	GSTM2
kaempferol	AHR
kaempferol	CDK1
kaempferol	CYP1B1
kaempferol	NR1I2
kaempferol	RPS6KA3
kaempferol	UGT1A3
kaempferol	UGT1A7
kaempferol	UGT1A8
kaempferol	UGT1A9
kaempferol	UGT3A1
kaempferol	NOS2

kaempferol	PTGS1
kaempferol	AR
kaempferol	PPARG
kaempferol	PTGS2
kaempferol	HSP90
kaempferol	PIK3CG
kaempferol	NCOA2
kaempferol	DPP4
kaempferol	PRSS1
kaempferol	PGR
kaempferol	CHRM1
kaempferol	NOS3
kaempferol	GABRA2
kaempferol	ACHE
kaempferol	SLC6A2
kaempferol	CHRM2
kaempferol	ADRA1B
kaempferol	GABRA1
kaempferol	TOP2
kaempferol	F7
kaempferol	CALM
kaempferol	RELA
kaempferol	IKBKB
kaempferol	AKT1
kaempferol	BCL2
kaempferol	BAX
kaempferol	TNF
kaempferol	JUN
kaempferol	AHSA1
kaempferol	CASP3
kaempferol	MAPK8
kaempferol	XDH
kaempferol	MMP1
kaempferol	STAT1
kaempferol	CDC2
kaempferol	PPARG
kaempferol	HMOX1
kaempferol	CYP3A4
kaempferol	CYP1A2
kaempferol	CYP1A1
kaempferol	ICAM1
kaempferol	SELE
kaempferol	VCAM1
kaempferol	NR1I2

kaempferol	CYP1B1
kaempferol	ALOX5
kaempferol	HAS2
kaempferol	GSTP
kaempferol	AHR
kaempferol	PSMD3
kaempferol	SLC2A4
kaempferol	NR1I3
kaempferol	INSR
kaempferol	DIO1
kaempferol	PPP3CA
kaempferol	PRXC1A
kaempferol	GSTM1
kaempferol	GSTM2
kaempferol	AKR1C3
kaempferol	SLPI
kaempferol	CYP2E1
kaempferol	GLP1R
kaempferol	GSK3A
kaempferol	GSK3B
kaempferol	HMOX1
kaempferol	IL6
kaempferol	SELE
kaempferol	VCAM1
kaempferol	CA2
kaempferol	BCL2
kaempferol	HMOX1
kaempferol	GAP43
kaempferol	PLB1
kaempferol	GCG
kaempferol	GSTM1
kaempferol	GSTM2
kaempferol	ABCG2
kaempferol	CYP19A1
kaempferol	CYP1A1
kaempferol	CYP1A2
kaempferol	CYP1B1
kaempferol	PYGB
kaempferol	PYGL
kaempferol	PYGM
kaempferol	RELA
kaempferol	TP53
kaempferol	PTGS1
kaempferol	AR

kaempferol	PTGS2
kaempferol	PDE3A
kaempferol	SLC6A4
kaempferol	GABRA1
kaempferol	DPP4
kaempferol	HSP90
kaempferol	PIK3CG
kaempferol	MAOB
kaempferol	PKIA
kaempferol	CDKN1
kaempferol	TGFB1
kaempferol	IL4
kaempferol	CYP19A1
kaempferol	IL13
kaempferol	MS4A2
geniposide	CYP2E1
geniposide	GLP1R
geniposide	GSK3A
geniposide	GSK3B
geniposide	HMOX1
geniposide	IL6
geniposide	SELE
geniposide	VCAM1
geniposide	CA2
geniposide	BCL2
geniposide	HMOX1
geniposide	GAP43
geniposide	PLB1
geniposide	GCG
geniposide	GSTM1
geniposide	GSTM2
chrysin	ABCG2
chrysin	CYP19A1
chrysin	CYP1A1
chrysin	CYP1A2
chrysin	CYP1B1
chrysin	PYGB
chrysin	PYGL
chrysin	PYGM
chrysin	RELA
chrysin	TP53
chrysin	PTGS1
chrysin	AR
chrysin	PTGS2

chrysin	PDE3A
chrysin	SLC6A4
chrysin	GABRA1
chrysin	DPP4
chrysin	HSP90
chrysin	PIK3CG
chrysin	MAOB
chrysin	PKIA
chrysin	CDKN1
chrysin	TGFB1
chrysin	IL4
chrysin	CYP19A1
chrysin	IL13
chrysin	MS4A2