

Supplementary Table S1. Potential active components of *Fructus Lycii*

Molecule ID	Molecule name	OB (%)	DL
MOL001323	Sitosterol alpha1	43.2813	0.78354
MOL003578	Cycloartenol	38.6857	0.78093
MOL001494	Mandenol	41.9962	0.19321
MOL001495	Ethyl linolenate	46.101	0.19716
MOL001979	LAN	42.1192	0.74787
MOL000449	Stigmasterol	43.8299	0.75665
MOL000358	beta-sitosterol	36.9139	0.75123
MOL005406	atropine	45.9706	0.19328
MOL005438	campesterol	37.5768	0.71488
MOL006209	cyanin	47.4209	0.75918
MOL007449	24-methylidenelophenol	44.1926	0.7533
MOL008173	daucosterol_qt	36.9139	0.75316
MOL008400	glycitein	50.4789	0.23826
MOL010234	delta-Carotene	31.8009	0.54639
MOL000953	CLR	37.8739	0.67677
MOL009604	14b-pregnane	34.7792	0.33723
MOL009612	(24R)-4alpha-Methyl-24-ethylcholesta-7,25-dien-3beta-ylacetate	46.3575	0.8398
MOL009615	24-Methylenecycloartan-3beta,21-diol	37.3173	0.79751
MOL009617	24-ethylcholest-22-enol	37.0945	0.7511
MOL009618	24-ethylcholesta-5,22-dienol	43.8299	0.75636
MOL009620	24-methyl-31-norlanost-9(11)-enol	37.9997	0.75092
MOL009621	24-methylenelanost-8-enol	42.3682	0.76769
MOL009622	Fucosterol	43.7764	0.75668
MOL009631	31-Norcyclolaudenol	38.6821	0.81391
MOL009633	31-norlanost-9(11)-enol	38.3539	0.7249
MOL009634	31-norlanosterol	42.2046	0.73012
MOL009635	4,24-methyllophenol	37.8347	0.74999
MOL009639	Lophenol	38.1294	0.714
MOL009640	4alpha,14alpha,24-trimethylcholesta-8,24-dienol	38.9099	0.75772
MOL009641	4alpha,24-dimethylcholesta-7,24-dienol	42.653	0.75297
MOL009642	4alpha-methyl-24-ethylcholesta-7,24-dienol	42.2951	0.78304
MOL009644	6-Fluoroindole-7-Dehydrocholesterol	43.726	0.72224
MOL009646	7-O-Methyluteolin-6-C-beta-glucoside_qt	40.7737	0.30497
MOL009650	Atropine	42.159	0.19299
MOL009651	Cryptoxanthin monoepoxide	46.9537	0.56103
MOL009653	Cycloeucalenol	39.7265	0.79446
MOL009656	(E,E)-1-ethyl octadeca-3,13-dienoate	41.9962	0.19364
MOL009660	methyl (1R,4aS,7R,7aS)-4a,7-dihydroxy-7-methyl-1-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-1,5,6,7a-tetrahydrocyclopenta[d]pyran-4-carboxylate	39.4285	0.46558
MOL009662	Lantadene A	38.6794	0.57405
MOL009664	Physalin A	91.7065	0.27207
MOL009665	Physcion-8-O-beta-D-gentiobioside	43.9036	0.62426
MOL009677	lanost-8-en-3beta-ol	34.2263	0.74036
MOL009678	lanost-8-enol	34.2263	0.74167
MOL009681	Obtusifoliol	42.552	0.7565
MOL000098	quercetin	46.4333	0.27525

Supplementary Table S2. Information of intersection target of components and exercise-induced fatigue

ID	Molecule name	Target name	Gene name
GQ1	Sitosterol alpha1	Progesterone receptor	PGR
GQ1	Sitosterol alpha1	Prostaglandin G/H synthase 2	PTGS2
GQ1	Sitosterol alpha1	Mineralocorticoid receptor	NR3C2
GQ2	Cycloartenol	Mineralocorticoid receptor	NR3C2
GQ3	Mandenol	Prostaglandin G/H synthase 1	PTGS1
GQ3	Mandenol	Prostaglandin G/H synthase 2	PTGS2
GQ4	Ethyl linolenate	Prostaglandin G/H synthase 1	PTGS1
GQ5	LAN	Progesterone receptor	PGR
GQ5	LAN	Mineralocorticoid receptor	NR3C2
GQ6	Stigmasterol	Progesterone receptor	PGR
GQ6	Stigmasterol	Mineralocorticoid receptor	NR3C2
GQ6	Stigmasterol	Ig gamma-1 chain C region	IGHG1
GQ6	Stigmasterol	Retinoic acid receptor RXR-alpha	RXRA
GQ6	Stigmasterol	Prostaglandin G/H synthase 1	PTGS1
GQ6	Stigmasterol	Prostaglandin G/H synthase 2	PTGS2
GQ6	Stigmasterol	Alpha-2A adrenergic receptor	ADRA2A
GQ6	Stigmasterol	Sodium-dependent noradrenaline transporter	SLC6A2
GQ6	Stigmasterol	Sodium-dependent dopamine transporter	SLC6A3
GQ6	Stigmasterol	Beta-2 adrenergic receptor	ADRB2
GQ6	Stigmasterol	Aldose reductase	AKR1B1
GQ6	Stigmasterol	Urokinase-type plasminogen activator	PLAU
GQ6	Stigmasterol	Leukotriene A-4 hydrolase	LTA4H
GQ6	Stigmasterol	Amine oxidase [flavin-containing] B	MAOB
GQ6	Stigmasterol	Amine oxidase [flavin-containing] A	MAOA
GQ6	Stigmasterol	Muscarinic acetylcholine receptor M3	CHRM3
GQ6	Stigmasterol	Beta-1 adrenergic receptor	ADRB1
GQ6	Stigmasterol	Sodium channel protein type 5 subunit alpha	SCN5A
GQ6	Stigmasterol	5-hydroxytryptamine 2A receptor	HTR2A
GQ6	Stigmasterol	Gamma-aminobutyric-acid receptor subunit alpha-3	GABRA3
GQ6	Stigmasterol	Muscarinic acetylcholine receptor M2	CHRM2
GQ6	Stigmasterol	Alpha-1B adrenergic receptor	ADRA1B
GQ6	Stigmasterol	Neuronal acetylcholine receptor subunit alpha-7	CHRNA7
GQ7	beta-sitosterol	Progesterone receptor	PGR
GQ7	beta-sitosterol	Prostaglandin G/H synthase 1	PTGS1
GQ7	beta-sitosterol	Prostaglandin G/H synthase 2	PTGS2
GQ7	beta-sitosterol	Heat shock protein HSP 90-alpha	HSP90AA1
GQ7	beta-sitosterol	Potassium voltage-gated channel subfamily H member 2	KCNH2
GQ7	beta-sitosterol	D(1A) dopamine receptor	DRD1
GQ7	beta-sitosterol	Muscarinic acetylcholine receptor M3	CHRM3
GQ7	beta-sitosterol	Sodium channel protein type 5 subunit alpha	SCN5A

Continued

ID	Molecule name	Target name	Gene name
GQ7	beta-sitosterol	cGMP-inhibited 3',5'-cyclic phosphodiesterase A	PDE3A
GQ7	beta-sitosterol	5-hydroxytryptamine 2A receptor	HTR2A
GQ7	beta-sitosterol	Gamma-aminobutyric-acid receptor subunit alpha-5	GABRA5
GQ7	beta-sitosterol	Gamma-aminobutyric-acid receptor subunit alpha-3	GABRA3
GQ7	beta-sitosterol	Muscarinic acetylcholine receptor M2	CHRM2
GQ7	beta-sitosterol	Alpha-1B adrenergic receptor	ADRA1B
GQ7	beta-sitosterol	Beta-2 adrenergic receptor	ADRB2
GQ7	beta-sitosterol	Neuronal acetylcholine receptor subunit alpha-2	CHRNA2
GQ7	beta-sitosterol	Sodium-dependent serotonin transporter	SLC6A4
GQ7	beta-sitosterol	Mu-type opioid receptor	OPRM1
GQ7	beta-sitosterol	Neuronal acetylcholine receptor subunit alpha-7	CHRNA7
GQ7	beta-sitosterol	Apoptosis regulator Bcl-2	BCL2
GQ7	beta-sitosterol	Apoptosis regulator BAX	BAX
GQ7	beta-sitosterol	Caspase-9	CASP9
GQ7	beta-sitosterol	Transcription factor AP-1	JUN
GQ7	beta-sitosterol	Caspase-3	CASP3
GQ7	beta-sitosterol	Caspase-8	CASP8
GQ7	beta-sitosterol	Protein kinase C alpha type	PRKCA
GQ7	beta-sitosterol	Transforming growth factor beta-1	TGFB1
GQ7	beta-sitosterol	Serum paraoxonase/arylesterase 1	PON1
GQ7	beta-sitosterol	Microtubule-associated protein 2	MAP2
GQ8	(-)-Hyoscyamine	D(1A) dopamine receptor	DRD1
GQ8	(-)-Hyoscyamine	Muscarinic acetylcholine receptor M3	CHRM3
GQ8	(-)-Hyoscyamine	Beta-1 adrenergic receptor	ADRB1
GQ8	(-)-Hyoscyamine	Alpha-2A adrenergic receptor	ADRA2A
GQ8	(-)-Hyoscyamine	Alpha-2C adrenergic receptor	ADRA2C
GQ8	(-)-Hyoscyamine	Delta-type opioid receptor	OPRD1
GQ8	(-)-Hyoscyamine	5-hydroxytryptamine 2A receptor	HTR2A
GQ8	(-)-Hyoscyamine	Sodium-dependent noradrenaline transporter	SLC6A2
GQ8	(-)-Hyoscyamine	Muscarinic acetylcholine receptor M2	CHRM2
GQ8	(-)-Hyoscyamine	Alpha-2B adrenergic receptor	ADRA2B
GQ8	(-)-Hyoscyamine	Alpha-1B adrenergic receptor	ADRA1B
GQ8	(-)-Hyoscyamine	Sodium-dependent dopamine transporter	SLC6A3
GQ8	(-)-Hyoscyamine	Beta-2 adrenergic receptor	ADRB2
GQ8	(-)-Hyoscyamine	Sodium-dependent serotonin transporter	SLC6A4
GQ8	(-)-Hyoscyamine	D(2) dopamine receptor	DRD5
GQ8	(-)-Hyoscyamine	Mu-type opioid receptor	OPRM1
GQ8	(-)-Hyoscyamine	5-hydroxytryptamine 1B receptor	HTR1B
GQ8	(-)-Hyoscyamine	Histamine H1 receptor	HRH1
GQ8	(-)-Hyoscyamine	5-hydroxytryptamine 1A receptor	HTR1A
GQ9	campesterol	Progesterone receptor	PGR

Continued

ID	Molecule name	Target name	Gene name
GQ10	cyanin	Prostaglandin G/H synthase 2	PTGS2
GQ10	cyanin	Heat shock protein HSP 90-alpha	HSP90AA1
GQ11	24-methylidenelophenol	Progesterone receptor	PGR
GQ11	24-methylidenelophenol	Mineralocorticoid receptor	NR3C2
GQ12	daucosterol_qt	Progesterone receptor	PGR
GQ13	glycitein	Prostaglandin G/H synthase 1	PTGS1
GQ13	glycitein	Estrogen receptor	ESR1
GQ13	glycitein	Androgen receptor	AR
GQ13	glycitein	Peroxisome proliferator-activated receptor gamma	PPARG
GQ13	glycitein	Prostaglandin G/H synthase 2	PTGS2
GQ13	glycitein	Retinoic acid receptor RXR-alpha	RXRA
GQ13	glycitein	cGMP-inhibited 3',5'-cyclic phosphodiesterase A	PDE3A
GQ13	glycitein	Estrogen receptor beta	ESR2
GQ13	glycitein	Mitogen-activated protein kinase 14	MAPK14
GQ13	glycitein	Heat shock protein HSP 90-alpha	HSP90AA1
GQ13	glycitein	Trypsin-1	PRSS1
GQ13	glycitein	Cyclin-A2	CCNA2
GQ13	glycitein	Nitric oxide synthase, inducible	NOS2
GQ13	glycitein	Collagenase 3	MMP13
GQ13	glycitein	Neutrophil collagenase	MMP8
GQ14	CLR	Progesterone receptor	PGR
GQ14	CLR	Mineralocorticoid receptor	NR3C2
GQ15	14b-pregnane	Prostaglandin G/H synthase 2	PTGS2
GQ15	14b-pregnane	Progesterone receptor	PGR
GQ16	24-ethylcholesta-5,22-dienol	Progesterone receptor	PGR
GQ16	24-ethylcholesta-5,22-dienol	Mineralocorticoid receptor	NR3C2
GQ17	Fucoesterol	Progesterone receptor	PGR
GQ17	Fucoesterol	Mineralocorticoid receptor	NR3C2
GQ18	31-norlanosterol	Progesterone receptor	PGR
GQ18	31-norlanosterol	Mineralocorticoid receptor	NR3C2
GQ19	4,24-methyllophenol	Progesterone receptor	PGR
GQ20	Lophenol	Progesterone receptor	PGR
GQ21	4alpha,14alpha,24-trimethylcholesta-8,24-dienol	Progesterone receptor	PGR
GQ22	4alpha,24-dimethylcholesta-7,24-dienol	Progesterone receptor	PGR
GQ22	4alpha,24-dimethylcholesta-7,24-dienol	Mineralocorticoid receptor	NR3C2
GQ23	4alpha-methyl-24-ethylcholesta-7,24-dienol	Progesterone receptor	PGR
GQ24	6-Fluoroindole-7-Dehydrocholesterol	Progesterone receptor	PGR
GQ24	6-Fluoroindole-7-Dehydrocholesterol	Mineralocorticoid receptor	NR3C2
GQ24	6-Fluoroindole-7-Dehydrocholesterol	Glucocorticoid receptor	NR3C1
GQ25	7-O-Methyluteolin-6-C-beta-glucoside_qt	Prostaglandin G/H synthase 2	PTGS2

Continued

ID	Molecule name	Target name	Gene name
GQ25	7-O-Methyluteolin-6-C-beta-glucoside_qt	DNA topoisomerase 2-alpha	TOP2A
GQ25	7-O-Methyluteolin-6-C-beta-glucoside_qt	Heat shock protein HSP 90-alpha	HSP90AA1
GQ26	Atropine	D(1A) dopamine receptor	DRD1
GQ26	Atropine	Muscarinic acetylcholine receptor M3	CHRM3
GQ26	Atropine	D(1B) dopamine receptor	DRD5
GQ26	Atropine	Beta-1 adrenergic receptor	ADRB1
GQ26	Atropine	Sodium channel protein type 5 subunit alpha	SCN5A
GQ26	Atropine	Alpha-2A adrenergic receptor	ADRA2A
GQ26	Atropine	5-hydroxytryptamine 1A receptor	HTR1A
GQ26	Atropine	Alpha-2C adrenergic receptor	ADRA2C
GQ26	Atropine	Delta-type opioid receptor	OPRD1
GQ26	Atropine	Histamine H1 receptor	HRH1
GQ26	Atropine	5-hydroxytryptamine 2A receptor	HTR2A
GQ26	Atropine	Sodium-dependent noradrenaline transporter	SLC6A2
GQ26	Atropine	Muscarinic acetylcholine receptor M2	CHRM2
GQ26	Atropine	Alpha-2B adrenergic receptor	ADRA2B
GQ26	Atropine	Alpha-1B adrenergic receptor	ADRA1B
GQ26	Atropine	Sodium-dependent dopamine transporter	SLC6A3
GQ26	Atropine	Beta-2 adrenergic receptor	ADRB2
GQ26	Atropine	Sodium-dependent serotonin transporter	SLC6A4
GQ26	Atropine	D(2) dopamine receptor	DRD5
GQ26	Atropine	Mu-type opioid receptor	OPRM1
GQ26	Atropine	5-hydroxytryptamine 1B receptor	HTR1B
GQ27	Physcion-8-O-beta-D-gentiobioside	DNA topoisomerase 2-alpha	TOP2A
GQ28	Ianost-8-en-3beta-ol	Progesterone receptor	PGR
GQ28	Ianost-8-en-3beta-ol	Mineralocorticoid receptor	NR3C2
GQ29	Obtusifoliol	Progesterone receptor	PGR
GQ29	Obtusifoliol	Mineralocorticoid receptor	NR3C2
GQ30	quercetin	Prostaglandin G/H synthase 1	PTGS1
GQ30	quercetin	Androgen receptor	AR
GQ30	quercetin	Peroxisome proliferator-activated receptor gamma	PPARG
GQ30	quercetin	Prostaglandin G/H synthase 2	PTGS2
GQ30	quercetin	Heat shock protein HSP 90-alpha	HSP90AA1
GQ30	quercetin	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma isoform	PIK3CG
GQ30	quercetin	Dipeptidyl peptidase 4	DPP4
GQ30	quercetin	Aldose reductase	AKR1B1
GQ30	quercetin	Trypsin-1	PRSS1
GQ30	quercetin	DNA topoisomerase 2-alpha	TOP2A
GQ30	quercetin	Prothrombin	F2
GQ30	quercetin	Potassium voltage-gated channel subfamily H member 2	KCNH2

Continued

ID	Molecule name	Target name	Gene name
GQ30	quercetin	Sodium channel protein type 5 subunit alpha	SCN5A
GQ30	quercetin	Coagulation factor X	F10
GQ30	quercetin	Beta-2 adrenergic receptor	ADRB2
GQ30	quercetin	Stromelysin-1	MMP3
GQ30	quercetin	Coagulation factor VII	F7
GQ30	quercetin	Nitric-oxide synthase, endothelial	NOS3
GQ30	quercetin	Retinoic acid receptor RXR-alpha	RXRA
GQ30	quercetin	Acetylcholinesterase	ACHE
GQ30	quercetin	Amine oxidase [flavin-containing] B	MAOB
GQ30	quercetin	Transcription factor p65	RELA
GQ30	quercetin	Epidermal growth factor receptor	EGFR
GQ30	quercetin	RAC-alpha serine/threonine-protein kinase	AKT1
GQ30	quercetin	G1/S-specific cyclin-D1	CCND1
GQ30	quercetin	Apoptosis regulator Bcl-2	BCL2
GQ30	quercetin	Bcl-2-like protein 1	BCL2L1
GQ30	quercetin	Proto-oncogene c-Fos	FOS
GQ30	quercetin	Cyclin-dependent kinase inhibitor 1	CDKN1A
GQ30	quercetin	Apoptosis regulator BAX	BAX
GQ30	quercetin	Caspase-9	CASP9
GQ30	quercetin	Urokinase-type plasminogen activator	PLAU
GQ30	quercetin	72 kDa type IV collagenase	MMP2
GQ30	quercetin	Matrix metalloproteinase-9	MMP9
GQ30	quercetin	Mitogen-activated protein kinase 1	MAPK1
GQ30	quercetin	Interleukin-10	IL10
GQ30	quercetin	Retinoblastoma-associated protein	RB1
GQ30	quercetin	Tumor necrosis factor	TNF
GQ30	quercetin	Transcription factor AP-1	JUN
GQ30	quercetin	Interleukin-6	IL6
GQ30	quercetin	Caspase-3	CASP3
GQ30	quercetin	Cellular tumor antigen p53	TP53
GQ30	quercetin	NF-kappa-B inhibitor alpha	NFKBIA
GQ30	quercetin	Xanthine dehydrogenase/oxidase	XDH
GQ30	quercetin	Caspase-8	CASP8
GQ30	quercetin	RAF proto-oncogene serine/threonine-protein kinase	RAF1
GQ30	quercetin	Superoxide dismutase [Cu-Zn]	SOD1
GQ30	quercetin	Protein kinase C alpha type	PRKCA
GQ30	quercetin	Interstitial collagenase	MMP1
GQ30	quercetin	Hypoxia-inducible factor 1-alpha	HIF1A
GQ30	quercetin	Signal transducer and activator of transcription 1-alpha/beta	STAT1
GQ30	quercetin	Cell division control protein 2 homolog	CDK1
GQ30	quercetin	Peroxisome proliferator-activated receptor gamma	PPARG

Continued

ID	Molecule name	Target name	Gene name
GQ30	quercetin	Heme oxygenase 1	HMOX1
GQ30	quercetin	Cytochrome P450 3A4	CYP3A4
GQ30	quercetin	Caveolin-1	CAV1
GQ30	quercetin	Myc proto-oncogene protein	MYC
GQ30	quercetin	Tissue factor	F3
GQ30	quercetin	Gap junction alpha-1 protein	GJA1
GQ30	quercetin	Cytochrome P450 1A1	CYP1A1
GQ30	quercetin	Intercellular adhesion molecule 1	ICAM1
GQ30	quercetin	Interleukin-1 beta	IL1B
GQ30	quercetin	Small inducible cytokine A2	CCL2
GQ30	quercetin	E-selectin	SELE
GQ30	quercetin	Vascular cell adhesion protein 1	VCAM1
GQ30	quercetin	Prostaglandin E2 receptor, EP3 subtype	PTGER3
GQ30	quercetin	Interleukin-8	CXCL8
GQ30	quercetin	Nitric oxide synthase, endothelial	NOS3
GQ30	quercetin	Heat shock protein beta-1	HSPB1
GQ30	quercetin	Transforming growth factor beta-1	TGFB1
GQ30	quercetin	Maltase-glucoamylase, intestinal	MGAM
GQ30	quercetin	Interleukin-2	IL2
GQ30	quercetin	Cytochrome P450 1B1	CYP1B1
GQ30	quercetin	Tissue-type plasminogen activator	PLAT
GQ30	quercetin	Thrombomodulin	THBD
GQ30	quercetin	Plasminogen activator inhibitor 1	SERPINE1
GQ30	quercetin	Interferon gamma	IFNG
GQ30	quercetin	Arachidonate 5-lipoxygenase	ALOX5
GQ30	quercetin	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase PTEN	PTEN
GQ30	quercetin	Interleukin-1 alpha	IL1A
GQ30	quercetin	Myeloperoxidase	MPO
GQ30	quercetin	DNA topoisomerase 2-alpha	TOP2A
GQ30	quercetin	Neutrophil cytosol factor 1	NCF1
GQ30	quercetin	Nuclear factor erythroid 2-related factor 2	NFE2L2
GQ30	quercetin	NAD(P)H dehydrogenase [quinone] 1	NQO1
GQ30	quercetin	Poly [ADP-ribose] polymerase 1	PARP1
GQ30	quercetin	Aryl hydrocarbon receptor	AHR
GQ30	quercetin	Solute carrier family 2, facilitated glucose transporter member 4	SLC2A4
GQ30	quercetin	Collagen alpha-1(III) chain	COL3A1
GQ30	quercetin	C-X-C motif chemokine 11	CXCL11
GQ30	quercetin	C-X-C motif chemokine 2	CXCL2
GQ30	quercetin	Serine/threonine-protein kinase Chk2	CHEK2
GQ30	quercetin	Insulin receptor	INSR

Continued			
ID	Molecule name	Target name	Gene name
GQ30	quercetin	Peroxisome proliferator-activated receptor alpha	PPARA
GQ30	quercetin	Peroxisome proliferator-activated receptor delta	PPARD
GQ30	quercetin	C-reactive protein	CRP
GQ30	quercetin	C-X-C motif chemokine 10	CXCL10
GQ30	quercetin	Inhibitor of nuclear factor kappa-B kinase subunit alpha	CHUK
GQ30	quercetin	Osteopontin	SPP1
GQ30	quercetin	Runt-related transcription factor 2	RUNX2
GQ30	quercetin	Ras association domain-containing protein 1	RASSF1
GQ30	quercetin	Cathepsin D	CTSD
GQ30	quercetin	Insulin-like growth factor-binding protein 3	IGFBP3
GQ30	quercetin	Insulin-like growth factor II	IGF2
GQ30	quercetin	CD40 ligand	CD40LG
GQ30	quercetin	Receptor tyrosine-protein kinase erbB-3	ERBB3
GQ30	quercetin	Serum paraoxonase/arylesterase 1	PON1
GQ30	quercetin	Type I iodothyronine deiodinase	DIO1
GQ30	quercetin	Ras GTPase-activating protein 1	RASA1
GQ30	quercetin	Glutathione S-transferase Mu 1	GSTM1

Supplementary Table S3. Information of targets of exercise-induced fatigue

Degree	Name	Neighborhood connectivity
117	MAPK1	15.31624
98	AKT1	16.81633
84	RAF1	15.54762
77	RELA	19.09091
68	TNF	16.77941
66	PRKCA	15.04545
62	MAPK14	16.27419
57	JUN	19.52632
54	CHUK	20.48148
52	BAX	19.34615
52	IL6	19.55769
51	TP53	19.23529
50	NFKBIA	20.4
48	EGFR	17.8125
47	CCND1	18.76596
46	CASP3	21.08696
46	FOS	20.28261
45	IL1B	18.93333
44	BCL2	20.56818
42	CDKN1A	19.33333

Continued

Degree	Name	Neighborhood connectivity
38	CASP8	22.10526
37	CASP9	21.48649
36	TGFB1	19.75
35	MYC	20.45714
34	CXCL8	21.73529
32	IFNG	18.5625
30	PGR	6.625
30	PTGS2	18.43333
30	STAT1	22.1
29	BCL2L1	21.2069
26	RB1	23
26	PTEN	20.80769
23	INSR	15.65217
22	IL10	17.18182
22	IL1A	21.04545
21	IL2	20.33333
20	HSP90AA1	23.8
19	RXRA	24.36842
19	NOS3	22.33333
18	NOS2	17.61111
18	CCL2	25.5
17	MMP9	27.76471
17	ICAM1	23.70588
15	NR3C2	3.714286
15	CXCL2	23.86667
14	ADRB2	23.57143
14	ADRB1	14.85714
14	HIF1A	23.78571
14	CD40LG	18.71429
13	CHRM3	15.92308
13	DRD1	14.53846
13	PPARG	25.16667
13	CCNA2	19.23077
13	PIK3CG	22.84615
13	CXCL10	24.46154
12	MMP2	28.16667
12	NCF1	24.75
11	MAOB	18.45455
11	GSTM1	26.45455
10	PTGS1	21.3
10	SLC6A3	13.2

Continued

Degree	Name	Neighborhood connectivity
10	MAOA	9.6
10	CHRM2	19.6
10	ADRA1B	17
10	VCAM1	27.6
10	PPARA	25.3
9	HTR2A	18.11111
9	CHRNA7	19.66667
9	ESR1	21.44444
9	F2	28.44444
9	SOD1	22.55556
9	MMP1	32.66667
9	CDK1	23.44444
9	CYP1A1	24.44444
9	CYP1B1	22.44444
9	SERPINE1	26
8	PLAU	29.5
8	GABRA3	13.125
8	ESR2	20.5
8	MMP3	33.375
8	SELE	31.5
8	NFE2L2	35.375
8	SLC2A4	22.125
8	ERBB3	29.625
7	GABRA5	11.71429
7	DRD5	18.16667
7	HMOX1	37.71429
7	CYP3A4	22.85714
7	PTGER3	36
7	COL3A1	28.42857
7	SPP1	28.85714
7	RASSF1	32
7	CTSD	29.28571
7	IGF2	37.57143
6	PDE3A	14.66667
6	OPRM1	19.5
6	HTR1B	17
6	HTR1A	17
6	AR	38
6	PRSS1	29.66667
6	CAV1	31.83333
6	PLAT	32.66667

Continued

Degree	Name	Neighborhood connectivity
6	ALOX5	26.83333
5	ADRA2A	20.4
5	SCN5A	38
5	SLC6A4	17.2
5	OPRD1	18.8
5	HRH1	17.4
5	TOP2A	31
5	MPO	30.2
5	NQO1	45.8
5	PARP1	34
5	AHR	36.4
5	CXCL11	33
5	CHEK2	35.2
5	PPARD	36.4
5	IGFBP3	34.2
4	SLC6A2	16.5
4	ADRA2C	19.75
4	ADRA2B	19.75
4	MMP13	17.25
4	HSPB1	38.75
4	THBD	43.25
4	RASA1	37
3	XDH	38.66667
3	F3	48
3	RUNX2	45.66667
2	AKR1B1	65
2	LTA4H	14
2	KCNH2	68
2	CHRNA2	27
2	PON1	68
2	NR3C1	14
2	DPP4	55.5
2	F10	58
2	F7	58
2	ACHE	59
2	GJA1	58.5
2	DIO1	60.5
1	IGHG1	23
1	MAP2	29
1	MMP8	15
1	MGAM	107
1	CRP	107

Supplementary Table S4. Information of pathways of exercise-induced fatigue

Pathway	Description	Degree	Neighborhood connectivity
hsa05200	Pathways in cancer	51	35.80392
hsa05417	Lipid and atherosclerosis	37	41.48649
hsa05418	Fluid shear stress and atherosclerosis	29	35.62069
hsa04933	AGE-RAGE signaling pathway in diabetic complications	28	44.89286
hsa05207	Chemical carcinogenesis - receptor activation	28	39.89286
hsa05161	Hepatitis B	27	56.66667
hsa05167	Kaposi sarcoma-associated herpesvirus infection	27	52.66667
hsa04151	PI3K-Akt signaling pathway	27	46.33333
hsa05163	Human cytomegalovirus infection	26	57
hsa04080	Neuroactive ligand-receptor interaction	25	15.12
hsa04657	IL-17 signaling pathway	24	46.25
hsa04668	TNF signaling pathway	23	49.73913
hsa05160	Hepatitis C	23	55.30435
hsa05164	Influenza A	23	54.52174
hsa05169	Epstein-Barr virus infection	23	52.47826
hsa05166	Human T-cell leukemia virus 1 infection	23	52.91304
hsa04010	MAPK signaling pathway	23	54.6087
hsa05205	Proteoglycans in cancer	22	49.04545
hsa05208	Chemical carcinogenesis - reactive oxygen species	22	45.72727
hsa05022	Pathways of neurodegeneration - multiple diseases	22	51.18182
hsa05215	Prostate cancer	21	50.66667
hsa05142	Chagas disease	21	54.85714
hsa05145	Toxoplasmosis	21	51.85714
hsa04218	Cellular senescence	21	49.90476
hsa05152	Tuberculosis	21	56.42857
hsa05171	Coronavirus disease - COVID-19	21	51.52381
hsa05132	Salmonella infection	21	61.42857
hsa05162	Measles	20	54.7
hsa05225	Hepatocellular carcinoma	20	49.65
hsa05165	Human papillomavirus infection	20	57.6
hsa05222	Small cell lung cancer	19	51.52632
hsa04926	Relaxin signaling pathway	19	53.89474
hsa04210	Apoptosis	19	60.94737
hsa04932	Non-alcoholic fatty liver disease	19	52.36842
hsa05202	Transcriptional misregulation in cancer	19	35.05263
hsa05170	Human immunodeficiency virus 1 infection	19	64.84211
hsa05206	MicroRNAs in cancer	19	46.84211
hsa01522	Endocrine resistance	18	56.55556
hsa04620	Toll-like receptor signaling pathway	18	58.38889
hsa04659	Th17 cell differentiation	18	51.94444

Continued

Pathway	Description	Degree	Neighborhood connectivity
hsa04621	NOD-like receptor signaling pathway	18	56
hsa04024	cAMP signaling pathway	18	45.5
hsa05010	Alzheimer disease	18	57.16667
hsa05168	Herpes simplex virus 1 infection	18	56.61111
hsa05140	Leishmaniasis	17	54.23529
hsa04625	C-type lectin receptor signaling pathway	17	64.88235
hsa04380	Osteoclast differentiation	17	59.76471
hsa04915	Estrogen signaling pathway	17	47.82353
hsa05224	Breast cancer	17	56.94118
hsa05130	Pathogenic Escherichia coli infection	17	61.29412
hsa05415	Diabetic cardiomyopathy	17	40.11765
hsa04020	Calcium signaling pathway	17	27.41176
hsa05212	Pancreatic cancer	16	64.125
hsa05210	Colorectal cancer	16	64.875
hsa04064	NF-kappa B signaling pathway	16	43.625
hsa04066	HIF-1 signaling pathway	16	53.9375
hsa05135	Yersinia infection	16	63.6875
hsa05131	Shigellosis	16	67.75
hsa04115	p53 signaling pathway	15	42.53333
hsa05220	Chronic myeloid leukemia	15	66.4
hsa05235	PD-L1 expression and PD-1 checkpoint pathway in cancer	15	66.2
hsa05323	Rheumatoid arthritis	15	43.8
hsa05146	Amoebiasis	15	48
hsa04660	T cell receptor signaling pathway	15	66.66667
hsa04071	Sphingolipid signaling pathway	15	64.86667
hsa04068	FoxO signaling pathway	15	61.13333
hsa04936	Alcoholic liver disease	15	59.6
hsa04022	cGMP-PKG signaling pathway	15	40.86667
hsa04062	Chemokine signaling pathway	15	54.53333
hsa04060	Cytokine-cytokine receptor interaction	15	39.66667
hsa05219	Bladder cancer	14	51.92857
hsa05223	Non-small cell lung cancer	14	63.71429
hsa05133	Pertussis	14	61.71429
hsa04726	Serotonergic synapse	14	43.14286
hsa04919	Thyroid hormone signaling pathway	14	57.64286
hsa05226	Gastric cancer	14	64.07143
hsa04630	JAK-STAT signaling pathway	14	55.85714
hsa05203	Viral carcinogenesis	14	58.78571
hsa05144	Malaria	13	42.61538
hsa01524	Platinum drug resistance	13	59
hsa04014	Ras signaling pathway	13	62.46154

Continued

Pathway	Description	Degree	Neighborhood connectivity
hsa05020	Prion disease	13	55.84615
hsa05213	Endometrial cancer	12	69.58333
hsa05321	Inflammatory bowel disease	12	55
hsa05214	Glioma	12	71.25
hsa01521	EGFR tyrosine kinase inhibitor resistance	12	68.5
hsa04921	Oxytocin signaling pathway	12	63.83333
hsa04510	Focal adhesion	12	66.5
hsa05012	Parkinson disease	12	39.5
hsa05134	Legionellosis	11	60
hsa05221	Acute myeloid leukemia	11	66.63636
hsa04917	Prolactin signaling pathway	11	70.54545
hsa05218	Melanoma	11	71.72727
hsa04658	Th1 and Th2 cell differentiation	11	67.63636
hsa04928	Parathyroid hormone synthesis, secretion and action	11	61
hsa04931	Insulin resistance	11	57.09091
hsa04725	Cholinergic synapse	11	56
hsa04722	Neurotrophin signaling pathway	11	80.90909
hsa04371	Apelin signaling pathway	11	55.90909
hsa04261	Adrenergic signaling in cardiomyocytes	11	58.27273
hsa04217	Necroptosis	11	50.36364
hsa05014	Amyotrophic lateral sclerosis	11	55.81818
hsa05143	African trypanosomiasis	10	51.8
hsa04370	VEGF signaling pathway	10	71.4
hsa05120	Epithelial cell signaling in Helicobacter pylori infection	10	64.1
hsa04012	ErbB signaling pathway	10	75.3
hsa04540	Gap junction	10	56
hsa04061	Viral protein interaction with cytokine and cytokine receptor	10	44.6
hsa04110	Cell cycle	10	46.2
hsa04728	Dopaminergic synapse	10	52
hsa04072	Phospholipase D signaling pathway	10	69
hsa05216	Thyroid cancer	9	63.66667
hsa04920	Adipocytokine signaling pathway	9	64.66667
hsa04622	RIG-I-like receptor signaling pathway	9	66
hsa05230	Central carbon metabolism in cancer	9	74.55556
hsa04662	B cell receptor signaling pathway	9	86.77778
hsa04610	Complement and coagulation cascades	9	26.77778
hsa05231	Choline metabolism in cancer	9	80.88889
hsa04914	Progesterone-mediated oocyte maturation	9	69.44444
hsa04935	Growth hormone synthesis, secretion and action	9	78.44444
hsa04611	Platelet activation	9	59.11111
hsa04140	Autophagy - animal	9	68.55556

Continued

Pathway	Description	Degree	Neighborhood connectivity
hsa04150	mTOR signaling pathway	9	81.55556
hsa04613	Neutrophil extracellular trap formation	9	79.88889
hsa04923	Regulation of lipolysis in adipocytes	8	49.25
hsa05416	Viral myocarditis	8	50.375
hsa04664	Fc epsilon RI signaling pathway	8	87.375
hsa05211	Renal cell carcinoma	8	80.75
hsa05031	Amphetamine addiction	8	51.375
hsa04912	GnRH signaling pathway	8	80.5
hsa04670	Leukocyte transendothelial migration	8	49.25
hsa04650	Natural killer cell mediated cytotoxicity	8	78.5
hsa04015	Rap1 signaling pathway	8	87
hsa05016	Huntington disease	8	55.375
hsa04215	Apoptosis - multiple species	7	63.42857
hsa05332	Graft-versus-host disease	7	62.57143
hsa05030	Cocaine addiction	7	53.71429
hsa04623	Cytosolic DNA-sensing pathway	7	69.85714
hsa04929	GnRH secretion	7	82.57143
hsa04211	Longevity regulating pathway	7	73
hsa05032	Morphine addiction	7	43.42857
hsa04152	AMPK signaling pathway	7	57
hsa04723	Retrograde endocannabinoid signaling	7	69.71429
hsa04934	Cushing syndrome	7	69
hsa04310	Wnt signaling pathway	7	65.57143
hsa05034	Alcoholism	7	63.28571
hsa04810	Regulation of actin cytoskeleton	7	68.42857
hsa01523	Antifolate resistance	6	82.33333
hsa05330	Allograft rejection	6	59.16667
hsa04940	Type I diabetes mellitus	6	64.33333
hsa04672	Intestinal immune network for IgA production	6	57.16667
hsa04913	Ovarian steroidogenesis	6	45.83333
hsa05204	Chemical carcinogenesis - DNA adducts	6	44
hsa04137	Mitophagy - animal	6	71
hsa03320	PPAR signaling pathway	6	42.16667
hsa04742	Taste transduction	6	39.66667
hsa04970	Salivary secretion	6	52.5
hsa04350	TGF-beta signaling pathway	6	81
hsa04666	Fc gamma R-mediated phagocytosis	6	95.83333
hsa04750	Inflammatory mediator regulation of TRP channels	6	64.16667
hsa04114	Oocyte meiosis	6	69.33333
hsa04910	Insulin signaling pathway	6	88
hsa04550	Signaling pathways regulating pluripotency of stem cells	6	99

Continued

Pathway	Description	Degree	Neighborhood connectivity
hsa04390	Hippo signaling pathway	6	55.33333
hsa04960	Aldosterone-regulated sodium reabsorption	5	83.6
hsa00380	Tryptophan metabolism	5	47.4
hsa04930	Type II diabetes mellitus	5	82.8
hsa00330	Arginine and proline metabolism	5	51
hsa00590	Arachidonic acid metabolism	5	49.2
hsa00982	Drug metabolism - cytochrome P450	5	47.4
hsa00980	Metabolism of xenobiotics by cytochrome P450	5	46.8
hsa00983	Drug metabolism - other enzymes	5	44.8
hsa04640	Hematopoietic cell lineage	5	77
hsa04270	Vascular smooth muscle contraction	5	95
hsa05322	Systemic lupus erythematosus	5	66.8
hsa04514	Cell adhesion molecules	5	49.4
hsa04141	Protein processing in endoplasmic reticulum	5	64.4
hsa04360	Axon guidance	5	93.8
hsa05310	Asthma	4	75.5
hsa05033	Nicotine addiction	4	55.5
hsa05320	Autoimmune thyroid disease	4	63.75
hsa04730	Long-term depression	4	116.25
hsa00140	Steroid hormone biosynthesis	4	55.75
hsa04213	Longevity regulating pathway - multiple species	4	82
hsa05217	Basal cell carcinoma	4	85.75
hsa04720	Long-term potentiation	4	116.25
hsa04924	Renin secretion	4	58
hsa04520	Adherens junction	4	96.5
hsa04612	Antigen processing and presentation	4	79.5
hsa04721	Synaptic vesicle cycle	4	54.25
hsa04146	Peroxisome	4	57
hsa04727	GABAergic synapse	4	69.75
hsa05410	Hypertrophic cardiomyopathy	4	88.5
hsa05414	Dilated cardiomyopathy	4	79
hsa04713	Circadian entrainment	4	106.75
hsa04916	Melanogenesis	4	116.25
hsa04972	Pancreatic secretion	4	70.75
hsa04974	Protein digestion and absorption	4	53.25

Supplementary Table S5. Summary of studies included in the systematic review

Study	Information of animals	Type of <i>Fructus Lycii</i>	Intervention vs. control	Time of intervention	Outcome measures used
Yang 2019	Kunming mice, weighing 12–22 g, half-male and half-female, SPF	Decoction of <i>Fructus Lycii</i>	3 mg/(g·d) (<i>n</i> = 10) vs. 6 mg/(g·d) (<i>n</i> = 10) vs. Placebo (distilled water 0.02 mL/(g·d), <i>n</i> = 10)	30 days	MDA, ROS, SOD, CAT, GSH-Px
Cao 2018	Kunming mice, weighing 18–22 g, half-male and half-female, SPF	Decoction of <i>Fructus Lycii</i>	3 mg/(g·d) (<i>n</i> = 10) vs. 6 mg/(g·d) (<i>n</i> = 10) vs. Placebo (distilled water 0.02 mL/(g·d), <i>n</i> = 10)	30 days	The time of exhaustive swimming, blood glucose, muscle glycogen and liver glycogen, BUN and lactic acid
Ji et al 2011	Eight-week-old Wistar rats, weighing 220 ± 23.19 g, female	Decoction of <i>Fructus Lycii</i>	Decoction of <i>Fructus Lycii</i> (<i>n</i> = 8) vs. Placebo (<i>n</i> = 8)	30 days	The time of exhaustive swimming, SOD, MAD
Ding et al 2001	Kunming mice, weighing 20–24 g, male	Decoction of <i>Fructus Lycii</i>	Decoction of <i>Fructus Lycii</i> (<i>n</i> = 10) vs. Placebo (<i>n</i> = 10)	2 weeks	The time of exhaustive swimming, SOD, MAD
Qin et al 2009	mice	Extract of <i>Fructus Lycii</i>	5 mg/(g·d) (<i>n</i> = 10) vs. 10 mg/(g·d) (<i>n</i> = 10) vs. 20 mg/(g·d) (<i>n</i> = 10) vs. Placebo (Equivalent saline, <i>n</i> = 10) 10 mL/(kg·d) (<i>n</i> = 10) vs. 20 mL/(kg·d) (<i>n</i> = 10)	2 weeks	The time of exhaustive swimming
Hu et al 2008	Kunming mice, weighing 18–22 g, female	Raw juice of <i>Fructus Lycii</i>	mL/(kg·d) (<i>n</i> = 10) vs. 30 mL/(kg·d) (<i>n</i> = 10) vs. Placebo (Equivalent saline, <i>n</i> = 10)	3 weeks	The time of exhaustive swimming, and liver glycogen, BUN
Liu et al 2011	Kunming mice, weighing 24 ± 5 g, female	Decoction of <i>Fructus Lycii</i>	5 mg/(g·d) (<i>n</i> = 10) vs. Placebo (Equivalent distilled water, <i>n</i> = 10)	10 days	The time of exhaustive swimming
Yi et al 2010	Kunming mice, weighing 24 ± 5 g, half-male and half-female	Decoction of <i>Fructus Lycii</i>	5 mg/(g·d) (<i>n</i> = 10) vs. 2.5 mg/(g·d) (<i>n</i> = 10) vs. Placebo (Equivalent running water, <i>n</i> = 10)	2 weeks	The time of exhaustive swimming
Wang et al 2002	Kunming mice, weighing 20 ± 2 g, male and female	Decoction of <i>Fructus Lycii</i>	0.2 mL/10 (g·d) (<i>n</i> = 10) vs. 0.1 mL/10 (g·d) (<i>n</i> = 10) vs. Placebo (Equivalent saline, <i>n</i> = 10)	1 week	The time of exhaustive swimming
Liu 2019	Kunming mice, 6 week, male	Extract of <i>Fructus Lycii</i>	0.3 mg/(g·d) (<i>n</i> = 10) vs. 0.6 mg/(g·d) (<i>n</i> = 10) vs. 0.9 mg/(g·d) (<i>n</i> = 10) vs. Placebo (<i>n</i> = 10)	2 weeks	The time of exhaustive swimming, muscle glycogen and liver glycogen, BUN and lactic acid, SOD, MDA
Yang et al 2018	Kunming mice, weighing 18–22 g, male, SPF	Extract of <i>Fructus Lycii</i>	0.5 mg/(g·d) (<i>n</i> = 10) vs. 1 mg/g/d (<i>n</i> = 10) vs. 1.5 mg/(g·d) (<i>n</i> = 10) vs. Placebo (<i>n</i> = 10)	30 days	The time of exhaustive swimming, muscle glycogen and liver glycogen, BUN and lactic acid
Ma 2019	Rats, SPF	Fruit of <i>Fructus Lycii</i>	0.5g/(kg·d) (<i>n</i> = 10) vs. 3g/(kg·d) (<i>n</i> = 15) vs. Placebo (5 mL/kg saline, <i>n</i> = 15)	6 weeks	The time of exhaustive swimming
Niu et al. 1994	Kunming mice, weighing 18–24 g, half-male and half-female, SPF	Decoction of <i>Fructus Lycii</i>	5g/(kg·d) (<i>n</i> = 10) vs. 2.5/(kg·d) (<i>n</i> = 10) vs. Placebo (Equivalent running water, <i>n</i> = 10)	2 weeks	The time of exhaustive swimming, blood glucose, and lactic acid
Wu et al. 2008	Kunming mice, 3 week, weighing 18–22 g, female	Raw juice of <i>Fructus Lycii</i>	0.2 mL/10 (g·d) (<i>n</i> = 10) vs. 0.25 mL/10 (g·d) (<i>n</i> = 10) vs. Placebo (Equivalent saline, <i>n</i> = 10)	3 weeks	The time of exhaustive swimming, BUN and lactic acid
Wang et al. 2017	Kunming mice, weighing 60–80 g, female	Extract of <i>Fructus Lycii</i>	0.2 mL/10 (g·d) (<i>n</i> = 10) vs. Placebo (<i>n</i> = 10)	3 weeks	The time of exhaustive swimming

Note. MDA, malondialdehyde; ROS, reactive oxygen species; SOD, superoxide dismutase; CAT, catalase; GSH-Px, glutathione peroxidase; BUN, blood urea nitrogen. A total 15 RCTs studies included, the information in detail were showed in the Supplementary Table S5. The exhaustive time, which the main parameter of anti-exercise-fatigue ability, were assessed in 14 articles. blood lactate (included in 6 articles) and BUN (included in 5 articles) were the main product of exercise metabolism and important marker for the evaluation of exercise fatigue. As the important energy source, muscle glycogen was included in 2 articles and liver glycogen in 3 articles. SOD (in 3 articles) and MAD (in 4 articles) also were the important outcomes included in our study. Based on the placebo group, the experimental group received decoction of *Fructus Lycii* (8 articles), extract of *Fructus Lycii* (4 articles), raw juice of *Fructus Lycii* (2 articles) and fruit of *Fructus Lycii* (1 article). Treatment duration ranged from 10 to 42 days.

Supplementary Table S6. Methodological quality assessment of the studies included

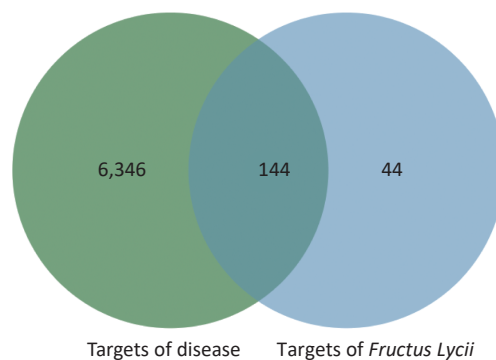
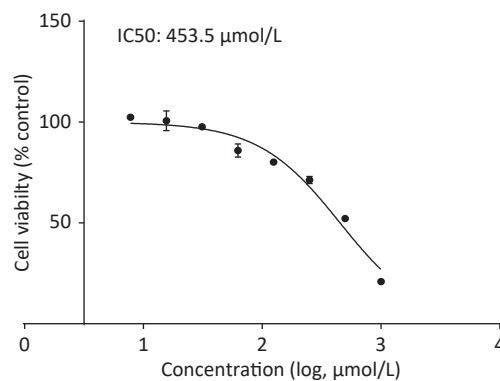
Quality score criterion	Peer-reviewed publication	Control of temperature	Random allocation to treatment or control	Blinded induction of model	Blinded assessment of outcome	Use of anesthetic without significant intrinsic neuroprotective activity	Appropriate animal model	Sample size calculation	Compliance with animal welfare regulations	Statement of potential conflict of interests	Total
Yang 2019 (30)	0	0	1	0	0	0	1	0	1	0	3
Cao 2018 (17)	0	0	1	0	0	0	1	0	1	0	3
Ji et al. 2011 (18)	1	1	1	0	0	1	1	0	1	0	6
Ding et al. 2001 (29)	1	0	1	0	0	0	1	0	1	0	4
Qin et al. 2009 (27)	1	0	1	0	0	0	1	0	1	0	4
Hu et al. 2008 (21)	1	1	1	0	0	0	1	0	1	0	5
Liu et al. 2011 (19)	1	0	1	0	0	0	1	0	1	0	4
Yi et al. 2010 (26)	1	0	1	0	0	0	1	0	1	0	4
Wang et al. 2002 (24)	1	0	1	0	0	0	1	0	1	0	4
Liu 2019 (22)	0	1	1	0	0	0	1	0	1	0	4
Yang et al. 2018 (20)	1	1	1	0	0	0	1	0	1	0	5
Ma 2019 (23)	1	0	1	0	0	0	1	0	1	0	4
Niu et al. 1994 (25)	1	0	1	0	0	0	1	0	1	0	4
Wu et al. 2008 (9)	1	1	1	0	0	0	1	0	1	0	5
Wang et al. 2017 (28)	1	0	1	0	0	0	1	0	1	0	4

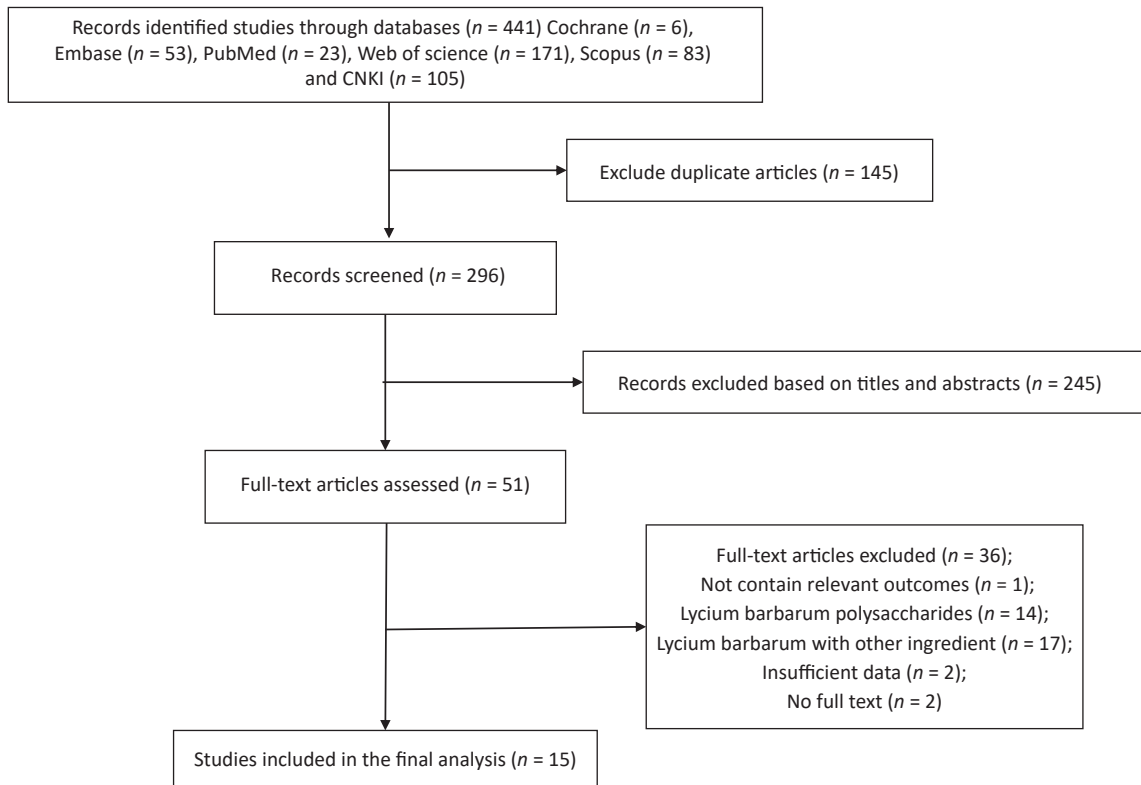
Note. As showed in Supplementary Table S6, the quality score of the included studies ranged from 3 to 5 and the average quality score was 4.2 points. All studies randomly allocated animals to the control group and the treatment group, adopted appropriate animal models and compliance with animal welfare regulations. However, the method of blinded induction of model and blinded assessment of outcome were not involved in those included studies. In addition, there was no statement of potential conflict of interests in those articles.

Supplementary Table S7. Meta-analysis for each sub-outcome measure

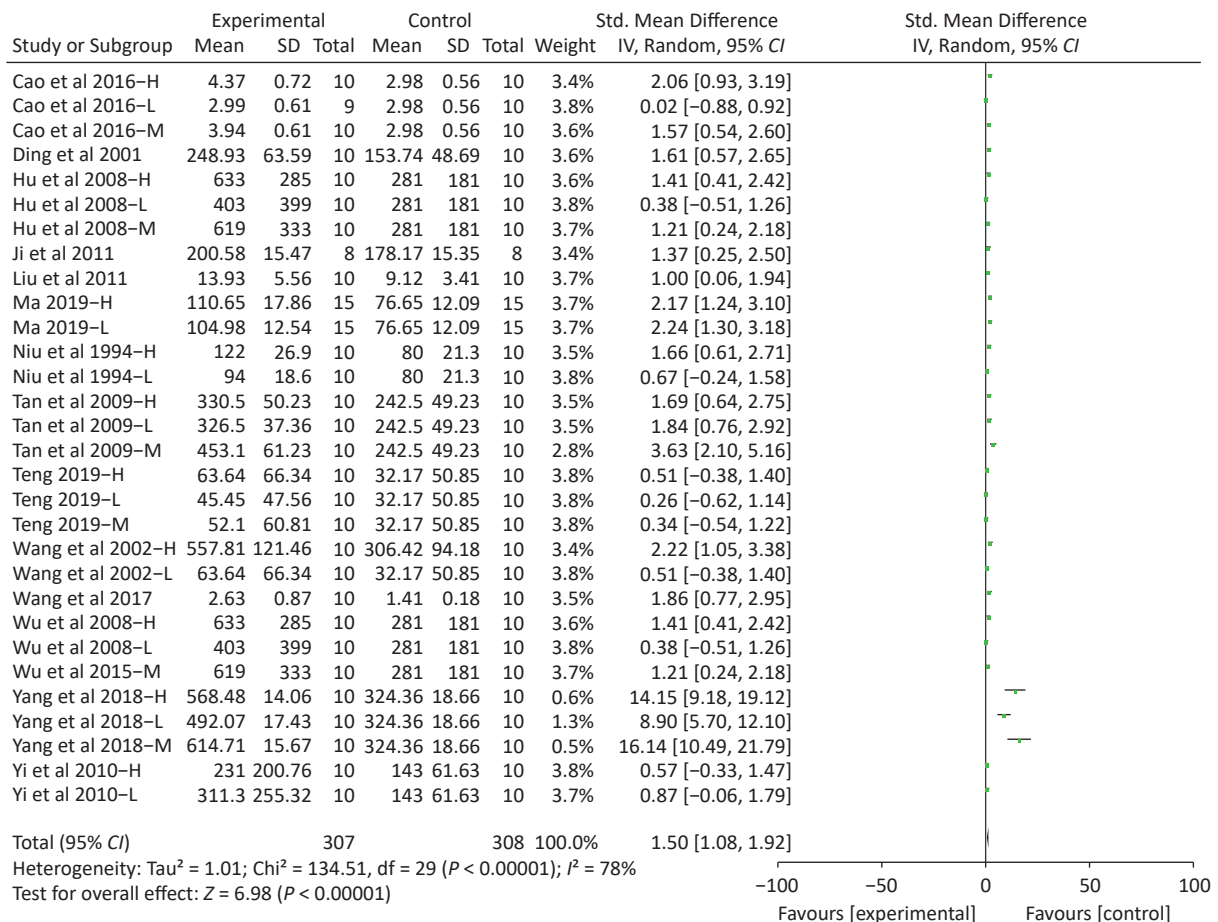
Outcome	Meta-analysis of outcome			Test of heterogeneity		Model used
	SMD	95% CI	P	I^2	P	
Blood lactates	-1.58	-1.58 to -0.97	< 0.01	80%	< 0.01	Random-effects
Muscle glycogen	0.85	0.04 to 1.67	< 0.01	76%	< 0.01	Random-effects
Liver glycogen	0.91	0.40 to 1.41	< 0.01	60%	< 0.01	Random-effects
SOD	1.30	0.45 to 2.14	< 0.01	78%	< 0.01	Random-effects
MAD	-0.84	-1.18 to -0.05	< 0.01	32%	0.18	Fixed-effects

Note. SMD, standardized mean difference; I^2 , I-squared statistic; CI, confidence interval; SOD, superoxide dismutase; MAD, malondialdehyde.

**Supplementary Figure S1.** Venn diagram of *Fructus Lycii*/exercise-induced fatigue related targets.**Supplementary Figure S2.** CCK-8 assay of cell viability.



Supplementary Figure S3. Flow diagram of the study selection. Supplementary Figure S3 showed that a total of 441 relevant literature sources were identified through the search strategy. After removing 145 duplicate articles, the titles and abstracts of the remaining papers were screened to exclude those that were not related to *Fructus Lycii* and exercise-induced fatigue. And then, we reviewed 51 articles with full texts and 15 randomized controlled trials (RCTs) involving animals were included in the final analysis.



Supplementary Figure S4. Forest plot of s standardized mean differences in exhausted time between *Fructus Lycii* and placebo. Weights have been calculated using random effects model. Degree of heterogeneity in the pooled estimates is represented at I^2 statistic. SMD, standardized mean difference; χ^2 , Chi-square test; df , degrees of freedom; I^2 , I -squared statistic; Z , Z -test; CI , confidence interval; H, high-dose intervention in each study; M, median-dose intervention in each study; L, low-dose intervention in each study. The exhausted time was the primary outcome. There was significant heterogeneity among the 14 studies ($I^2 = 78\%$, $P < 0.01$) and therefore a random effect model was used as shown in the Supplementary Figure S4. Meta-analysis of 14 studies showed significant effects of *Fructus Lycii* on increasing the time to exhaustion compared with control groups (SMD 1.5; 95% CI 1.08 to 1.92; $P < 0.01$).