Supplementary Tables

Table S1 The main active substance of triterpenoids of G. lucidum

Compound	CAS Number	Molecular formula	Molecular weight	Extract content (triterpenoids per g of feed) (mg/g)
Ganoderenic acid C	100665-42-7	$C_{30}H_{44}O_7$	516.666	0.00017
Ganoderic acid C2	103773-62-2	$C_{30}H_{46}O_7$	518.682	0.00025
Ganoderic acid G	98665-22-6	$C_{30}H_{44}O_8$	532.666	0.00061
Ganoderenic acid B	100665-41-6	$C_{30}H_{42}O_7$	514.65	0.00021
Ganoderic acid B	81907-61-1	$C_{30}H_{44}O_7$	516.666	0.00045
Ganoderic acid A	81907-62-2	$C_{30}H_{42}O_7$	514.65	0.00156
Ganoderic acid H	98665-19-1	$C_{31}H_{42}O_9$	558.66	0.00098
Ganoderenic acid D	100665-43-8	$C_{30}H_{40}O_7$	512.634	0.00036
Ganoderic acid D	108340-60-9	$C_{30}H_{42}O_7$	514.65	0.00102

Table S2 Pharmacokinetic parameters of triterpenes of G. lucidum

Object of study	Triterpenoids	Dosage of administration	Administration route	Absorption parameters			Distribution parameter	Elimination parameter		
				T_{max}	C_{max}	AUC	V_d/L ·kg^{-1}	$t_{1/2\alpha}$	$t_{1/2\beta}$	CL
SD rat (Cao et al., 2017)	Ganoderic acid A	20 mg ·kg^{-1}	ig	(0.15±0.03)h	(0.91±0.57) μmol·L^{-1}	(1.35±0.46) μmol·h·L^{-1}	106.24±26.42		(2.46±0.75)h	32.38±13.45*
		20 mg ·kg^{-1}	iv			(14.34±4.54) μmol·h·L^{-1}	10.21±3.47		(2.40±0.35)h	2.91±0.81*
		20 mg ·kg^{-1}(brain microdialysis)	iv	(0.25±0) h	(0.61±0.18) μmol·L^{-1}	(0.45±0.09)μmol·h·L^{-1}	190.61±146.36		(1.40±0.93)h	89.21±16.21*
SD rat (Cheng et al., 2013)	Ganoderic acid D	15 mg ·kg^{-1}	iv		(3582.93±888.57) μg·L^{-1}	(2320.18±221.44) μg·h·L^{-1}	4.42±0.47		(0.92±0.02)h	72.36±6.57$^{\#}$
		15 mg ·kg^{-1}	ig (Conventional solution)		(107.18±4.84)μg·L^{-1}	(550.64±23.09) μg·h·L^{-1}	18.51±0.72		(2.05±0.08)h	303.11±12.78$^{\#}$
		15 mg ·kg^{-1}	ig (Nano preparation)		(1555.59±237.56)μg·L^{-1}	(1629.29±186.23) μg·h·L^{-1}	6.53±0.45		(1.87±0.12)h	103.25±10.12$^{\#}$
	Ganoderic acid B (the metabolite of Ganoderic acid D)	15 mg ·kg^{-1}(Ganoderic acid D)	iv		(998.76±108.72)μg·L^{-1}	(2765.89±483.61) μg·h·L^{-1}	3.79±0.78		(1.62±0.46)h	61.98±13.10$^{\#}$
		15 mg ·kg^{-1}(Ganoderic acid D)	ig (Conventional solution)		(271.06±18.02)μg·L^{-1}	(1643.90±92.28) μg·h·L^{-1}	6.38±0.41		(4.12±0.14)h	101.59±5.69$^{\#}$
		15 mg ·kg^{-1}(Ganoderic acid D)	ig (Nano preparation)		(883.95±35.74)μg·L^{-1}	(1900.99±39.53) μg·h·L^{-1}	6.68±0.26		(3.10±0.13)h	87.80±1.81$^{\#}$
SD rat (Guo et al., 2013)	Ganoderic acid C2	20 mg ·kg^{-1}	per os	25.19 min	145.42 μg·L^{-1}	56600.12 μg·min·L^{-1}		3.912	213.5607min	
SD rat (Wang et al., 2007)	Ganoderic acid C2	55.3 mg ·kg^{-1}	ig	16.79 min	5.23 mg ·L^{-1}	1125.29 mg ·min ·L^{-1}	4.85	11.61	376.08 min	47.9$^{\#}$
	Ganoderic acid B	258.0 mg ·kg^{-1}	ig	6.26 min	13.15 mg ·L^{-1}	5771.93 mg ·min ·L^{-1}	18.03	37.63	852.59 min	44.7$^{\#}$
	Ganoderic acid K	75.8 mg ·kg^{-1}	ig	32.10 min	2.86 mg ·L^{-1}	923.59 mg ·min ·L^{-1}	15.99	32.26	697.48 min	82.1$^{\#}$
	Ganoderic acid H	155.0 mg ·kg^{-1}	ig	24.88 min	4.92 mg ·L^{-1}	986.00 mg ·min ·L^{-1}	14.77	17.13	293.75 min	157.2$^{\#}$
Human (Teekachunhatean et al., 2012)	Ganoderic acid A	(4253.4±122.22) μg	per os (abrosia)	(0.54±0.18)h	(10.99±4.02) μg·L^{-1}	(10.53±4.32) μmin·L^{-1}		(0.62±0.17)h		
		(4253.4±122.22) μg	per os(no abrosia)	(1.67±0.88)h	(3.84±1.56) μg·L^{-1}	(11.02±5.54) μmin·L^{-1}		(1.34±0.65)h		
	Ganoderic acid F	(672.45±24.06) μg	per os (abrosia)	(0.52±0.13)h	(2.57±0.91) μg·L^{-1}	(2.42±0.93) μmin·L^{-1}		(0.48±0.22)h		
		(672.45±24.06) μg	per os(no abrosia)	ND	ND	ND		ND		

Note: Tmax, time to peak; Cmax, Peak blood concentration; Vd, apparent volume of distribution; t1/2α, Distribution half-life; t1/2β, Elimination half-time; ig, intragastric administration; iv, intravenous immunoglobulin; per os, oral administration; #, mL ·min^{-1} ·kg^{-1}; *, L ·h^{-1} ·kg^{-1}

Table S3 G. lucidum and its effects (Phu et al., 2020)

Effects	Bioactive Components	Potential Mechanisms	Models	References
Anti-aging	Total water extract of G. lucidum	Improves the resistance to oxidative stress via the mTOR/S6K signaling	Caenorhabditis elegans	(Cuong et al., 2019)
	G. lucidum ethanol extract	Increases the expression of Nrf2/ HO-1	C2C12 mouse myoblast cell line	(Lee et al., 2016)
	Ganodermanontriol	Increases the expression of Nrf2/ HO-1 via PI3K/Akt	Hepa1c1c7 cells	(Ha et al., 2013)
	Ganodermanondiol	Increases the expression of Nrf2/ HO-1 via AMPK	HepG2 cells	(Li et al., 2013)
Cognitive impairments	G. lucidum polysaccharides (RF3)	Activates the expression of DAF-16 via TIR-1 receptor and MAPK	Caenorhabditis elegans	(Chuang et al., 2009)
	G. lucidum aqueous extract	Inhibits the apoptotic-associated signaling pathways JNK-c-Jun, p38MAP kinase signaling	Cortical neurons	(Lai et al., 2008)
	G. lucidum aqueous extract	Up-regulates MAP kinase and cAMP-response element binding protein (CREB) signaling pathways	rat PC12 cells	(Cheung et al., 2000)
	G. lucidum ethanol extract	Regulate DNA methylation in Rodents	D-galactose induced Sprague-Dawley rats; APP/PS1 mice; SAMP8 mice	(Lai et al., 2019)
Hypoglycemic effects	G. lucidum polysaccharides (containing 89% total carbohydrate and 11% uronic acid.)	Decreases the expression of PEPCK	Obese/diabetic (+db/+db) mice	(Liang et al., 2018)
	G. lucidum polysaccharides	Decreases the mRNA expression of hepatic glycogen phosphorylase, glucose-6-phosphatase, fructose-1,6-bisphosphatase	Type 2 diabetic mice	(Xiao et al., 2012)
	G. lucidum polysaccharides (F31)	Decreases the mRNA levels of hepatic glucose regulatory enzymes via AMPK activation	Type 2 diabetic mice	(Xiao et al., 2017)
	G. lucidum polysaccharides	Facilitates $Ca2^{+}$ entry into pancreatic β cells beta cells	Normal fasted mice	(Zhang et al., 2004)
	GLPs proteoglycan extract (FYGL)	Suppress the expression of protein tyrosine phosphatase 1B (PTP1B)	Type 2 diabetes mellitus(T2DM) rats.	(Teng et al., 2012)
	GLPs proteoglycan extract (FYGL)	Inhibits the expression of PTP1B, activate PI3K/Akt increases phosphorylation of AMPK, up-regulate the expression of GLUT 4	Obese C57BL/6(ob/ob) mice, rat myoblast L6 cells	(Yang et al., 2018)
Antihyperlipidemic effects	G. lucidum spores	Up-regulates acyl-CoA oxidase 1 (Acox1) and Insig-1/2 gene expression	Diabetic rats	(Wang et al., 2015)
	G. lucidum ethanol extract (GL95)	Reduces the mRNA levels of FAS, ACAT2, SREBP-1C, HMGCR elevates the mRNA levels of CYP7A1, PPARα, ApoB and Acox1	HFD-fed Wistar rats	(Guo et al., 2018)
	G. lucidum ethanol extract	Activates leptin-mediated signaling to improve metabolic regulation	HFD-fed mice	(Diling et al., 2020)
Antitumous effect	Ganoderic acid A/DM	Induced NDRG2 over-expression	In vitro cell culture and in vivo cell-line-derived orthotopic xenograft animal models of anaplastic meningioma	(Das et al., 2020)

Table S4 The IPA analysis showed that the function and diseases, including the Carbohydrate Metabolism, Lipid Metabolism, were influenced (APP/PS1).

Category	p-value	Category	p-value
Cancer	1.49E-29-1.69E-04	Nervous System Development and Function	6.47E-08-1.91E-05
Dermatological Diseases and Conditions	1.49E-29-1.8E-04	Hematological Disease	1.44E-07-1.61E-04
Organismal Injury and Abnormalities	1.49E-29-1.89E-04	Auditory Disease	1.44E-07-1.44E-07
Neurological Disease	3.5E-24-1.89E-04	Developmental Disorder	3.3E-07-1.76E-04
Gastrointestinal Disease	1.86E-23-1.83E-04	Cellular Movement	3.81E-07-1.6E-04
Hereditary Disorder	4.26E-21-5.65E-05	Hematological System Development and Function	3.81E-07-1.6E-04
Psychological Disorders	4.26E-21-1.73E-04	Immune Cell Trafficking	3.81E-07-1.6E-04
Skeletal and Muscular Disorders	4.26E-21-1.44E-04	Cell Signaling	4.61E-07-1E-04
Cardiovascular Disease	1.64E-13-1.73E-04	Vitamin and Mineral Metabolism	4.61E-07-6.88E-06
Nutritional Disease	8.43E-13-9.04E-09	Nucleic Acid Metabolism	7.47E-07-1E-04
Endocrine System Disorders	1.46E-12-1.69E-04	Small Molecule Biochemistry	7.47E-07-1.8E-04
Hepatic System Disease	8.77E-12-9.65E-05	Tumor Morphology	3.38E-06-1.1E-05
Metabolic Disease	9.01E-11-9.72E-05	Cell-mediated Immune Response	8.41E-06-2.56E-05
Reproductive System Disease	2.97E-10-1.85E-04	Hair and Skin Development and Function	1.5E-05-1.5E-05
Immunological Disease	3.19E-10-1.8E-04	Renal and Urological System Development and Function	1.59E-05-1.59E-05
Inflammatory Disease	3.19E-10-1.8E-04	DNA Replication, Recombination, and Repair	2.8E-05-4.8E-05
Respiratory Disease	3.19E-10-1.44E-04	Embryonic Development	6.85E-05-1.38E-04
Renal and Urological Disease	6.43E-10-1.84E-04	Organismal Development	6.85E-05-1.38E-04
Inflammatory Response	2.17E-09-1.8E-04	Post-Translational Modification	1E-04-1E-04
Connective Tissue Disorders	5.98E-09-1.44E-04	Carbohydrate Metabolism	1.1E-04-1.23E-04
Infectious Diseases	1.69E-08-1.39E-04	Lipid Metabolism	1.1E-04-1.23E-04
Ophthalmic Disease	1.91E-08-1.8E-04	Hypersensitivity Response	1.6E-04-1.6E-04
Behavior	3.21E-08-1.04E-05	Cellular Assembly and Organization	1.88E-04-1.88E-04
Molecular Transport	6.37E-08-1E-04	Cellular Function and Maintenance	1.88E-04-1.88E-04
Cell-To-Cell Signaling and Interaction	6.47E-08-6.8E-05		

Table S5 The different expressed mRNAs enriched into the sphingolipid metabolism (APP/PS1).

Ingenuity Canonical Pathways	-log(p-value)	Molecules
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	1.76	INPP5J, INPP5D, ITPKB, ITPKA, INPP5A
3-phosphoinositide Biosynthesis	0.901	DUSP10, PTPRM, PIK3R3, PHOSPHO1, CDC25A, IRS1, PTPN22, KIT, VAV1, EPHX2, CD28, DUSP5, DUSP14, PPP1R1A, PPP1R1B, CD86, PIP5K1B, SGPP2, PXYLP1, PTPN7, DUSP16
3-phosphoinositide Degradation	1.11	DUSP10, INPP5J, PTPRM, PHOSPHO1, CDC25A, PTPN22, EPHX2, MTM1, INPP5D, DUSP5, DUSP14, PPP1R1A, INPP4B, PPP1R1B, SGPP2, PXYLP1, PTPN7, DUSP16
Adipogenesis pathway	1.08	AGPAT2, KAT2B, FGF1, FZD2, FZD7, SMAD9, KAT6A, LPIN1, SLC2A4, FZD1, CTBP2, SAP30, EBF1, LPL, RPS6KA1, KLF5
Ceramide Biosynthesis	0.341	SPTSSB
Ceramide Degradation	0.341	ASAH2
Ceramide Signaling	0.287	TNFRSF11B, FOS, PIK3R3, SMPD3, CERK, MRAS, MAP3K1, IRS1
Complement System	1.13	C1QC, ITGAM, CFB, C3, C1QB, ITGAX
CREB Signaling in Neurons	3.63	GNG11, PRKAR2B, MRAS, GNG10, GNG7, IRS1, PLCE1, GRIN2C, GRM3, GRM4, GNG3, PRKCB, ADCY2, ITPR1, GRM1, GNG13, PRKCH, GRIA4, GRM5, NOTUM, GRIK5, PIK3R3, ADCY5, PLCB4, CAMK4, CAMK2A, ITPR3, GRID2, RPS6KA1, PLCZ1
GDNF Family Ligand-Receptor Interactions	1.64	FOS, DOK4, PIK3R3, ITPR3, GFRA1, MRAS, MAPK12, RET, GFRA4, DOK6, IRS1, ITPR1
GDP-glucose Biosynthesis	0.3	HK2
Glucose and Glucose-1-phosphate Degradation	0.265	HK2
Glutathione-mediated Detoxification	0.218	GSTT2/GSTT2B, HPGDS
Glycoaminoglycan-protein Linkage Region Biosynthesis	0.341	B3GAT1
Granulocyte Adhesion and Diapedesis	1.03	ITGAM, ITGAL, MMP9, ITGA3, EZR, CLDN19, MMP17, CCL21, CCL27, CX3CL1, SDC1, TNFRSF11B, IL18, HRH3, SELPLG, IL1RL2, CXCL14, MMP23B, MMP24

NAD Phosphorylation and Dephosphorylation	0.236	PXYLP1
Phenylalanine Degradation I (Aerobic)	0.532	PCBD1
Phospholipase C Signaling	1.48	GNG11, ITGA3, RHOD, PLD3, MRAS, GNG10, GNG7, PLCE1, LCP2, SYK, GNG3, PRKCB, ADCY2, ITPR1, GNG13, PRKCH, BLNK, FNBP1, MYL4, ADCY5, PLCB4, CAMK4, PLA2G3, MEF2C, FCGR2A, ITPR3, PPP3R1, CD247
Phospholipases	1.27	PNPLA3, PLCB4, PLD3, PLCE1, PLCZ1, PLB1, PLA2G3, NOTUM, LIPG
Renin-Angiotensin Signaling	2.36	PIK3R3, ADCY5, PRKAR2B, MRAS, MAPK12, IRS1, AGTR2, SHC3, AGT, FOS, ITPR3, PAK6, PTK2B, MAP3K1, MAPK13, PRKCB, ADCY2, ITPR1, PRKCH
Sphingomyelin Metabolism	0.3	SMPD3
Sphingosine and Sphingosine-1-phosphate Metabolism	0.772	ASAH2, SGPP2
Sphingosine-1-phosphate Signaling	0.861	PIK3R3, SMPD3, ADCY5, RHOD, PLCB4, ASAH2, IRS1, PLCE1, PDGFB, PTK2B, ADCY2, PLCZ1, NOTUM, FNBP1