Supplemental Data to *Drug Metabolism and Disposition*

Multi-omics profiling reveals protective function of *Schisandra* lignans against acetaminophen-induced hepatotoxicity

Caixia Yan[1a], Huimin Guo[1a], Qingqing Ding[1b], Yuhao Shao[a], Dian Kang[a], Tengjie Yu[a],Changjian Li[a], Haoran Huang[a], Yisha Du[a], He Wang[a], Kangrui Hu[a], Lin Xie[a], Guangji Wang[**a], Yan Liang[*a]

a. Key Lab of Drug Metabolism & Pharmacokinetics, State Key Laboratory of Natural Medicines, China Pharmaceutical University, Tongjiaxiang 24, Nanjing 210009, P.R. China

b. Department of Geriatric Oncology, First Affiliated Hospital of Nanjing Medical University (Jiangsu People's Hospital), No. 300 Guangzhou Road, Nanjing210029, P.R. China

[*] Corresponding author. Tel.: +86 25 83271060; fax: +86 25 83271060;

E-mail addresses: liangyan0679@163.com; guangjiwang@hotmail.com

[1] These authors contributed equally to this work.

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Table S1 The contents of schizandrol A, schizandrol B, schisantherin A, schizandrin A, schizandrin B in SLE.

Schisandra Lignans	Content (%)
Schizandrol A	**0.047**
Schizandrol B	**0.397**
Schisantherin A	**4.610**
Schizandrin A	**7.670**
Schizandrin B	**0.019**

Table S2 The primer sets for the target genes.

	Forward	Reverse
FASN	GGAGGTGGTGATAGCCGGTAT	TGGGTAATCCATAGAGCCCAG
DGAT2	TGGGTCCAGAAGAAGTTCCAGAAGTA	ACCTCAGTCTCTGGAAGGCCAAAT
ACC1	AATGAACGTGCAATCCGATTTG	ACTCCACATTTGCGTAATTGTTG
CD36	GAACCACTGCTTTCAAAAACTGG	TGCTGTTCTTTGCCACGTCA
PKCα	CAAGGGATGAAATGTGACACC	CCTCTTCTCTGTGTGATCCATTC
PKCβ	CCTCGGGAAGCAGAAAGTAAC	TCCATACTGAGTTTTGGTGGAG
PKCγ	GTCGACTGGTGGTCTTTTGG	CTCATCTTCCCCATCAAAGG
PKCδ	CAAGAAGAACAACGGCAAGG	TGCACACACATCAGCACCT
PKCθ	GGCCAAGGACCTTCTAGTGA	TCCCAGTTGATCTCTCGAAAC
ACC2	CCTTTGGCAACAAGCAAGGTA	AGTCGTACACATAGGTGGTCC
FATP5	GACCACTGGACTCCCAAAGC	GACAGCACGTTGCTCACTTGT
L-FABP	CCATGAACTTCTCCGGCAAGTACC	CTTTGGGTCCATAGGTGATGGTGAG

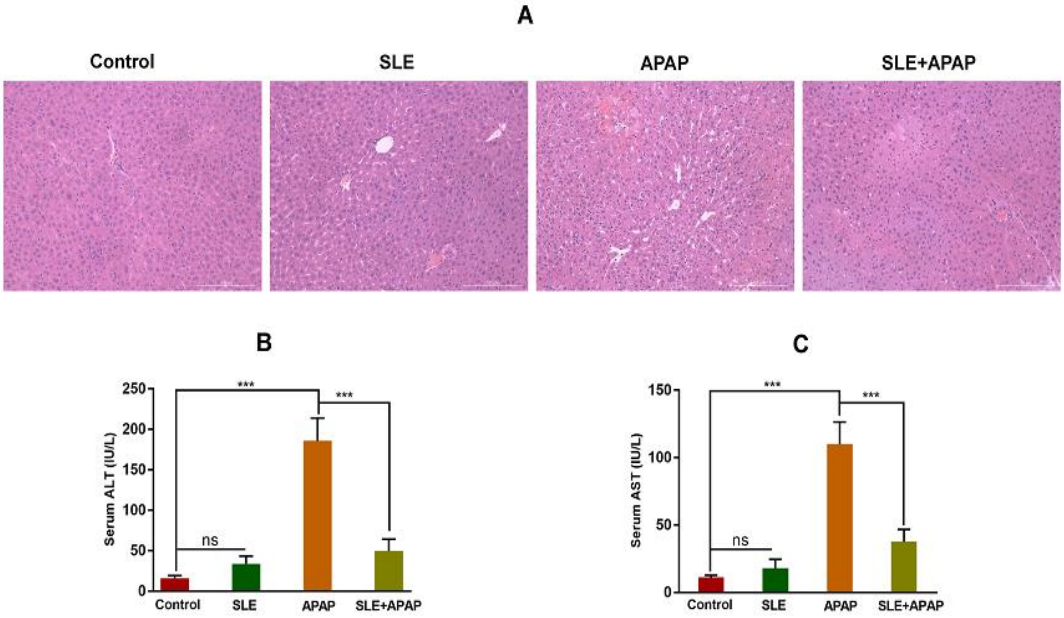

Figure S1 The effect of SLE on liver pathological sections (A), intrahepatic ALT (B) and AST (C) of mice via intragastric administration of SLE (500 mg/kg) twice a day for 3 consecutive days.

Table S3 Metabolism pathways of APAP induced hepatotoxicity and hepatoprotective effect of SLE

	Total	Hits	P value
Urea Cycle	25	8	3.28E-07
Ammonia Recycling	27	7	9.90E-06
Arginine and Proline Metabolism	47	8	5.86E-05
Purine Metabolism	66	9	0.000115
Glutamate Metabolism	44	7	0.000291
Alanine Metabolism	13	4	0.000508
Malate-Aspartate Shuttle	8	3	0.001502
Aspartate Metabolism	30	5	0.00197
Gluconeogenesis	32	5	0.002659
Glucose-Alanine Cycle	10	3	0.003079
Nicotinate and Nicotinamide Metabolism	34	5	0.003509
Phenylalanine and Tyrosine Metabolism	21	4	0.003545
Glutathione Metabolism	22	4	0.004235
Selenoamino Acid Metabolism	26	4	0.007905
Galactose Metabolism	33	4	0.018465
Glycine and Serine Metabolism	52	5	0.02167
Phenylacetate Metabolism	8	2	0.024684
Lactose Degradation	9	2	0.031107
Glycolysis	23	3	0.034205
Cysteine Metabolism	23	3	0.034205
Starch and Sucrose Metabolism	26	3	0.047052

Table S4 Fold change of DAGs in APAP-induced liver injury and SLE-treated mice

Name	Formula	Mass	A vs C	P value	AS vs A	P value	AS vs C	P value
DAG(12:0/18:2/0:0)	$OHC_{33}H_{59}O_4$	554.4735	2.99	0.01	0.68	0.13	2.03	0.02
DAG(16:1/16:0/0:0)	$OHC_{35}H_{65}O_4$	584.5226	2.29	0.01	0.33	0.00	0.76	0.14
DAG(16:0/18:1/0:0)	$OHC_{37}H_{69}O_4$	612.5531	2.42	0.01	0.30	0.00	0.73	0.14
DAG(16:0/18:2/0:0)	$OHC_{37}H_{67}O_4$	610.5386	3.14	0.02	0.37	0.01	1.16	0.56
DAG(16:1/18:2/0:0)	$OHC_{37}H_{65}O_4$	608.5213	3.61	0.01	0.38	0.01	1.37	0.32
DAG(18:0/18:1/0:0)	$OHC_{39}H_{73}O_4$	640.5865	1.52	0.05	0.55	0.02	0.84	0.18
DAG(18:1/18:1/0:0)	$OHC_{39}H_{71}O_4$	638.5703	3.13	0.05	0.30	0.02	0.94	0.64
DAG(18:1/18:2/0:0)	$OHC_{39}H_{69}O_4$	636.5556	6.00	0.02	0.27	0.01	1.62	0.01
DAG(18:2/18:2/0:0)	$OHC_{39}H_{67}O_4$	634.5397	4.20	0.05	0.35	0.04	1.47	0.05
DAG(18:2/18:3/0:0)	$OHC_{39}H_{65}O_4$	632.5227	3.84	0.03	0.34	0.04	1.31	0.31
DAG(18:2/18:4/0:0)	$OHC_{39}H_{63}O_4$	630.5104	3.53	0.05	0.34	0.04	1.20	0.41
DAG(18:1/20:1/0:0)	$OHC_{41}H_{75}O_4$	666.6028	1.05	0.84	0.33	0.00	0.35	0.02
DAG(18:2/20:1/0:0)	$OHC_{41}H_{73}O_4$	664.5855	2.07	0.01	0.31	0.00	0.64	0.03
DAG(18:0/20:4/0:0)	$OHC_{41}H_{71}O_4$	662.5696	1.77	0.04	0.62	0.03	1.10	0.62
DAG(18:1/20:4/0:0)	$OHC_{41}H_{69}O_4$	660.5528	2.64	0.04	0.45	0.03	1.19	0.55
DAG(16:0/22:6/0:0)	$OHC_{41}H_{67}O_4$	658.5382	1.61	0.01	0.81	0.18	1.30	0.38
DAG(18:2/20:5/0:0)	$OHC_{41}H_{65}O_4$	656.5233	2.87	0.06	0.50	0.16	1.44	0.09
DAG(18:1/20:4/0:0)	$OHC_{43}H_{73}O_4$	688.5881	1.31	0.32	0.66	0.09	0.86	0.18
DAG(18:0/22:6/0:0)	$OHC_{43}H_{71}O_4$	686.5698	2.14	0.02	0.86	0.50	1.84	0.03
DAG(18:1/22:6/0:0)	$OHC_{43}H_{69}O_4$	684.5538	3.15	0.05	0.36	0.03	1.13	0.59
DAG(18:2/22:6/0:0)	$OHC_{43}H_{67}O_4$	682.5379	4.75	0.03	0.48	0.04	2.28	0.03

Table S5 Fold change of TAGs in APAP-induced liver injury and SLE-treated mice

Name	Formula	Mass	A vs C	P value	AS vs A	P value	AS vs C	P value
TAG 42:1	$C_{45}H_{84}O_6$	720.6268	2.49	0.03	0.89	0.62	2.22	0.03
TAG 44:1	$C_{47}H_{88}O_6$	748.6581	2.14	0.00	0.68	0.02	1.46	0.01
TAG 44:2	$C_{47}H_{86}O_6$	746.6424	6.77	0.02	0.94	0.84	6.36	0.02
TAG 46:1	$C_{49}H_{92}O_6$	776.6894	3.17	0.01	0.56	0.04	1.78	0.02
TAG 46:2	$C_{49}H_{90}O_6$	774.6737	7.23	0.01	0.71	0.26	5.13	0.01
TAG 48:1	$C_{51}H_{96}O_6$	804.7207	3.11	0.00	0.59	0.10	1.83	0.02
TAG 48:2	$C_{51}H_{94}O_6$	802.705	6.25	0.03	0.37	0.09	2.31	0.03
TAG 48:3	$C_{51}H_{92}O_6$	800.6894	6.85	0.01	0.46	0.05	3.15	0.02
TAG 50:1	$C_{53}H_{100}O_6$	832.752	1.96	0.03	0.60	0.07	1.18	0.11
TAG 50:2	$C_{53}H_{98}O_6$	830.7363	2.41	0.01	0.55	0.04	1.33	0.09
TAG 50:3	$C_{53}H_{96}O_6$	828.7207	3.53	0.01	0.42	0.03	1.48	0.04
TAG 50:4	$C_{53}H_{94}O_6$	826.705	4.57	0.01	0.48	0.06	2.19	0.03
TAG 50:5	$C_{53}H_{92}O_6$	824.6894	5.63	0.00	0.65	0.13	3.66	0.01
TAG 52:4	$C_{55}H_{98}O_6$	854.7363	1.33	0.04	0.80	0.04	1.06	0.14
TAG 52:5	$C_{55}H_{96}O_6$	852.7207	2.83	0.00	0.74	0.20	2.09	0.03
TAG 52:6	$C_{55}H_{94}O_6$	850.705	3.41	0.01	0.65	0.15	2.22	0.03
TAG 52:7	$C_{55}H_{92}O_6$	848.6894	4.60	0.01	0.71	0.25	3.27	0.02
TAG 52:8	$C_{55}H_{90}O_6$	846.6737	4.27	0.01	0.86	0.56	3.67	0.02
TAG 54:3	$C_{57}H_{104}O_6$	884.7833	2.01	0.00	0.73	0.07	1.47	0.05
TAG 54:4	$C_{57}H_{102}O_6$	882.7676	1.65	0.01	0.74	0.03	1.22	0.09
TAG 54:5	$C_{57}H_{100}O_6$	880.752	1.66	0.02	0.78	0.07	1.29	0.08
TAG 54:6	$C_{57}H_{98}O_6$	878.7363	2.04	0.03	0.93	0.71	1.90	0.03
TAG 54:7	$C_{57}H_{96}O_6$	876.7207	1.93	0.01	0.87	0.57	1.68	0.02
TAG 56:6	$C_{59}H_{102}O_6$	906.7676	1.68	0.02	1.11	0.55	1.86	0.02
TAG 58:8	$C_{61}H_{102}O_6$	930.7676	1.84	0.04	1.12	0.46	2.06	0.02